Resumen

Los insecticidas botánicos son sustancias de origen vegetal con propiedades repelentes y tóxicas contra gran variedad de insectos. Durante siglos constituyeron la única estrategia disponible para el control de plagas hasta que el desarrollo de los insecticidas sintéticos los relegó a un segundo plano. Sin embargo, los problemas provocados por el uso intensivo de los insecticidas sintéticos durante las últimas décadas, ha renovado el interés por los insecticidas botánicos como alternativa para el manejo de plagas.

Schinus areira L. (Anacardiacea) es una especie vegetal con propiedades repelentes e insecticidas. Dicha actividad ha sido comprobada en varias especies de insectos plaga de interés en la sanidad vegetal, animal y humana. Sin embargo, la introducción de nuevos plaguicidas en el mercado, aunque éstos sean de origen natural, requiere no sólo la evaluación de su efectividad como insecticidas sino también el estudio de los efectos adversos que implicaría su utilización sobre el humano y el ambiente.

El objetivo del presente trabajo fue evaluar la toxicidad de los extractos etanólicos y hexánicos de frutos y hojas de *S. areira* utilizando ratones y ratas como modelos experimentales de mamíferos.

Por un lado, se evaluó en ratones la toxicidad de los extractos por vía oral mediante la incorporación de los mismos en el alimento. En primera instancia, se realizaron los estudios por exposición aguda a través de la administración de los extractos en una única dosis de 2000 mg/kg de peso corporal. Los ratones se evaluaron luego de la exposición y a los 14 días de realizada la misma, para detectar la reversibilidad de los efectos o la aparición tardía de los mismos. Se evaluaron la funcionalidad del sistema nervioso central (SNC) a nivel neuromotor, sensorial y autonómico mediante una batería de observaciones funcionales (BOF), y la actividad locomotora mediante observaciones en el open

field (OF). También se llevó a cabo el estudio histopatológico en hígado, riñón, estómago, intestino y cerebro de los animales. En segundo lugar, se realizaron los estudios por exposición repetida del extracto a mediano y largo plazo. En los estudios subagudos se administró una dosis diaria de extracto de 1000 mg/kg de peso corporal durante 28 días, mientras que en los estudios subcrónicos, dicha dosis se administró durante un período de 90 días. Los efectos producidos por los extractos se evaluaron una vez finalizada la exposición mediante una BOF, observaciones en el OF, determinaciones hematológicas y bioquímicas, y estudios histopatológicos de los diversos órganos.

Por otro lado, se evaluó la toxicidad aguda por vía dérmica de los extractos mediante la administración sobre la piel de ratas de una dosis única de 2000 mg/kg de peso corporal durante un período de 24 h. Transcurrido dicho período, se determinaron los efectos locales sobre la piel expuesta a los extractos y los efectos sistémicos a través de una BOF y de observaciones en el OF. Dichas evaluaciones volvieron a realizarse luego de 14 días. Finalmente, se efectuó el estudio histopatológico de los órganos.

Los resultados obtenidos en los diferentes estudios demostraron que ninguno de los extractos de *S. areira* evaluados produjo alteraciones en el crecimiento y desarrollo de los ratones durante las exposiciones a corto, mediano y largo plazo. En particular, el extracto etanólico de frutos sólo provocó un efecto estimulante transitorio del SNC, alteraciones en la fórmula leucocitaria de las hembras, disminución del nivel de colesterol total en las hembras y aumento de dicho parámetro en los machos, y signos leves y transitorios de irritación dérmica. El extracto hexánico de frutos sólo causó un efecto estimulante transitorio del SNC y un aumento leve y temporal de la actividad locomotora. Por otro lado, el extracto etanólico de hojas produjo un efecto diurético leve, aumento transitorio de la cantidad de eritrocitos y alteraciones en otros parámetros eritrocitarios relacionados, disminución del nivel plasmático de glucosa en los machos y generó irritación dérmica leve y reversible. Por su parte,

el extracto hexánico de hojas provocó un efecto diurético leve, alteraciones transitorias de los niveles plasmáticos de glucosa y colesterol total, y signos de irritación leves y reversibles en piel. Ninguno de los extractos causó efectos adversos sobre la funcionalidad hepática y renal, así como tampoco lesiones tisulares en los órganos evaluados.

Los efectos detectados en los animales expuestos a los extractos no pudieron considerarse como deletéreos o adversos ya que no produjeron cambios en la morfología, fisiología, crecimiento y desarrollo del organismo que originaran la pérdida de la funcionalidad o el deterioro de alguna capacidad esencial para su subsistencia. Considerando que dichos efectos, en todos los casos, fueron leves y transitorios, y que las dosis a las cuales podrán ser aplicados como repelentes e insecticidas serán muy inferiores a las evaluadas en los estudios de toxicidad, puede concluirse que los extractos etanólicos y hexánicos de frutos y hojas de *S. areira* son seguros para su utilización en el control de plagas domiciliarias, peri-domiciliarias y agrícolas.

Además, debido a las numerosas propiedades medicinales que se le adjudican a esta especie, los resultados obtenidos en este trabajo también son válidos para inferir que el uso terapéutico de los extractos no provocará toxicidad sobre el organismo.

Abstract

Botanical insecticides are plant substances with repellent and toxic properties against many insects. Until the development of the synthetic insecticides, they represented the only available strategy for pest control. However, health problems caused by the intensive use of synthetic insecticides in recent decades have renewed the interest for botanical insecticides as an alternative for pest management.

Schinus areira L. (Anacardiacea) is a plant species with repellent and insecticidal properties. This activity has been demonstrated in several species of insect pest with impact in plant, animal and human health. However, the insertion of new pesticides in the market, even if they are of natural origin, not only requires assessing their effectiveness as insecticides but also avoiding possible adverse effects on human and environment that would involve their use.

The aim of this study was to evaluate the toxicity of ethanolic and hexanic extracts of fruits and leaves of *S. areira,* using mice and rats as experimental models in mammals.

The oral toxicity of the extracts was evaluated by incorporating them in the diet of mice. These studies were performed by acute exposure through the administration of the extracts in a single dose of 2000 mg/kg body weight, and mice were evaluated after the exposure. After 14 days, they were tested again to detect the possible reversibility or the delayed onset of the effects. The neuromotor, sensorial and autonomic functionality of the central nervous system (CNS) was assessed through a functional observational battery (FOB), and motor activity was evaluated by observations in an open field (OF). Histopathological studies were also conducted on liver, kidney, stomach, intestine and brain of animals. In addition, the effects of repeated exposure to

the extracts were evaluated at medium and long term. In subacute studies, a daily dose of extract of 1000 mg/kg of body weight was administered during 90 days. The effects of the extracts were evaluated after exposure by a BOF, observations in the OF, hematological and biochemical determinations, and histopathological studies of different organs.

The acute dermal toxicity of the extracts was assessed through the topical exposure of a single dose of 2000 mg/kg body weight on rat skin during 24 h. After this period, local effects on tested skin and systemic effects were evaluated through a FOB and observations in an OF. After 14 days, these tests were assessed again. Finally, the histopathological examinations of the organs were performed.

