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"Salud global, genes y sociedad"

I Jornada Paraguaya de Genética

Asunción - Paraguay
25 al 27 de abril de 2019

Universidad Católica Nuestra Señora de la Asunción
CAMPUS ASUNCIÓN

IAEMGS

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MEMORIAS DEL XI CONGRESO LATINOAMERICANO DE MUTAGÉNESIS, CARCINOGÉNESIS Y TERATOGÉNESIS AMBIENTAL

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- EMGS (Environmental Mutagenesis Genomic Society) o Hollaender Fund
- UKEMS (United Kingdom Environmental Mutagen Society)

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- Sociedad Científica del Paraguay
- Asociación Latinoamericana de Mutagénesis Carcinogénesis y Teratogénesis Ambiental (ALAMCTA)
- International Association of Environmental Mutagenesis and Genomics Societies (IAEMGS)
- Sociedad Paraguaya de Mutagénesis Carcinogénesis y Teratogénesis Ambiental (SPAMCTA)
- Sociedad Paraguaya de Genética

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PRÓLOGO

La Asociación Latinoamericana de Mutagénesis Carcinogénesis y Teratogénesis Ambiental (ALAMCTA), conformada por sociedades científicas de países de América Latina que reúnen a científicos dedicados al estudio de la interacción del ambiente con los genes y sus consecuencias para la salud humana., tiene como misión congregar a científicos para la colaboración, el intercambio de ideas y la promoción del desarrollo de la Genética Toxicológica y la Mutagénesis Ambiental en la región. Fundada en México en 1980, ha tenido 10 ediciones de Congreso, desde el año 1992, realizados en México, Colombia, Brasil, Chile, Argentina y Uruguay. En el último congreso de ALAMCTA llevado a cabo en este último país, se eligió a PARAGUAY para ser sede de la XI versión del congreso de ALAMCTA.

El XI Congreso, realizado en la ciudad de Asunción entre el 25 y el 27 de abril de 2019, tuvo como eje central "SALUD GLOBAL GENES Y SOCIEDAD", en el que se integraron conceptos de Mutagénesis Ambiental y de Genética Toxicológica con la salud humana bajo una mirada global, buscando evitar o mitigar su impacto en las poblaciones humanas

Los ejes temáticos principales fueron, entre otros: Salud Global, Nutrigenómica, Epigenética, Epigenómica y Cáncer, Salud y Ambiente, Genotoxicidad y Mutagénesis Ambiental, Genotoxicidad y antigenotoxicidad de Productos Naturales, Genómica del Cáncer, estrés oxidativo celular, daño oxidativo del DNA y envejecimiento, genotoxicidad de Agroquímicos, dosimetría Biológica y radio protección y por último daño y Reparación de DNA.

Un total de 500 participantes se inscribieron al Congreso, de los cuales 340 eran locales y 160 extranjeros, de países como Italia, España, Canadá, Argentina, Uruguay, Ecuador, Colombia, México, Estados Unidos, Chile y Cuba.

Durante el Congreso se dictaron los cursos de Radio protección, dosimetría biológica, Mutagénesis ambiental y un taller de Mentoring, hubo 12 simposios, 2 videoconferencias y 9 conferencias Magistrales, los idiomas oficiales fueron el inglés y el español. Como producto del congreso, se creó la Red Latinoamericana de investigación en exposición a agroquímicos y genotoxicidad y se fortaleció la red latinoamericana de investigación en Genotoxicidad y antigenotoxicidad de Productos naturales.

Sin duda éste fue un espacio de reflexión y de discusión de resultados de las últimas investigaciones en el área para investigadores y para estudiantes de los diferentes países y un lugar donde se han establecido lazos para promover el desarrollo científico de jóvenes investigadores a través de la cooperación entre los países participantes.

Agradezco especialmente a los directivos de las instituciones co organizadoras, de la Facultad de Ciencias de la Salud de la Universidad Católica Nuestra Señora de la Asunción (FCS-UC), y de la Facultad de Ciencias Exactas y Naturales de la Universidad Nacional de Asunción (FACEN - UNA), a las agencias Internacionales quienes otorgaron las becas y que hicieron posible la participación de jóvenes investigadores de diversos países, al Comité organizador, a los estudiantes de Medicina de la FCS -UC y a estudiantes de la FACEN -UNA, a la empresa CEDIAL que sin el apoyo de todos ellos, este evento de tan grande envergadura, hubiera sido imposible de realizar.