None of the *S. areira* extracts produced changes in the growth and development of the mice during the short, medium and long term exposures. The ethanolic extract from fruits caused a transient stimulatory effect of the CNS, changes in the differential leukocyte count in the female mice, a decrease of the total cholesterol level in females, an increase of this parameter in male mice, and mild and transient signs of dermal irritation. The hexanic extract from fruits produced a temporary stimulatory effect of the CNS and a slight and transient increase of motor activity. The ethanolic extract from leaves caused a mild diuretic effect, a transiently increased total erythrocyte count accompanied by changes in other related hematological parameters, a decrease of plasma glucose level in males, and generated a mild and temporary dermal irritancy. The hexanic extract from leaves caused a mild diuretic effect, transient variations of plasma levels of glucose and total cholesterol, and slight temporary signs of skin irritation. None of the extracts produced adverse effects on hepatic and renal functionality, nor histologically evident signs of tissue damage in the tested organs.

The effects observed in the animals exposed to the extracts could not be considered as deleterious or adverse as they did not produce changes in the

morphology, physiology, growth or development of the organism that could cause the loss of functionality or the impairment of essential abilities for survival. Their effects in all cases were mild and transient, and the doses in which the extracts may be applied to be used as repellents or insecticides are much lower than those evaluated in the present toxicity studies. Moreover, because of the many medicinal properties that are attributed to this species, the results obtained in this work are also valid to infer that the possible therapeutic use of *S. areira* extracts will cause no toxicity to the body.

In conclusion, the ethanolic and hexanic extracts from fruits and leaves of *Schinus areira* are safe for use to control domiciliary, peri-domiciliary and agricultural pests.

Bibliografía

- Aimola, I.A.; Inuwa, H.M.; Mamman, A.I.; Habila, N.; Agbaji, A.S.; Omoniwa, D., 2011. *Terminalia cappata* extract enhances erythropoiesis in adult Balb/C mice. Journal of Molecular Biology Research 1 (1), 40-46.
- Alanís, A.D.; Calzada, F.; Cervantes, J.A.; Torres, J.; Ceballos, G.M., 2005. Antibacterial properties of some plants used in Mexican traditional medicine for the treatment of gastrointestinal disorders. Journal of Ethnopharmacology 100, 153-157.
- Alanís-Garza, B.A.; González-González, G.M.; Salazar-Aranda, R.; Waskman de Torres, N.; Rivas-Galindo, V.M., 2007. Screening of antifungal activity of plants from the northeast of Mexico. Journal of Ethnopharmacology 114, 468-471.
- Allen, S.L., 2010. Regulatory aspects of acute neurotoxicity assessment. En: Hayes' Handbook of pesticide toxicology, Third Edition. Editor: Robert Krieger. Academic Press. Elsevier. pp: 587-602.
- Alonso, J., Desmarchelier, C., 2006. Aguaribay. En: Plantas medicinales autóctonas de la Argentina. Bases científicas para su aplicación en atención primaria de la salud. Editorial L.O.L.A. 1ra Edición. Buenos Aires. pp.: 26-33. ISBN 987-22875-0-3.
- Anila, L.; Vijayalakshmi, N.R., 2002. Flavonoids of *Emblica officinalis* and *Mangifera indica* – effectiveness for dyslipidemia. Journal of Ethnopharmacology 79, 81-87.
- Ayoka, A.O.; Akomolafe, R.O.; Iwalewa, E.O.; Akanmu, M.A.; Ukponmwan, O.E., 2006. Sedative, antiepileptic and antipsychotic effects of *Spondias mombin* L. (Anacardiaceae) in mice and rats. Journal of Ethnopharmacology 103, 166-175.
- Baird, S.J.S.; Catalano, P.J.; Ryan, L.M.; Evans, J.S., 1997. Evaluation of effect profiles: functional observational battery outcomes. Fundamental and Applied Toxicology 40, 37-51.
- Barrachina, M.D.; Bello, R.; Martínez-Cuesta, M.A.; Primo-Yúfera, E.; Esplunges, J., 1997. Analgesic and central depressor effects of the dichloromethanol extract from *Schinus molle* L. Phytotherapy Research 11 (4), 317-319.
- Baumans, V., 2010. The laboratory mouse. En: The UFAW handbook on the care and management and other research animals. Eighth edition. Editores: Robert Hubrecht y James Kirkwood. Wiley-Blackwell. pp: 276-310.
- Baynes, R.E.; Hodgson, E., 2010. Absorption and distribution of toxicants. En: A textbook of modern toxicology. Fourth edition. Editor: Ernest Hodgson. John Wiley & Sons, Inc. pp: 79-114.

- Bello, R.; Barrachina, M.D.; Moreno, L.; Primo-Yúfera, E.; Esplugues, J., 1996. Effects on arterial blood pressure of the methanol and dichloromethanol extracts from *Schinus molle* L. in rats. Phytotherapy Research 10 (7), 634-635.
- Bello, R.; Beltrán, B.; Moreno, L.; Calatayud, S.; Primo-Yúfera, E.; Esplugues, J., 1998. *In vitro* pharmacological evaluation of the dichloromethanol extract from *Schinus molle* L. Phytotherapy Research 12 (7), 523-525.
- Bendaoud, H.; Romdhane, M.; Souchard, J.P.; Cazaux, S.; Bouajila, J., 2010. Chemical composition and anticancer and antioxidant activities of *Schinus molle* L. and *Schinus terebinthifolius* Raddi berries essential oils. Journal of Food Science 75 (6), 466-472.
- Benzi, V.; Stefanazzi, N.; Ferrero, A.A., 2009. Biological activity of essential oils from leaves and fruits of pepper tree (*Schinus molle* L.) to control rice weevil (*Sitophilus oryzae* L.). Chilean Journal of Agricultural Research 69 (2), 154-159.
- Bidart-Bouzat, M.G., Imeh-Nathaniel, A., 2008. Global change effects on plant chemical defenses against insect hervibores. Journal of Integrative Plant Biology 50 (11), 1339-1354.
- Blazka, M.E.; Hayes, A.W., 2008. Acute toxicity and eye irritancy. En: Principles and methods of toxicology, Fifth Edition. Editor: A. Wallace Hayes. CRC Press. pp: 1131-1177.
- Bloomquist, J.R., 2003. Insecticidas: Químicas y características. En: E.B. Radcliffe y W.D. Hutchinson (Eds.), Radcliffe: Texto Mundial de MIP. URL: http//ipmworld.umn.edu, Universidad de Minnesota, St. Paul, MN.
- Bowen, S.E.; Balster, R.L., 2006. Tolerance and sensitization to inhaled 1,1,1-trichloroethane in mice: results from open-field behavior and functional observational battery. Psychopharmacology 185, 405-415.
- Breckenridge, C.B.; Stevens, J.T., 2008. Crop protection chemicals: Mechanism of action and hazard profiles. En: Principles and Methods of Toxicology. 5th Edition. Editado por A. Wallace Hayes. pp.: 727-792.
- Brenes, J.C.; Padilla, M.; Fornaguera, J., 2009. A detailed analysis of open-field habituation and behavioral and neurochemical antidepressant-like effects in postweaning enriched rats. Behavioural Brain Research 197, 125-137.
- Bussmann, R.W.; Glenn, A., 2010. Medicinal plants used in Northern Peru for reproductive problems and female health. Journal of Ethnobiology and Ethnomedicine 6, 30.
- Camaño, R.M., 1996. Method for treating bacterial infections. United States Patent Number 5.512.284, Apr. 30.
- Camaño, R.M., 1997. Essential oil composition with bactericidal activity. United States Patent Number 5.635.184, Jun. 3.

- Casida, J.E., 2010. Pest toxicology: The primary mechanisms of pesticide action. En: Hayes´ Handbook of Pesticide Toxicology, Third Edition. Edited by Robert Krieger. Academic Press. Elsevier. pp: 103-117.
- Casida, J.E.; Quistad, G.B., 1998. Golden age of insecticide research: Past, present or future? Annual Reviews of Entomology 43, 1-16.
- Cerón-Martínez, C.E., 2006. Plantas medicinales de los Andes ecuatorianos. En: Botánica Económica de los Andes Centrales. Editores: M. Moraes R., B. Øllgaard, L.P. Kvist, F. Borchsenius, H. Balslev. Universidad Mayor de San Andrés. La Paz. pp.: 285-293.
- Charles River Laboratories International, Inc., 2011. Research animal models: CF-1™ mouse (on-line). Fecha de acceso 09/02/2011. Disponible en: http://www.criver.com/en-US/ProdServ/ByType /ResModOver/ResMod/Pages/CF_1_Mice.aspx
- Chirino, M.; Cariac, M.; Ferrero, A.A., 2001. Actividad insecticida de extractos crudos de drupas de *Schinus molle* L. (Anacardiaceae) sobre larvas neonatas de *Cydia pomonella* L. (Lepidoptera: Tortricidae). Boletín de Sanidad Vegetal. Plagas 27, 305-314.
- Choleris, E.; Thomas, A.W.; Kavaliers, M.; Prato, F.S., 2001. A detailed ethological analysis of the mouse open field test: effects of diazepam, chlordiazepoxide and an extremely low frequency pulsed magnetic field. Neuroscience and Biobehavioral Reviews 25, 235-260.
- Coats, J.R., 1994. Risks from natural versus synthetic insecticides. Annual Reviews of Entomology 39, 489-515.
- Cochran, R., 2010. Risk assessment for acute exposure to pesticides. En: Hayes' Handbook of pesticide toxicology, Third Edition. Editor: Robert Krieger. Academic Press. Elsevier. pp: 337-355.
- Corey-Slechta, D.A.; Weiss, B., 2008. Assessment of behavioral toxicity. En: En: Principles and methods of toxicology. Fifth Edition. Editor: A. Wallace Hayes. CRC Press. pp: 1797-1864.
- Costa, L.G., 2010. Toxic effects of pesticides. En: Casarett & Doull's Essentials of toxicology. Second Edition. Editores: Curtis D. Klaassen y John B. Watkins III. The McGraw-Hill Companies. pp: 309-321.
- Crawley, J.N.; Paylor, R., 1997. A proposed test battery and constellations of specific behavioral paradigms to investigate the behavioral phenotypes of transgenic and knockout mice. Hormones and Behavior 31,197-211.
- Crozier, A.; Jaganath, I.B.; Clifford, M.N., 2006. Phenols, polyphenols and tannins: an overview. In: Plant secondary metabolites: occurrence, structure and role in the human diet. Editado por A. Crozier, M.N. Clifford y H. Ashihara. Blackell Publishing. 372p.

- Davicino, R.; Mattar, M.A.; Casali, Y.A.; Correa, S.G.; Pettenati, E.M.; Micalizzi, B., 2007. Actividad antifúngica de extractos de plantas usadas en medicina popular en Argentina. Revista peruana de Biología 14 (2), 247-251.
- De Feo, V., 2003. Ethnomedical field study in northern Peruvian Andes with particular reference to divination practices. Journal of Ethnopharmacology 85, 243-256.
- Descamps, L.R.; Stefanazzi, N.; Sánchez Chopa, C.; Ferrero, A.A., 2008. Actividad biológica de extractos vegetales de *Schinus molle* var. *areira* (Anacardiaceae) en *Tribolium castaneum* Herbst. (Insecta, Coleoptera, Tenebrionidae), plaga de grano almacenado.
- Després, L.; David, J.P.; Gallet, C., 2007. The evolutionary ecology of insect resistance to plant chemicals. Trends in Ecology and Evolution 22 (6), 298-307.
- Deveci, O.; Sukan, A.; Tuzun, N.; Kocabas, E.E.H., 2010. Chemical composition, repellent and antimicrobial activity of *Schinus molle* L. Journal of Medicinal Plants Research 4 (21), 2211-2216.
- Devine, G.J.; Eza, D.; Ogusuku, E.; Furlong, M.J., 2008. Uso de insecticidas: contexto y consecuencias ecológicas. Revista Peruana de Medicina Experimental y Salud Pública 25 (1), 74-100.
- Díaz, C.; Quesada, S.; Brenes, O.; Aguilar, G.; Cicció, J.F., 2008. Chemical composition of *Schinus molle* essential oil and its cytotoxic activity on tumour cell lines. Natural Products Research 22 (17), 1521-1534.
- Dikshit, A.; Naqvi, A.A.; Husain, A., 1986. *Schinus molle*: a new source of natural fungitoxicant. Applied and Environmental Microbiology 51 (5), 1085-1088.
- Dimo, T.; Rakotonirina, S.V.; Tan, P.V.; Azay, J.; Dongo, E.; Kamtchouing, P.; Cros, G., 2007. Effect of *Sclerocarya birrea* (Anacardiaceae) stem bark methylene chloride/methanol extract on streptozotocin-diabetic rats. Journal of Ethnopharmacology 110, 434-438.
- Dixon, A.K., 2004. The social behaviour of mice and its sensory control. En: The laboratory mouse. Editor: Hans Hedrich. Elsevier. pp: 287-300.
- Drai, D.; Kafkafi, N.; Benjamini, Y.; Elmer, G.; Golani, I., 2001. Rats and mice share common ethologically relevant parameters of exploratory behavior. Behavioural Brain Research 125, 133-140.
- Duke, S.O.; Cantrell, C.L.; Meepagala, K.M.; Wedge, D.E.; Tabanca, N.; Schrader, K.K., 2010. Natural toxins for use in pest managements. Toxins 2, 1943-1962.
- Eaton, D.L.; Gilbert, S.G., 2008. Principles of toxicology. En: Casarett & Doull's Toxicology. The basic science of poisons. Seventh Edition. Editor: Curtis D. Klaassen. The McGraw-Hill Companies. pp: 11-43.

- Eaton, D.L.; Gilbert, S.G., 2010. Principles of toxicology. En: Casarett & Doull's Essentials of Toxicology. Second Edition. Editores: Curtis D. Klaassen y John B. Watkins III. McGraw-Hill LANGE. pp: 5-19.
- Enan, E., 2001. Insecticidal activity of essential oils: octopaminergic sites of action. Comparative Biochemistry and Physiology Part C 130, 325-337.
- Everds, N., 2004. Hematology of the mouse. En: The laboratory mouse. Editor: Hans Hedrich. Elsevier Academic Press. pp: 271-286.
- Everds, N., 2007. Hematology of the laboratory mouse. En: The mouse in biomedical research. Second Edition. Volumen III: Normative biology, husbandry and models. Editores: James G. Fox, Stephen W. Barthold, Muriel T. Davison, Christian E. Newcomer, Fred W. Quimby y Abigail L. Smith. Elsevier Academic Press. pp: 133-170.
- Ferrero, A.; Minetti, A.; Bras, C.; Zanetti, N., 2007a. Acute and subacute toxicity evaluation of ethanolic extract from fruits of *Schinus molle* in rats. Journal of Ethnopharmacology 113, 441-447.
- Ferrero, A.A.; Sánchez Chopa, C.; Werdin González, J.O.; Alzogaray, R., 2007b. Repellence and toxicity of *Schinus molle* extracts on *Blattella germanica.* Fitoterapia 78, 311-314.
- Ferrero, A.A.; Werdin González, J.O.; Sánchez Chopa, C., 2006. Biological activity of *Schinus molle* on *Triatoma infestans.* Fitoterapia 77, 381-383.
- Ferry, N.; Edwards, M.G.; Gatehouse, J.A.; Gatehouse, A.M.R., 2004. Plant-insect interactions: molecular approaches to insect resistance. Current Opinion in Biotechnology 15, 155-161.
- Fukuta, K., 2004. Collection of body fluids. En: The laboratory mouse. Editor: Hans Hedrich. Elsevier Academic Press. pp: 543-554.
- Gentz, M.C.; Murdoch, G.; King, G.F., 2010. Tandem use of selective insecticides and natural enemies for effective, reduced-risk pest management. Biological Control 52, 208-215.
- Gondwe, M.; Kamadyaapa, D.R.; Tufts, M.; Chuturgoon, A.A.; Musabayane, C.T., 2008. *Sclerocarya birrea* [(A. Rich.) Hochst.] [Anacarciaceae] stem-bark ethanolic extract (SBE) modulates blood glucose, glomerular filtration rate (GFR) and mean arterial blood pressure (MAP) of STZ-induced diabetic rats. Phytomedicine 15, 699-709.
- Gregus, Z., 2008. Mechanisms of toxicity. En: Casarett & Doull's Toxicology. The basic science of poisons. Seventh Edition. Editor: Curtis D. Klaassen. The McGraw-Hill Companies. pp: 45-106.
- Gregus, Z., 2010. Mechanisms of toxicity. En: Casarett & Doull´s Essentials of Toxicology. Second Edition. Editor: Curtis D. Klaassen y John B. Watkins III. McGraw-Hill Lange. pp: 472.