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XI CONGRESO DE LA ASOCIACION LATINOAMERICANA DE MUTAGENESIS, CARCINOGENESIS Y TERATOGENESIS AMBIENTAL

CONFERENCIAS

CONFERENCIA 1

CONFERENCIA INAUGURAL

THE MUTAGENIC AND CARCINOGENIC ACTIVITY OF COMBUSTION-DERIVED COMPLEX

Paul A. White[1], Rebecca Maertens [2], Christine Lemieux [2] and Alexandra S. Long [1]

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Combustion-derived complex mixtures contain a wide range of known mutagens and carcinogens. Humans encounter these mixtures via contact with contaminated environmental matrices such as soil, urban air, and indoor air. Assessing the mutagenic and/or carcinogenic hazards of combustion-derived mixtures in complex matrices constitutes a significant challenge. In vitro mutagenicity assays provide a means to characterise samples without a priori information about mutagen sources and identity. For example, analysis of atmospheric mutagenicity worldwide, expressed per m^3 equivalent, permits general statements about the spatial and temporal distribution of mutagenic hazard. A review of published data revealed that atmospheric Salmonella mutagenicity in rural areas is ~70% lower than urban areas; summer levels are ~60% lower than winter levels. Analyses of cannabis smoke condensates revealed that they contain lower amounts of PAHs (polycyclic aromatic hydrocarbons) relative to experimentally-matched tobacco samples; however, Salmonella mutagenicity was higher. Comparisons of observed mutagenicity with values predicted using the concentrations and activity of known mutagens permits an assessment of activity attributable to known substances/sources. Analyses of SHD (settled house dust), contaminated soil, and coal tar indicates that PAHs account for a variable proportion of mutagenic activity; with magnitude related to sample type and bioassay. For example, mutagenic priority PAHs generally account for a small fraction (~20%) of SHD Salmonella mutagenicity. In contrast, PAH levels in coal-tar- contaminated soils yield predictions of mutagenicity that are within 2-fold of actual observations for the soils themselves. Use of bioassay responses to determine levels of BaP equivalents in contaminated soils permits an evaluation of the additive assumption employed for cancer risk assessment. The results of chemical analyses, in combination with in vitro and in vivo mutagenicity assessments, indicate that BaP equivalent levels based on PAH concentrations are within 10-fold of those derived from bioassay results. The results support use of a chemical- specific, additive paradigm for cancer risk assessment of combustion-derived PAH mixtures in contaminated matrices.

CONFERENCIA 2

NUESTRO AMBIENTE, NUESTRA SALUD

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El cambio climático y la contaminación ambiental afectan nuestro ambiente que incluye nuestra dieta y la contaminación de agua, suelo, del aire y de otros factores que afectan la salud humana y la calidad de vida de esta y de las generaciones futuras. Se estima que unas 9 millones de muertes pueden ser atribuidas a los distintos tipos de contaminación ambiental durante el año 2015, lo que representa el 16% de la mortalidad global. La mayoría de estas muertes ocurren en países menos desarrollados. Esta cantidad es 3 veces mayor que las causadas por el SIDA, la tuberculosis y malaria combinadas. Más aún, las evidencias sugieren que cuando la exposición empieza temprano en la vida de los individuos esta causa más morbilidad y mortalidad. Discutiremos información de estudios de campo en poblaciones en riesgo en donde se intenta identificar biomarcadores de efectos tempranos e identificación de individuos susceptibles. Además de estudios en modelos de laboratorio empleados para identificar los mecanismos de toxicidad de los xenobióticos. Los estudios epidemiológicos muestran que la exposición durante la gestación o la infancia se asocian con el desarrollo de enfermedades en la vida adulta como la diabetes, obesidad, hipertensión, neurodegeneración y cáncer.

CONFERENCIA 3

BIOMARKERS OF DNA DAMAGE IN CLINICAL PRACTICE: THE EXAMPLE OF FRAILTY STATUS IN ELDERLY

Stefano Bonassi

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Measuring DNA damage and early events of pathogenesis is extensively applied in population studies to explore exposure to genotoxic agents, dose-response relationships, mechanisms of action, disease causality, and in some cases to monitor public health interventions. On the other hand, the recent implementation of systems approaches in clinical practice, and the development of complex predictive models which include social, psychological, and life-style parameters in the diagnostic and therapeutic process, has determined the inclusion of molecular/cellular profiling into clinical studies. The possibility to model in the same playground the complexity generated by the interaction between early molecular events and the variety of real clinical practice may help to have a better insight into the pathways of chronic diseases, and to improve disease recognition and treatment. In particular it will be presented a practical example of their use in the clinical assessment of frailty in older adult, discussing the use of these biomarkers in the personalized complexity.