- Gundidza, M., 1993. Antimicrobial activity of essential oil from *Schinus molle* Linn. Central African Journal of Medicine 39 (11), 231-234.
- Gurib-Fakim, A., 2006. Medicinal plants: traditions of yesterday and drugs of tomorrow. Molecular Aspects of Medicine 27 (1), 1-93.
- Gutiérrez, M.M.; Stefanazzi, N.; Werdin González, J.; Benzi, V.; Ferrero, A.A., 2009. Actividad fumigante de aceites esenciales de *Schinus molle* (Anacardiaceae) y *Tagetes terniflora* (Astereaceae) sobre adultos de *Pediculus humanus capitis* (Insecta; Anoplura; Pediculidae). Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas 8 (3), 176-179.
- Hajtó, T.; Fodor, K.; Perjési, P.; Németh, P., 2011. Difficulties and perspectives of immunomodulatory therapy with mistletoe lectins and standardized mistletoe extracts in evidence-based medicine. Evidence-based Complementary and Alternative Medicine, Vol. 2011, Article ID 298972, 6 pages.
- Hall, R.L.; Everds, N.E., 2008. Principles of clinical pathology for toxicology studies. En: Principles and Methods of Toxicology, 5th Edition. Editor: A. Wallace Hayes. CRC Press. pp: 1317-1358.
- Hanson, L.; Ritter, L., 2010. Toxicity and safety evaluation of pesticides. En: Hayes' Handbook of Pesticide Toxicology. Third Edition. Volume 1. Edited by Robert Krieger. Academic Press, Elsevier. pp: 333-336.
- Hartmann, T., 2007. From waste products to ecochemicals: fifty years research of plant secondary metabolism. Phytochemistry 68, 2831-2846.
- Hayes, B.B.; Patrick, E.; Maibach, H.J., 2008. Dermatotoxicology. En: Principles and methods of toxicology. Fifth Edition. Editor: A. Wallace Hayes. CRC Press. pp: 1359-1405.
- Hedrich, H.J.; Mossmann, H.; Nicklas, W., 2004. Housing and maintenance. En: The laboratory mouse. Editor: Hans Hedrich. Elsevier Academic Press. pp: 395-408.
- Himmel, H.M., 2008. Safety pharmacology assessment of central nervous system function in juvenile and adult rats: effects of pharmacological reference compounds. Journal of Pharmacological and Toxicological Methods 58, 129-146.
- Hogenhout, S.A.; Bos, J.I.B., 2011. Effector proteins that modulate plant-insect interactions. Current Opinion in Plant Biology 14, 1-7.
- Hossain, M.S.; Khan, M.R.I.; Anisuzzaman, A.S.M.; Ahmed, M.; Amran, M.S.; Islam, A., 2010. Antidiabetic and glycogenesis effects of different fractions of ethanolic extract of leaves of *Mangifera indica* (Linn.) in normal and alloxan induced diabetic rats. Journal of Medical Sciences 10 (4), 80-86.
- Howe, G.A.; Jander, G., 2008. Plant Immunity to insect herbivores. Annual Review of Plant Biology 59, 41-46.

- Hübler, N.; Gottschling, B.; Jacobs, M.; von Landenberg, F.; Hewicker-Trautwein, M., 2005. Functional observational battery and motor activity in rats after single administration of two NHE 1 inhibitors. Toxicology and Applied Pharmacology 208, 266-276.
- Huerta, A.; Chiffelle, I.; Puga, K.; Azúa, F.; Araya, J.E., 2010. Toxicity and repellence of aqueous and ethanolic extracts from *Schinus molle* on elm leaf beetle *Xanthogaleruca luteola.* Crop Protection 29, 1118-1123.
- Iannacone, J.; Alvariño, L., 2010. Toxicidad de *Schinus molle* L. (Anacardiaceae) a cuatro controladores biológicos de plagas agrícolas en el Perú. Acta Zoológica Mexicana 26 (3), 603-615.
- Iannacone, J.; Lamas, G., 2003a. Efecto insecticida de cuatro extractos botánicos y del cartap sobre la polilla de la papa *Phthorimaea operculella* (Zeller) (Lepidoptera: Gelechiidae), en el Perú. Entomotropica 18 (2), 95-105.
- Iannacone, J.; Lamas, G., 2003b. Efectos toxicológicos de extractos de molle (*Schinus molle*) y lantana (*Lantana cámara*) sobre *Chysoperla externa* (Neuroptera: Chrysopidae), *Trichogramma pintoi* (Hymenoptera: Trichogrammatidae) y *Copidosoma koehleri* (Hymenoptera: Encyrtidae) en el Perú. Agricultura Técnica 63 (4), 347-360.
- Irwin, S., 1968. Comprehensive observational assessment: Ia. A systematic, quantitative procedure for assessing the behavioral and physiologic state of the mouse. Psychopharmacology 13, 222-257.
- Isman, M.B., 2006. Botanical insecticides, deterrents and repellents in modern agriculture and an increasingly regulated world. Annual Review of Entomology 51, 45-66.
- Isman, M.B., 2008. Botanical insecticides: for richer, for poorer. Pest Management Science 64, 8-11.
- Jaya, A.; Shanti, P.; Sachdanandam, P., 2010. Hypolipidemic activity of *Semecarpus anacardium* in streptozotocin induced diabetic rats. Endocrine 38 (1), 11-17.
- Jilge, B.; Kunz, E., 2004. Circadian rhythms of the mouse. En: The laboratory mouse. Editor: Hans Hedrich. Elsevier. pp: 311-325.
- Juárez de Varela, F.; Novara, L.J., 2007. Flora del Valle de Lerma: Anacardiaceae Lindl. Aportes Botánicos de Salta, Serie Flora 8 (6), 1-28. ISSN 0327-506X.
- Kalueff, A.V.; Tuohimaa, P., 2005. Mouse grooming microstructure is a reliable anxiety marker bidirectionally sensitive to GABAergic drugs. European Journal of Pharmacology 508, 147-153.
- Kamtchouing, P.; Sokeng, S.D.; Moundipa, P.F.; Watcho, P.; Jatsa, H.B.; Lontsi, D., 1998. Protective role of *Anacardium occidentale* extract against streptozotocin-induced diabetes in rats. Journal of Ethnopharmacology 62, 95-99.

- Kask, A.; Harro, J.; von Hörsten, S.; Redrobe, J.P.; Dumont, Y.; Quirion, R., 2002. The neurocircuitry and receptor subtypes mediating anxiolytic-like effects of neuropeptide Y. Neuroscience and Biobehavioral Reviews 26, 259-283.
- Kassa, J.; Karasova, J.Z.; Musilek, K.; Kuca, K.; Jung, Y., 2009. A comparison of the neuroprotective efficacy of newly developed oximes (K117, K127) and currently available oxime (obidoxime) in tabun-poisoned rats. Toxicology Mechanisms and Methods 19 (3), 232-238.
- Kaushik, G.; Satya, S.; Khandelwal, R.K.; Naik, S.N., 2010. Commonly consumed Indian plant food materials in the management of diabetes mellitus. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 4, 21-40.
- Koffuor, G.A.; Sam, G.H.; Dadzeasah, P.E.; Owiafe, E.O.; Asante-Gyapong, A., 2012. Erythropoietic effect of the ethanolic root bark extract of *Carissa edulis* in phenylhydrazine-induced anemic Sprague-Dawley rats. Research Journal of Pharmacology 6 (2), 20-24.
- Kumar, S.V.; Kumar, S.P.; Rupesh, D.; Nitin, K., 2011. Immunomodulatory effects of some traditional medicinal plants. Journal of Chemical and Pharmaceutical Research 3 (1), 675-684.
- Lamarque, A.; Zygadlo, J.; Labuckas, D.; López, L.; Torres, M.; Maestri, D., 2008. Fundamentos teórico-prácticos de química orgánica. Coordinado por: Alicia Lamarque y Damián Maestri. 1ra Edición. Encuentro Grupo Editor. pp: 128.
- Lewinsohn, E.; Gijzen, M., 2009. Phytochemical diversity: the sounds of silent metabolism. Plant Science 176, 161-169.
- Liu, P.J.; Hsieh, W.T.; Huang, S.H.; Liao, H.F.; Chiang, B.H., 2010. Hematopoietic effect of water-soluble polisaccharides from *Angelica sinensis* on mice with acute blood loss. Experimental Hematology 38 (6), 437-455.
- López, M.D.; Pascual-Villalobos, M.J., 2010. Mode of inhibition of acetylcholinesterase by monoterpenoids and implications for pest control. Industrial Crops and Products 31, 284-288.
- Lund, J.E., 2006. Toxicologic effects on blood and bone marrow. En: Schalm´s veterinary hematology, 5th Edition. Editores: Bernard V. Feldman, Joseph G. Zinkl, Nemi, C. Jain. Blackwell Publishing. pp: 44-50.
- Machado, D.G.; Bettio, L.E.B.; Cunha, M.P.; Santos, A.R.S.; Pizzolatti, M.G.; Brighente, I.M.C.; Rodrigues, A.L.S., 2008. Antidepressant-like effect of rutin isolated from the ethanolic extract from *Schinus molle* L. in mice: evidence for the involvement of the serotonergic and noradrenergic systems. European Journal of Pharmacology 587, 163-168.
- Machado, D.G.; Kaster, M.P.; Binfaré, R.W.; Dias, M.; Santos, A.R.S.; Pizzolatti, M.G.; Brighente, I.M.C.; Rodrigues, A.L.S., 2007. Antidepressant-like effect of the extract from leaves of *Schinus molle* L. in mice: evidence for the involvement of the

monoaminergic system. Progress in Neuro-Psychopharmacology & Biological Psychiatry 31, 421-428.

- Maia, M.F.; Moore, S.J., 2011. Plant-based insect repellents: a review of their efficacy, development and testing. Malaria Journal 10 (1): S11.
- Mareggiani, G., 2001. Manejo de insectos plaga mediante sustancias semioquímicas de origen vegetal. Manejo Integrado de Plagas (Costa Rica) 60, 22-30.
- Markgraf, C.G.; Cirino, M.; Meredith, J., 2010. Comparisons of methods for analysis of functional observational battery (FOB) data. Journal of Pharmacological and Toxicological Methods 62, 89-94.
- Martínez, G.J.; Barboza, G.E., 2010. Natural pharmacopoeia used in traditional Toba medicine for the treatment and parasitosis and skin disorders (Central Chaco, Argentina). Journal of Ethnopharmacology 132, 86-100.
- Martínez, M.R.; Pochettino, M.L.; Cortella, A.R., 2004. Environment and illness in the Calchaquí Valley (Salta, Argentina): phytotherapy for osteo-articular and cardio-circulatory diseases. Journal of Ethnopharmacology 95, 317-327.
- Marzouk, M.S.; Moharram, F.A.; Haggag, E.G.; Ibrahim, M.T.; Badary, O.A., 2006. Antioxidant flavonol glycosides from *Schinus molle*. Phytotherapy Research 20 (3), 200-205.
- Massebo, F.; Tadesse, M.; Bekele, T.; Balkew, M.; Gebre-Michael, T., 2009. Evaluation on larvicidal effects of essential oils of some local plants against *Anopheles arabiensis* Patton and *Aedes aegypti* Linnaeus (Diptera, Culicidae) in Ethiopia. African Journal of Biotechnology 8 (17), 4183-4188.
- Molina-Salinas, G.M.; Pérez-López, A.; Becerril-Montes, P.; Salazar-Aranda, R.; Said-Fernández, S.; Waskman de Torres, M., 2007. Evaluation of the flora of Northern Mexico for *in vitro* antimicrobial y antituberculosis activity. Journal of Ethnopharmacology 109, 435-441.
- Moscardo, E.; Maurin, A.; Dorigatti, R.; Champeroux, P.; Richard, S., 2007. An optimised methodology for the neurobehavioural assessment in rodents. Journal of Pharmacological and Toxicological Methods 56, 239-255.
- Moser, V.C., 2000. The functional observational battery in adult and developing rats. Neurotoxicology 21(6), 989-996.
- Moser, V.C.; Aschner, M.; Richardson, R.J.; Philbert, M.A., 2010. Toxic responses of the nervous system. En: Casarett & Doull's Essentials of toxicology. Second Edition. Editores: Curtis D. Klaassen y John B. Watkins III. The McGraw-Hill Companies. pp: 217-232.
- Moser, V.C.; MacPhail, R.C.; Gennings, C., 2003. Neurobehavioral evaluations of mixtures of trichloroethylene, heptachlor, and di(2-ethylhexyl)phthalate in a full-factorial design. Toxicology 188, 125-137.