CONFERENCIA 4

QUANTITATIVE ANALYSIS OF GENETIC TOXICITY DOSE-RESPONSE DATA FOR POTENCY RANKING AND RISK ASSESSMENT

Paul A. White[1], Nikolai Chepelev [1], George E. Johnson [2], Mirjam Luijten [3], Alexandra S. Long [1], Andreas Zeller [4], John W. Wills [5], Wout Slob [3]

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Interpretations of genetic toxicity test results have historically employed a qualitative "screen-and-bin" approach to identify genotoxic substances. However, a paradigm shift is advocating use of quantitative methods to analyse and interpret genetic toxicity dose-response data. The benchmark dose (BMD) approach, which is the preferred method for dose-response analysis, determines a Reference Point (RP) on the dose-response function (i.e., the BMD) that reflects genotoxic potency. The BMD approach has been employed to analyse numerous in vitro and in vivo dose-response datasets; the results were employed for compound potency ranking and examinations of covariates related to cell type, tissue, sampling time, sex, and TGR (transgenic rodent) assay variant. Additional analyses investigated the correlation between genotoxic potency and carcinogenic potency; the relationship can be used to facilitate regulatory evaluations of substances that have never been tested for carcinogenic activity. More recent work is scrutinising dose-response data in an effort to determine endpoint-specific CES (Critical Effect Size) values for genotoxicity endpoints. Current work is comparing the outcome of regulatory evaluations based on genotoxicity and carcinogenicity data. Specifically, using modeled exposure estimates, case studies are comparing MOE (Margin of Exposure) values based on in vivo genotoxicity dose-response data with those based on carcinogenicity data. The results obtained, which are based on 43 substances, indicate that regulatory evaluations based on genotoxicity data would be more conservative (i.e., lower MOE). Analyses of NDMA (N- nitrosodimethylamine) and BaP (benzo[a]pyrene) dose-response data are comparing genotoxicity-derived exposure limit values (e.g., PDE or Permitted Daily Exposure) with those based on linear low-dose extrapolations of carcinogenicity data. Finally, quantitative analyses of benzene dose-response data are being used to evaluate the recently-updated OEL (Occupational Exposure Limit) value. The analyses collectively demonstrate the utility of quantitative dose-response analyses for regulatory assessments of genotoxic substances, particularly ubiquitous substances that have never been tested for carcinogenic activity.

CONFERENCIA 5

THE MINING AND BURNING OF COAL: EFFECTS ON HEALTH AND THE ENVIRONMENT

Juliana da Silva

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Coal dust is constituted from carbon, hydrogen, oxygen, nitrogen, quartz (crystalline silica), and inorganic minerals, such as beryllium, cadmium, cobalt, chromium, iron, boron, copper, nickel, antimony, zinc, aluminum, titanium, magnesium, manganese, mercury, and lead. The presence of mineral matter in coal may result in a number of environmental and human health problems related to its mining, preparation, and combustion. As observed, coal is a mixture of a variety of chemicals, and includes hydrocarbons, which may generate polycyclicaromatic hydrocarbons (PAH). Compounds such as PAHs once activated by the organisms have been shown to have mutagenic and carcinogenic activity due to its ability to form adducts with purines. Coal induced DNA damage is related to macrophage activation and the recruitment of polymorphonuclear cells. This cell activation induces the release of inflammatory mediators, such as cytokines, ROS and reactive nitrogen species (RNS). The proinflammatory properties of ROS and RNS include endothelial cell damage, lipid peroxidation and oxidation, the formation of chemostatic factors, the recruitment of neutrophils, and DNA damage. Interaction of ROS with DNA can result in DNA structural and transcriptional errors. Damage caused by ROS is recognized by DNA glycosylases, apurinic/apyrimidinic endonucleases of the base excision repair (BER) mechanism, and in some cases by the nucleotide excision repair (NER) machinery, leading to DNA strand-breaks. The relationship between chronic exposure to coal and coal ash particles and cancer is still widely debated.

CONFERENCIA 6

MICRONUCLEI, CHROMOTHRIPSIS, CHROMOANAGENESIS AND INFLAMMATION

Prof. Michael Fenech

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Micronuclei (MN) originate mainly from acentric chromosome fragments or whole chromosomes that are not included in the daughter nuclei during mitosis. Their exclusion occurs because of failure to engage with the mitotic spindle due to defects in the chromosome segregation mechanisms. The obvious consequence of MN formation is generation of daughter cells that have either gained or lost genetic material. Until recently the fate of cells with MN was not so clear although Grote *et al*. had shown that they may divide more slowly than normal. In the past 5-10 years new research has revealed a much more complicated picture based on the following observations: (i) DNA of a chromosome entrapped in an MN is not replicated properly resulting in chromosome shattering (chromothripsis) possibly due to failure of ligation of Okazaki fragments; (ii) the shattered chromosome fragments are subsequently randomly rearranged and re-ligated in the next division cycle leading to the generation of a hypermutated chromosome (chromoanagenesis) a phenomenon often seen in cancer and (iii) the presence of MN in a cell and the leakage of shattered DNA from the MN into the cytoplasm trigger two pro-inflammatory pathways namely the Senescence Associated Secretory Phenotype (SASP) and the cGAS-STING mechanism of innate immunity respectively. This new knowledge highlights the additional central roles that MN formation plays in generating chromosomal hypermutation within one cell cycle, and the stimulation of inflammation which is likely to result in a vicious cycle of ever-increasing MN formation and hyper-inflammation with ageing if not resolved. The presentation will provide a succinct summary of these new and exciting developments on the increased relevance of MN formation in genome instability, enhanced inflammation and unhealthy ageing.

CONFERENCIA 7

NUTRIGENOMICS AND HEALTHY AGING

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In each of the stages of our lives, good nutrition is key to our health. However, what foods are part of healthy nutrition has been a controversial topic in the scientific and popular field. In order to provide health professionals and the public with a more solid basis to recommend and practice this good nutrition, different national and international institutions periodically publish nutritional guides that incorporate current scientific knowledge. However, what these guidelines do not include is the great interindividual variability in response to the food consumed. The molecular basis of this variability is complex, but part of it is associated with our genome and its multiple differences. The study of the relationship between the variations in the genome and the response to the diet is what is known as nutrigenetics or nutrigenomics and its results will be the basis for the implementation of personalized recommendations as instruments of prevention or even therapy of common chronic diseases. Nutrigenetics is a growing science and the results of the research in this area are promising thanks to advances in genetic techniques and there are already some applications that allow some limited dietary personalization. However, greater precision is needed in terms of obtaining information about the habitual diet of individuals. Other aspects that will contribute to the progress of nutrigenetics will be the integration of other technologies that define who we are and how we function, such as epigenetics, metabolomics and microbiota. In addition, nutrigenetics will require demonstration that its implementation is more effective than global recommendations and do so at the highest level of scientific evidence through randomized clinical intervention trials. Although there is still a way to go, the incorporation of this knowledge into daily practice will allow a more effective prevention of the diseases associated with aging and therefore a healthier and more vital life.

CONFERENCIA 8

THE USE OF XERODERMA PIGMENTOSUM CELLS TO UNDERSTAND HOW SUNLIGHT DAMAGE HUMAN SKIN CELLS

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The UVA component of sunlight is responsible for 95% of UV reaching Earth surface, and penetrates deep on skin. UVA light causes direct DNA lesions, such as pyrimidine dimers, but indirect action effects may generate reactive oxygen species, which also damage cellular components, including the genetic material. Despite many decades of investigation, the discrimination of how UVA light causes lesion on DNA is not clear. Genetic defects in DNA damage processing mechanisms have clear harmful effects, as disclosed by the human syndrome xeroderma pigmentosum (XP), whose patients have increased skin photodamage, including tumors and photoaging, in sunlight exposed areas. Our proposal is to use cells from XP patients to amplify and, thus, better comprehend the effects of UVA light irradiation in human cells. Initial studies were performed in cells from XP-V patients, who are defective on translesion synthesis (TLS). Basically, results indicate that although pyrimidine dimers are important in the deleterious action of UVA-light, oxidative stress is also triggered several hours after irradiation and, mainly, affect the capacity of DNA repair probably due to protein oxidation. The use of antioxidant gives almost full protection of the irradiated cells, including DNA replication and cell survival, although pyrimidine dimers are still induced in the genome. UVA-induced mutagenesis was also investigated using exome sequencing, to identify point mutations in the cells. Mainly C>T mutations at dipyrimidine sites were detected in UVA irradiated XP-V cells, probably due to pyrimidine dimers. However, the data disclosed also C>A mutations that may also occur due to oxidative stress, and, curiously, these mutations were also increased in non-irradiated XP-V cells, compared to TLS proficient cells. This information is highly relevant for XP patients, but may also help us to understand what occurs during skin sunlight exposure from normal human population.