- Moser, V.C.; McCormick, J.P.; Creason, J.P.; MacPhail, R.C., 1988. Comparison of chlordimeform and carbaryl using a functional observational battery. Fundamental and Applied Toxicology 11, 189-206.
- Moser, V.C.; Ross, J.F., 1996. Training video and reference manual for a functional observational battery. Co-Sponsors: Neurotoxicology Division, National Health and Environmental Effects Research Laboratory, U.S. Environmental Protection Agency and Neurotoxicology Subcommittee, American Industrial Health Council.
- Murray, A.P.; Gurovic, M.S.; Rodriguez, S.A.; Murray, M.G.; Ferrero, A.A., 2009. Acetilcholinesterase inhibition and antioxidant activity of essential oils from *Schinus areira* L. and *Schinus longifolia* (Lindl.) Speg. Natural Products Communications 4 (6), 873-876.
- Muruganandan, S.; Srinivasan, K.; Gupta, S.; Gupta, P.K.; Lal, J., 2005. Effect of mangiferin on hyperglycemia and atherogenicity in streptozotocin induced diabetic rats. Journal of Ethnopharmacology 97, 497-501.
- Newland, C.M., 1995. Motor function and the physical properties of the operant: applications to screening and advanced techniques. En: Neurotoxicology approaches and methods. Editores: Louis W. Chang y William Slikker, Jr. Elsevier Inc. pp: 265-299.
- Nijveldt, R.J.; van Nood, E.; van Hoorn, D.E.C.; Boelens, P.G.; van Norren, K.; Leeuwen, P.A.M., 2001. Flavonoids: a review of probable mechanisms of action and potential applications. The American Journal of Clinical Nutrition 74, 418-425.
- O' Malley, M., 2010. The regulatory evaluation of the skin effects of pesticides. En: Hayes' Handbook of Pesticide Toxicology. Third Edition. Volume 1. Edited by Robert Krieger. Academic Press, Elsevier. pp: 701-787.
- OECD, 1987. Test N° 402: Acute dermal toxicity, OECD Guidelines for the testing of chemicals, Section 4: Health Effects, OECD Publishing.
- OECD, 1997. Test N° 424: Neurotoxicity study in rodents, OECD Guidelines for the testing of chemicals, Section 4: Health Effects, OECD Publishing.
- OECD, 1998. Test N° 408: Repeated dose 90-day oral toxicity study in rodents, OECD Guidelines for the testing of chemicals, Section 4: Health Effects, OECD Publishing.
- OECD, 2001. Series on testing and assessment N° 24: Guidance document on acute oral toxicity testing. OECD Environment, Health and Safety Publications, París, Francia.
- OECD, 2002a. Test N° 404: Acute dermal Irritation/Corrosion, OECD Guidelines for the testing of chemicals, Section 4: Health Effects, OECD Publishing.

- OECD, 2002b. Test N° 423: Acute oral toxicity – Acute toxic class method, OECD Guidelines for the testing of chemicals, Section 4: Health Effects, OECD Publishing.
- OECD, 2008. Test N° 407: Repeated dose 28-day oral toxicity study in rodents, OECD Guidelines for the testing of chemicals, Section 4: Health Effects, OECD Publishing.
- Olafsson, K.; Jaroszewski, J.W.; Smitt, U.W.; Nyman, U., 1997. Isolation of angiotensin converting enzyme (ACE) inhibiting triterpenes from *Schinus molle*. Planta Medica 63 (4), 352-355.
- Otto, K., 2004. Anesthesia, analgesia and euthanasia. En: The laboratory mouse. Editor: Hans Hedrich. Elsevier Academic Press. pp: 555-569.
- Oyesomi, T.O.; Ajao, M.S.; Olayaki, I.A.; Adekomi, D.A., 2012. Effect of essential oil of the leaves of *Eucaliptus globulus* on heamatological parameters of Wistar rats. African Journal of Biochemistry Research 6 (4), 46-49.
- Panagiotakopulu, E.; Buckland, P.C.; Day, P.M., 1995. Natural insecticides and insect repellents in Antiquity: a review of the evidence. Journal of Archeological Science 22, 705-710.
- Peluso, M.R., 2006. Flavonoids attenuate cardiovascular disease, inhibit phosphodiesterase, and modulate lipid homeostasis in adipose tissue and liver. Experimental Biology and Medicine 231, 1287-1299.
- Philogène, B.J.R.; Renault-Roger, C.; Vincent, C., 2004. Productos fitosanitarios insecticidas de origen vegetal: promesas de ayer y de hoy. En: Biopesticidas de origen vegetal. Ediciones Mundi-Prensa. Madrid, España. pp: 1-18.
- Prut, L.; Belzung, C., 2003. The open field as a paradigm to measure the effects of drugs on anxiety-like behaviors: a review. European Journal of Pharmacology 463, 3-33.
- Quimby, F.W.; Luong, R.H., 2007. Clinical chemistry of the laboratory mouse. En: The mouse in biomedical research, 2nd Edition. Editores: J.G. Fox, S.W. Barthold, M.T. Davison, C.E. Newcomer, F.W. Quimby, A.L. Smith. Academic Press. pp: 171-216.
- Quiroga, E.N.; Sampietro, A.R.; Vattuone, M.A., 2001. Screening antifungal activities of selected medicinal plants. Journal of Ethnopharmacology 74, 89-96.
- Ramsingh, D., 2010. The assessment of the chronic toxicity and carcinogenicity of pesticides. En: Hayes' Handbook of Pesticide Toxicology. Third Edition. Volume 1. Edited by Robert Krieger. Academic Press, Elsevier. pp: 463-482.
- Ranilla, L.G.; Kwon, Y.; Apostolidis, E.; Shetty, K., 2010. Phenolics compounds, antioxidant activity and *in vitro* inhibitory potential against key enzymes relevant for hyperglycemia and hypertension of commonly used medicinal plants, herbs and spices in Latin America. Bioresource Technology 101, 4676-4689.

- Rattan, R.S., 2010. Mechanism of action of insecticidal secondary metabolites of plant origin. Crop Protection 29, 913-920.
- Redfern, W.S.; Strang, I.; Storey, S.; Heys, C.; Barnard, C.; Lawton, K.; Hammond, T.G.; Valentin, J.P., 2005. Spectrum of effects detected in the rat functional observational battery following oral administration of non-CNS targeted compounds. Journal of Pharmacological and Toxicological Methods 52, 77-82.
- Regnault-Roger, C., 2004. ¿Nuevos fitoinsecticidas para el tercer milenio? En: Biopesticidas de origen natural. Ediciones Mundi-Prensa. Madrid, España. pp: 19-40.
- Rehecho, S.; Uriarte-Pueyo, I.; Calvo, J.; Vivas, L.A.; Calvo, M.I., 2011. Ethnopharmacological survey of medicinal plants in Nor-Yauyos, a part of the Landscape Reserve Nor-Yauyos-Cochas, Peru. Journal of Ethnopharmacology 133, 75-85.
- Repetto Jiménez, M.; Repetto Kuhn, G., 2009a. Conceptos y definiciones: Toxicología. Toxicidad. En: Toxicología fundamental. Cuarta Edición. Ediciones Díaz de Santos. pp: 21-58.
- Repetto Jiménez, M.; Repetto Kuhn, G., 2009b. Procesos fisiopatológicos de origen tóxico. En: Toxicología fundamental. Cuarta Edición. Ediciones Díaz de Santos. pp: 219-339.
- Ríos, J.P., 2010. Effects of triterpenes on the immune system. Journal of Ethnopharmacology 128, 1-14.
- Ritskes-Hoitinga, M., 2004. Nutrition of laboratory mouse. En: The laboratory mouse. Editor: Hans Hedrich. Elsevier. pp: 463-479.
- Ruffa, M.J.; Ferraro, G.; Wagner, M.L.; Calcagno, M.L.; Campos, R.H.; Cavallaro, L., 2002. Cytotoxic effect of Argentine medicinal plant extracts on human hepatocellular carcinoma cell line. Journal of Ethnopharmacology 79, 335-339.
- Ruffinengo, S.; Eguaras, M.; Floriz, I.; Faverin, C.; Bailac, P.; Ponzi, M., 2005. LD_{50} and repellent effects of essential oils from argentinian wild plant species on *Varroa destructor*. Journal of Economic Entomology 98 (3), 651-655.
- Ruiz, A.I.; Mercado, M.I.; Guantay, M.E.; Ponessa, G.I., 2009a. Morfoanatomía y arquitectura foliar de *Schinus areira* (Anacardiaceae). Lilloa 46 (1-2), 137-146.
- Ruiz, M.J.; Fernández, M.; Picó, Y.; Mañes, J.; Asensi, M.; Carda, C.; Asensio, G.; Estela, J.M., 2009b. Dietary administration of high doses of pterostilbene and quercetin to mice is not toxic. Journal of Agricultural and Food Chemistry 57 (8), 3180-3186.
- Sánchez Chopa, C.; Alzogaray, R.; Ferrero, A., 2006. Repellency assays with *Schinus molle* var. *areira* L. (Anacardiaceae) essential oils against *Blattella germanica* L. (Blattodea: Blattellidae). Bioassay 1 (6), 1-3.