CONFERENCIA 9

SALUD GLOBAL

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La Salud Global (SG) según Koplan y colaboradores es el área de la investigación que prioriza el mejoramiento y la obtención de la equidad en salud para toda la población mundial. El término Global está ligado al alcance o impacto de los problemas de salud en la comunidad mundial, por lo tanto, está íntimamente relacionado con las enfermedades con mayor carga de morbilidad. La Organización Mundial de la Salud ha definido diez desafíos que tiene que afrontar la SG y en el 13° Programa de Salud Mundial la estrategia pretende proteger a 3 mil millones de personas, un mil millones con cobertura de salud universal, un mil millones protegidos en las emergencias y un mil millones con mejor salud y bienestar. Los múltiples retos de la salud se centran en la contaminación del aire y el cambio climático: 9 de cada 10 personas respiran aire contaminado. Ocurren 7 millones de óbitos por año a causa de la contaminación del aire y aunque todos los países cumplan su compromiso del Acuerdo de París con relación al Cambio Climático la temperatura aumentará 3 °C. La diabetes, el Cáncer y las enfermedades cardíacas causan el 70% de todas las muertes anuales, siendo los principales factores de riesgo: el tabaquismo, inactividad física, el alcohol, dietas no saludables, y la contaminación del aire. La OMS prepara a los países para enfrentar una nueva epidemia de influenza que, sin duda ocurrida, pero no se sabe cuándo. La resistencia antimicrobiana es otro desafío: Cada año enferman 10 millones de personas con microorganismos resistentes y mueren 1.6 millones de personas. Los virus altamente morales con el Ébola están avanzando a zonas urbanas, aumentando los contextos críticos. Aumentar la Atención Primaria de la Salud y apoyar la Cobertura Integral de Salud es uno de los desafíos más importante, así como la renuencia o rechazo al uso de vacunas, ocurren 2 a 3 millones de muertes por año, pudiendo evitarse 1.5 millones de muertes con un aumento de la cobertura. El dengue sido declarado como emergencia mundial, 390 millones de personas se infectan anualmente y el 20% de los dengues graves fallecen. Para el 2020 se espera reducir la mortalidad en un 50%. Existen 37 millones de personas que viven con HIV, 22 millones están bajo tratamiento y un millón muere anualmente. Para el 2030 se espera que sea la tercera enfermedad que cause más enfermedades en el mundo. Para lograr cumplir el objetivo de desarrollo sostenible (ODS) 3: Salud y Bienestar, debemos todos juntos ser promotores de éste y todos los otros objetivos que interactúan para apoyar a la población global.

SIMPOSIOS

SIMPOSIO ECOTOXICOLOGÍA Y GENOTOXICIDAD AMBIENTAL

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CONTAMINATION IN SURFACE WATERS IN TRANSITIONAL AREAS OF THE ATLANTIC FOREST AND CERRADO IN THE CENTRAL-WEST REGION OF BRAZIL*

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Industrial, domestic and agricultural effluents promote the contamination of water resources due to the existence of chemical compounds that can cause genetic damage to living beings. We evaluated toxicogenic potential of surface water and analyzed the contamination by metals and emerging contaminants (ECs) to understand the relationship between their presence in the water and the use and land cover and physicochemical parameters in genetic damage. We determined whether ECs mixtures that are present in the surface waters cause effects on zebrafish gene expression. Samples were collected from Dourados and Brilhante Rivers (MS/Brazil). The metals were analyzed using ICP-OES and EC using LC-MS/MS. The Al exceeded acceptable by Brazilian Resolution and ECs detected were caffeine, imidacloprid, 2-hydroxy atrazine, tebuthiuron, atrazine, and bisphenol A. The toxicogenic variables were analyzed in meristematic cells of *Allium cepa*; and micronuclei, nuclear abnormalities, and DNA strand breaks using erythrocytes of *Astyanax lacustris*. The rivers presented physicochemical values outside the Brazilian laws. The results of *A. cepa* test indicated that the water samples from rivers showed cytotoxic and genotoxic effects. In blood cells of *A. lacustris*, the genotoxic effect of the water samples was observed for nuclear abnormalities and DNA breaks. Land use and cover and physicochemical parameters were correlated with DNA damage. We demonstrated toxigenic potential of water samples from rivers and land use and land cover and physicochemical parameters have influence on toxicogenomic damages. We reported changes in the expression of zebrafish target genes. Areas with agricultural practices and absence of ciliary forest favor the contamination of water resources.

Key words: surface water, toxigenetic -emerging contaminants

*We acknowledge FUNDECT, FUNASA and UFGD by the financial support.

EVALUATION OF THE ATMOSPHERIC PARTICULATE MATTER MUTAGENICITY FROM CITIES WITH DISTINCT METEOROLOGICAL CONDITIONS USING A COMPREHENSIVE SET OF SALMONELLA STRAINS