- Schmidt, C.; Fronza, M.; Goettert, M.; Geller, F.; Luik, S.; Flores, E.M.M.; Bittencourt, C.F.; Zanetti, G.D.; Heinzmann, B.F.; Laufer, S.; Merfort, I., 2009. Biological studies on Brazilian plants used in wound healing. Journal of Ethnopharmacology 122, 523-532.
- Schmitz, H.; Chevaux, K., 2000. Defining the role of dietary phytochemicals in modulating human immune function. En: Nutrition and Immunology, Principles and practice. Editores: M.E. Gershwin, J.B. German, C.L. Keen. Humana Press. 505 pp.
- Schmourlo, G.; Mendonça-Filho, R.R.; Alviano, C.S.; Costa, S.S., 2005. Screening of antifungal agents using ethanol precipitation and bioautography of medicinal and food plants. Journal of Ethnopharmacoloy 96, 563-568.
- Seymour, R.; Ichiki, T.; Mikaelian, I.; Boggess, D.; Silva, K.A.; Sundberg, J.P., 2004. Necropsy methods. En: The laboratory mouse. Editor: Hans Hedrich. Elsevier Academic Press. pp: 495-516.
- Shalaan, E.A.S.; Canyon, D.; Younes, M.W.F.; Abdel-Wahab, H.; Mansour, A.H., 2005. A review of botanical phytochemicals with mosquitocidal potential. Environment International 31, 1149-1166.
- Silva-Aguayo, G., 2002. Insecticidas vegetales. En: E.B. Radcliffe y W.D. Hutchinson (Eds.), Radcliffe: Texto Mundial de MIP. URL: http//ipmworld.umn.edu, Universidad de Minnesota, St. Paul, MN.
- Sutko, J.L.; Aired, J.A.; Welch, W.; Ruest, L., 1997. The pharmacology of ryanodine and related compounds. Pharmacological Reviews 49 (1), 53-98.
- Taiz, L.; Zeiger, E., 2002. Plant Physiology. Third Edition. Sunderland, MA. Sinauer Associates. 690p.
- Tang, X.; Sandford, L.D., 2005. Home cage and activity-based measures if anxiety in 129P3/J, 129X1/SvJ and C57BL/6J mice. Physiology and Behavior 84, 105-115.
- Tang, X.; Xiao, J.; Liu, X.; Sanford, L.D., 2004. Strain differences in the influence of open field exposure on sleep in mice. Behavioural Brain Research 154, 137-147.
- Taylor, L., 2005. Brazilian Peppertree (*Schinus molle*). En: The Healing Power of the Rainforest Herbs. A guide to understanding and using herbal medicinal. Square One Publishers, Inc. New York. ISBN 0-7570-0144-0.
- Tédong, L.; Dimo, T.; Dzeufiet, P.D.D.; Asongalem, A.E.; Sokeng, D.S.; Callard, P.; Flejou, J.F.; Kamtchouing, P., 2006. Antihyperglycemic and renal protective activities of *Anacardium occidentale* (Anacardiaceae) leaves in streptozotocin induced diabetic rats. African Journal of Tradicional, Complementary and Alternative Medicines 3 (1), 23-35.

- Tédong, L.; Dzeufiet, P.D.D.; Dimo, T.; Asongalem, E.A.; Sokeng, S.N.; Flejou, J.F.; Callard, P.; Kamtchouing, P., 2007. Acute and subchronic toxicity of *Anacardium occidentale* Linn (Anacardiaceae) leaves hexane extract in mice. African Journal of Tradicional, Complementary and Alternative Medicines 4 (2), 140-147.
- Tegeris, J.; Balster, R.L., 1994. A comparison of the acute behavioral effects of alkylbenzenes using a functional observational battery in mice. Fundamental and Applied Toxicology 22, 240-250.
- Thiel, C.M.; Müller, C.P.; Huston, J.P.; Schwarting, R.K.W., 1999. High versus low reactivity to a novel environment: behavioral, pharmacological and neurochemical assessment. Neuroscience 93 (1), 243-251.
- U.S. EPA, 1998. Guidelines for neurotoxicity risk assessment. U.S. Environmental Protection Agency, Risk Assessment Forum, Washington, DC, 630/R-95/001F.
- Ujváry, I., 2010. Pest control agents from natural products. En: Hayes´ Handbook of Pesticide Toxicology, Third Edition. Edited by Robert Krieger. Academic Press. Elsevier. pp: 119-229.
- Wang, D.X.; Liu, P.; Chen, Y.H.; Chen, R.Y.; Guo, D.H.; Ren, H.Y.; Chen, M.L., 2008. Stimulating effect of catechin, an active component of *Spatholobus suberectus* Dunn, on bioactivity of hematopoietic growth factor. Chinese Medical Journal (English Edition) 121 (8), 752-755.
- Weiner, M.L.; Nemec, M.; Sheets, L.; Sargent, D.; Breckenridge, C., 2009. Comparative functional observational battery study of twelve commercial pyrethroids insecticides in male rats following acute oral exposure. Neurotoxicology 30S, 1S-16S.
- Werdin González, J.O., 2011. Alternativas para el manejo integrado de *Nezara viridula* (L.), insecto plaga de la soja. Tesis Doctoral. Universidad Nacional del Sur. Bahía Blanca. 253 pág.
- Werdin, J.O.; Gutiérrez, M.M.; Murray, A.P.; Ferrero, A.A., 2010. Biological activity of essential oils from *Aloysia polystachia* y *Aloysia citriodora* (Verbenaceae) against the soybean pest *Nezara viridula* (Hemiptera: Pentatomidae). Natural Products Communications 5 (2), 301-306.
- Werdin, J.O.; Murray, A.P.; Ferrero, A.A., 2008. Bioactividad de aceites esenciales de *Schinus molle* var. *areira* (Anacardiaceae) en ninfas II de *Nezara viridula* (Hemiptera, Pentatomidae). Boletín de Sanidad Vegetal Plagas 34, 367-376.
- Wilson, N.H.; Hardisty, J.F.; Hayes, J.R., 2008. Short-term, subchronic and chronic toxicology studies. En: Principles and methods of toxicology. Fifth Edition. Editor: A. Wallace Hayes. CRC Press. pp: 1223-1264.