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The organic fractions of urban atmospheric particulate material (PM) are often mutagenic for the Salmonella/microsome assay. The PM mutagenicity is related to many chemical classes (e.g. PAHs and nitro-PAHs). Thus, the type and intensity of pollution sources and meteorological conditions such as temperature, and sunlight period are known to influence the atmospheric reactions of pollutants degradation and the formation of secondary pollutants and may directly influence the PM mutagenicity. Our work compared the mutagenic profiles of atmospheric total suspended particulates (TSP) from three cities with marked different meteorological conditions and TSP concentrations: Limeira (Brazil), with 99.0 μg/m^3, Stockholm (Sweden) with 6.2 μg/m^3, and Kyoto (Japan) with 28.0 μg/m^3. In order to make direct comparisons we used the same batch of filters, sample extraction method and Salmonella/microsome protocol with 11 strains of Salmonella. All samples were mutagenic for all strains, except for TA102. Based on the selectivity of these strains, we could verify that the mutagens present in the samples are able to induce DNA intercalation, DNA adducts, DNA cross-linking, DNA alkylation and oxidizing DNA damage. The mutagenicity profiles expressed by extracted organic material mass (EOM) (revertants/μg of EOM) obtained for Limeira, Stockholm and Kyoto were similar despite the differences in meteorological conditions and TSP concentrations. Mutagenic potencies expressed by air volume (rev./m^3) directly correlate to the TSP concentrations from the three (Limeira > Kyoto > Stockholm). In general, the frameshift strains sensitivity was YG1041 > YG1024 > YG1021 ≈ TA1538 > TA98 > TA97a ≈ YG5185. For the base-pare substitution the sensitivity was TA100 > YG7108 > TA104. In the both cases samples were more mutagenic without S9. We found small mutagenic potencies' variations as already observed by IARC (2006) highlighted by the use of the same extraction method and Salmonella/microsome protocol. We acknowledge FAPESP (2015/23364-3) by the financial support.

Key words: urban atmospheric particulate**,** mutagenicity- Salmonella strains

ECOTOXICITY FOR SUSTAINABILITY

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Ecotoxicity is the study of environmental toxicity. Sustainability is a set of ideas, strategies and attitudes ecologically correct, economically viable, socially fair and culturally diverse that ensures the maintenance of natural resources and allows the survival of living beings. Anthropic activities generate many toxic wastes, which interfere with the environment and human health. Among the sources of pollution are the contaminants generated in Sewage Treatment Plant (STP). STP are intended to minimize or exempt the presence of toxic contaminants from wastewater. During the treatment carried out in the STP, a decontaminated liquid effluent, to be released in a water resource, and a toxic solid waste (Sewage Sludge - SS), to be disposed in a specific sanitary landfill, are formed. SS toxicity comes from toxic sewage compounds and chemical agents used in the decontamination process. SS also contains different pathogens. Although the SS shows toxicity, it also has a rich composition in organic matter and nutrients, ideal for biodegradation, which allows a more sustainable destination for it, such as reconditioning agricultural soils. The biodegradation of wastes can be obtained, for example, by processes such as natural attenuation, bio-augmentation and biostimulation. Studies with SS + soil associations (ratio 1: 1), bioremediated by natural attenuation for 6 and 12 months, showed a decrease in toxicity and total exemption of contaminants and pathogens, respectively. Biostimulation with agricultural wastes has also proved to be a promising tool for decreasing decontamination time. Thus, biodegradation allowed to transform a highly ecotoxic wastes into an interesting agent to be used sustainably in agriculture.

Key words: Sewage, wastewater, biodegradation, natural attenuation, bio-augmentation and biostimulation

SIMPOSIO GENÓMICA Y CÁNCER

COORDINACIÓN: Ruth Zarate, PhD

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DEVELOPMENT OF EPIGENETIC DRUGS IN BREAST CANCER

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Breast cancer is one of the most common cancers in women worldwide and is a leading cause of cancer-related death in women. Comprehensive whole exome sequencing, DNA copy-number determination, and transcriptomic analyses of breast cancers have greatly expanded the therapeutic landscape opening the door for the new era of precision medicine in breast cancer. Epigenetic modification emerged as a key player in breast cancer development and progression. Three main epigenetic modifications play a key role in several cancers including DNA methylation, histone modifications and no coding RNA which are affecting gene expression, in a reversible way, and without changes in the DNA chain. Several data support the pivotal role of epigenetic mechanism in breast cancer development, prognosis and as mechanism of resistance to current therapies. In addition, recent lines of evidence support that epigenetic modulation of cancer or immune cells could modify their immunological properties and sensitize tumours to immune therapies. Drugs targeting the epigenome therefore appear as having a promising potential as immunomodulators, to overcome resistance to hormonal therapies and in combination with PPARP inhibitors. Development of epigenetic drugs in breast cancer is a field of great interest, highly attractive that need to be clinically exploited.

Key words: epigenetic drugs, breast cancer

GENOMIC PROFILING OF LEUKEMIAS

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For more than three decades, genomic aberrations have been known to play an important role in the pathogenesis of acute myeloid leukemia (AML), and cytogenetic aberrations have become well established diagnostic and prognostic markers. Major advances in genomic profiling by "omis" technologies, as next-generation sequencing (NGS), have improved the understanding of the biologically heterogeneity of leukemias and have facilitated the risk stratification of patients. These achievements have also provided relevant insights into improved disease classification, clinical care, and novel therapeutic approaches, allowing potentially targetable lesions for the development of new therapeutic approaches in the era of precision medicine. This presentation aims to show the increasing use if NGS technologies in research and clinical routine for more comprehensive knowledge that serve as valuable tools to advance individualized treatment approaches for diseases as leukemia.

Key words: leukemias, genomic profiling

IDENTIFICATION OF SOMATIC MUTATIONS IN HETEROGENOUS CONTEXT AND ITS THERAPEUTIC IMPLICATIONS IN SOLID TUMOURS

Dr. David Olivares Osuna

Centro para el Desarrollo de la Investigación Científica

For more than three decades, genomic aberrations have been known to play an important role in the pathogenesis of acute myeloid leukemia (AML), and cytogenetic aberrations have become well established diagnostic and prognostic markers. Major advances in genomic profiling by "omis" technologies, as next-generation sequencing (NGS), have improved the understanding of the biologically heterogeneity of leukemias and have facilitated the risk stratification of patients. These achievements have also provided relevant insights into improved disease classification, clinical care, and novel therapeutic approaches, allowing potentially targetable lesions for the development of new therapeutic approaches in the era of precision medicine. This presentation aims to show the increasing use if NGS technologies in research and clinical routine for more comprehensive knowledge that serve as valuable tools to advance individualized treatment approaches for diseases as leukemia.

Key words: somatic mutations, next-generation sequencing- leukemia

CÁNCER Y TRABAJO: UNA RELACIÓN PERFECTA

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Sociedad Paraguaya de Medicina del Trabajo

Una persona de 60 años aproximadamente ha dormido 20 años y se mantuvo despierto 40 años, de los cuales 35 años aproximadamente estuvo trabajando o estudiando, son estas las bases por las cuales podemos considerar al trabajo como un factor de exposición importante. Las estadísticas nos hablan de que el cáncer es la segunda causa de muerte de los seres humanos a nivel mundial; y por ello él es una patología para seguir combatiendo desde varias aristas. El tiempo de exposición, las diferentes sustancias a las que estamos expuestos, el mal o incorrecto uso de elementos de protección personal son elementos a tener en cuenta a la hora de buscar mecanismos disparadores de cambios a niveles celulares. Desde la medicina laboral tenemos la obligación de buscar los mecanismos de reducción a la exposición a sustancias peligrosas, a la detección precoz de procesos que induzcan a la aparición de cánceres profesionales, principalmente en las poblaciones de riesgos considerando no solo el ambiente de trabajo si no en busca de sus bases genéticas y familiares que lo pueden predisponer a ello.

Palabras claves: medicina del trabajo, cáncer y trabajo -

SIMPOSIO PRODUCTOS NATURALES EN LATINOAMERICA: RIESGO Y/O BENEFICIO DE SU USO

COORDINACIÓN: Marta Carballo, PhD

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HYPERLIPIDEMIA AND THE MODULATION OF THE GENOTOXICITY USING *Campomanesia xanthocarpa* MEDICINAL PLANT

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Hypercholesterolemia is associated with overweight and obesity which have been increasing in many countries including Brazil. This condition increases the cardiovascular risks to atherosclerosis and stroke as well as the genomic instability making the discovery of new approach therapies needed. In this sense, *Campomanesia xanthocarpa* (Mart.) O. Berg (Myrtaceae) popularly known as Guabiroba is a plant spread in Latin America, more specifically in Brazil, Argentina, Paraguay, and Uruguay, empirically used to decreasing cholesterol. The aim of this study was to evaluate hypolipidemic effects and to assess protective actions against oxidative stress and DNA damages of a *C. xanthocarpa* aqueous leaf extract (CxAE). The tyloxapol- induced hyperlipidemia model was used to evaluate the hypolipidemic properties of CxAE and its genotoxic/antigenotoxic effects. Wistar rats were treated with CxAE 250 and 500 mg/kg by gavage for 7 consecutive days before tyloxapol administration. Biochemical analyses and oxidative stress levels measuring thiobarbituric acid reactive substances (TBARS), superoxide dismutase (SOD), and catalase (CAT) enzyme activities, and glutathione S-transferase (GST) activity were performed. DNA damages were assessed using alkaline comet assay in several tissues and micronucleus test in bone marrow. The data were analyzed using the one-way analysis of variance (ANOVA) followed by Tukey's test or Newman-Keuls Multiple Comparison test with statistical significance at $p<0.05$. CxAE decreased cholesterol and triglyceride levels in serum and DNA damage in liver and kidney tissues of tyloxapol-treated rats. There was no effect on the micronucleus frequency in bone marrow. The extract increased CAT activity and decreased GST activity in kidney tissue. In conclusion, CxAE showed hypolipidemic effects, reinforcing its value in folk medicine by lowering cholesterol, it improved oxidative stress parameters, and protected DNA against damage induced by tyloxapol-induced hyperlipidemia, providing chemopreventive properties associated with its hypolipidemic effect.