- Wimalaratne, P.D.C.; Slessor, K.N.; Borden, J.H.; Chong, L.J.; Abate, T., 1996. Isolation and identification of house fly, *Musca domestica* L., repellents from pepper tree, *Schinus molle* L. Journal of Chemical Ecology 22 (1), 49-59.
- Wink, M., 2003. Evolution of secondary metabolites from an ecological and molecular phylogenetic perspective. Phytochemistry 64, 3-19.
- Wink, M., 2009. Functions and biotechnology of plant secondary metabolites. 2nd Edition. In: Annual Plant Reviews 39, 1-20. ISBN: 978-1-4051-85-28-8.
- Wink, M., 2010. Biochemistry of plant secondary metabolism. 2nd Edition. In: Annual Plant Reviews 40, 1-19. ISBN: 978-1-4051-8397-0.
- Wolansky, M.J.; Harrill, J.A., 2008. Neurobehavioral toxicology of pyrethroid insecticides in adult animals: a critical review. Neurotoxicology and Teratology 30, 55-78.
- Wu, J.; Baldwin, I.J., 2010. New insights into plant responses to the attack from insect herbivores. Annual Review of Genetic 44, 1-24.
- Yueqin, Z., 2007. Identificación y actividad farmacológica de principios de especies antiinflamatorias. Tesis doctoral. Universitat de València, Servei de Publicacions. Valencia. pp.: 5-10. ISBN 978-84-370-6676-9.
- Yueqin, Z.; Recio, M.C.; Máñez, S.; Giner, R.M.; Cerdá-Nicolás, M.; Ríos, J.L., 2003. Isolation of two triterpenoids and a biflavanone with anti-inflamatory activity from *Schinus molle* fruits. Planta Medica 69 (10), 893-898.
- Zanetti, N.; Minetti, A.; Ferrero, A., 2006. Evaluación de toxicidad aguda de extractos etanólicos de frutos y hojas de *Schinus areira* L. en ratas. Acta Toxicológica Argentina 14 (2), 52.
- Zar, J.H., 1999. Biostatistical Analysis. Forth Edition. Prentice Hall, New Jersey. 663 pp.
- Zehnder, G.; Gurr, G.M.; Kühne, S.; Wade, M.R.; Wratten, S.D.; Wyss, E., 2007. Arthropod pest management in organic crops. Annual Review of Entomology 52, 57-80.
- Zuloaga, F.O.; Morrone, O.; Belgrano, M.J., 2008. Catálogo de las Plantas Vasculares del Cono Sur (Argentina, sur de Brasil, Chile, Paraguay y Uruguay). Missouri Botanical Garden Press. St. Louis. pp.: 389. ISBN 193-07237-0-9.

Artículos publicados en revistas científicas internacionales

Las publicaciones derivadas del presente trabajo son:

- Ferrero, A.; Minetti, A.; Bras, C. y Zanetti, N., 2007. "Acute and subacute toxicity evaluation of ethanolic extract from fruits of *Schinus molle* in rats". Journal of Ethnopharmacology 113: 441-447. Elsevier Ed.
- Bras, C.; Domínguez, S.; Codón, S.; Minetti, A.; Ferrero, A., 2010. "Consequences of subchronic exposure to ethanolic extract from fruits and leaves of *Schinus molle* var. *areira* L. in mice". Journal of Ethnopharmacology 132: 321-327. Elsevier Ed.
- Bras, C.; Gumilar, F.; Gandini, N.A.; Minetti, A.; Ferrero, A., 2011. "Evaluation of the acute dermal exposure of the ethanolic and hexanic extracts from leaves of *Schinus molle* var. *areira* L. in rats". Journal of Ethnopharmacology 137: 1450-1456. Elsevier Ed.

Presentaciones a Congresos, Simposios y Jornadas

Durante el transcurso de la realización del presente trabajo, se realizaron las siguientes presentaciones en reuniones científicas de carácter nacional e internacional:

- Bras, C.; Minetti, A. y Ferrero, A. "Estudio de neurotoxicidad del extracto hexánico de hojas de *Schinus areira* L. en ratones". XV Congreso Argentino de Toxicología. Neuquén, Argentina. 26 al 28 de Septiembre de 2007. Trabajo presentado en modalidad póster. Resumen publicado en: Acta Toxicológica Argentina 15 (Suplemento): 65.

- Bras, C.; Minetti, A. y Ferrero, A. "Estudio subcrónico del extracto etanólico de frutos de *Schinus areira* L. en ratones". XXVI Jornadas Interdisciplinarias de Toxicología. Buenos Aires, Argentina. 17 al 19 de Septiembre de 2008. Trabajo presentado en modalidad póster. Resumen publicado en: Acta Toxicológica Argentina 16 (Suplemento): 20.
- Bras, C.; Minetti, A. y Ferrero, A. "Evaluación de neurotoxicidad por exposición subcrónica al extracto etanólico de hojas de *Schinus areira* L.". 1° Congreso Internacional de Farmacobotánica Chile. Chillán, Chile. 6 al 10 de Enero de 2009. Trabajo presentado en modalidad póster. Resumen publicado en: CD-ROM del Congreso.
- Bras, C.; Domínguez, S.; Codón, S.; Minetti, A. y Ferrero, A. "Estudios bioquímicos e histopatológicos por exposición subcrónica al extracto etanólico de frutos de *Schinus areira* L.". 1er Congreso Internacional de Farmacobotánica Chile. Chillán, Chile. 6 al 10 de Enero de 2009. Trabajo presentado en modalidad póster. Resumen publicado en: CD-ROM del Congreso.
- Bras, C.; Minetti, A. y Ferrero, A. "Evaluación de la toxicidad aguda del extracto hexánico de frutos de *Schinus areira* L.". XVI Congreso Argentino de Toxicología. Puerto Madryn, Argentina. 24 al 27 de Junio de 2009. Trabajo presentado en modalidad póster. Resumen publicado en: Acta Toxicológica Argentina 17 (Suplemento): 37.
- Bras, C.; Domínguez, S.; Codón, S.; Minetti, A. y Ferrero, A. "*Schinus areira* L.: estudios bioquímicos e histopatológicos en ratones expuestos en forma subcrónica al extracto etanólico de sus hojas". Vth Internacional Congress of Ethnobotany ICEB 2009. San Carlos de Bariloche, Argentina. 21 al 24 de Septiembre de 2009. Trabajo presentado en modalidad póster. Resumen publicado en: CD- ROM del Congreso, ISBN: 978-84-96023-68-0.

- Bras, C.; Domínguez, S.; Minetti, A. y Ferrero, A. "*Schinus molle* var. *areira* L.: consequences of subacute exposure to ethanolic extract from its fruits in mice". 1º Reunión Internacional de Ciencias Farmacéuticas. Córdoba, Argentina. 24 y 25 de Junio de 2010. Trabajo presentado en modalidad póster. Resumen próximamente publicado con formato proceeding por la revista AAPS Pharm Sci Tech.
- Bras, C.; Bucciarelli, A.; Minetti, A. y Ferrero, A. "Efectos de la exposición subaguda al extracto hexánico de frutos de *Schinus molle* var. *areira* (Anacardiaceae)". X Simposio Argentino y XIII Simposio Latinoamericano de Farmacobotánica. Córdoba, Argentina. 24 al 26 de Noviembre de 2010. Trabajo presentado en modalidad póster. Resumen publicado en el Libro de resúmenes del Simposio.
- Bras, C.; Gandini, N.A.; Minetti, A.; Ferrero, A. "Evaluación de la toxicidad aguda por vía dérmica del extracto etanólico de frutos de *Schinus molle* var. *areira* L. en ratas". XVII Congreso Argentino de Toxicología. Tandil, Argentina. 29 de Septiembre al 1 de Octubre de 2011. Trabajo presentado en modalidad póster. Resumen publicado en Acta Toxicológica Argentina 19 (Suplemento): 86.