Key words: hyperlipidemia, *Campomanesia xanthocarpa*, modulation of genotoxicity

Financial Support: ULBRA, CNPq, CAPES, and FAPERGS

RUTAS DE MUERTE CELULAR INDUCIDAS POR ESPECIES ECUATORIANAS*

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La especies vegetales constituyen una alternativa importante para el aislamiento de nuevas terapias contra el cáncer, incluido el cáncer de colon, uno de los más frecuentes en la zona Sur del Ecuador. Además de conocer si un extracto o molécula presenta un efecto citotóxico es necesario conocer sobre los mecanismos involucrados en dicho proceso. Es así por ejemplo, que a partir de *Hedyosmun racemosum* se obtuvo una lactona sesquiterpénica denominada Onoseriolide, que tiene efecto citotóxico sobre RKO, línea tumoral humana de cáncer de colon. Al exponer a las células a dosis cercanas a la IC_{50} observamos un incremento en expresión de p53, seguido de un incremento en la expresión de p21, los mismos que están involucrados en la detención del ciclo celular en la fase G2/M. Además de la activación de caspasa-3 y la escisión de PARP-1, que son marcadores apoptóticos. También se estudiaron marcadores de autofagia (Beclin 1, LC-3II y SQSTM1 / p62). Donde podemos concluir que el Onoseriolide ejerce efectos citotóxicos y citostáticos, activando la vía de autofagia como mecanismo de protección y la apoptosis como vía de muerte celular. Por otro lado, en el caso de *Grias neuberthii,* el extracto de tallos *fue* citotóxico sobre celulares de carcinoma de colon, RKO (p53 normal) y SW613-B3 (p53 mutado). El efecto citotóxico fue similar en ambas líneas celulares. Se observaron diferencias significativas después del análisis de la formación de colonias, siendo las células RKO más sensibles que SW613-B3. No se observó activación de marcadores apoptóticos, pero si de muerte celular por autofagia, incluyendo el aumento de Beclin-1 y LC3-II, y la disminución de p62. Finalmente, se identificaron tres compuestos químicos, posibles responsables del efecto observado: Lupeol, ácido 3'-O-Metil elágico 4-O-β-D-ramnopiranosido y 19-α - Monoglucósido del ácido hidroxi-asiático.

Palabras clave: muerte celular, citotoxicidad, *Hedyosmun racemosum, Grias neuberthii*

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NATURAL PRODUCTS AS POSSIBLE ANTICANCER AGENTS

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The complexity of cancer is reflected in the fact that currently there is no drug or treatment to eliminate this condition. Since 1942 when chlormethine (mustine), the first synthetic compound with therapeutic properties against leukemia, was used, the synthesis and use of cytotoxic drugs were privileged. Unfortunately, the vast majority of these drugs lack selectivity, which leads to substantial side effects. Against this background, several approaches have been tried, including the use of secondary metabolites of plant origin. In the clinic, there are several drugs of plant origin such as taxol, vinca alkaloids, and podophyllotoxin. However, these drugs also lack selectivity. Recently, our group has studied the antitumor activities of several natural compounds belonging to the triterpene group. Most of the triterpenes studied have two things in common: they have an excellent anti-inflammatory effect and a moderate cytotoxic activity to human cancer lines. These properties induced us to suppose that possibly these triterpenes could have a tumor effect in an in vivo model using nu/nu mice xenotransplanted with human cancer cells. Our results indicated that administration three times a week of low doses inhibited tumor growth by almost 80% concerning the control. A significant point in favor of the use of these natural compounds is that they do not present problems of toxicity.

Key words: anticancer agents, natural products, triterpene group.

FRUITS OF POPULAR CONSUMPTION, ITS CYTOTOXIC AND GENOTOXIC ACTIVITY

Gloria Rodrigo Lira

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Passiflora tripartita var. *mollisima* (tumbo), *Garcinia humilis* (achachairu) and *Garcinia madruno* (ocoro) are fruits widely consumed by the Bolivian population due to the high content of vitamin C. Our study analyzed the antiproliferative activity of the fruits and the parts of these plants in four cancer cell lines (Hela, A549, CaCo-2 and JIMT-1) by MTT cytotoxicity assay, in addition their genotoxicity were analyzed. The ethereal extracts of the bark and stem of the achachairu showed cytotoxic activity against the 4 cell lines with IC_{50} between 8 to 48 µg/ml. The ethereal extracts of leaves and stems of ocoro were cytotoxic for CaCo-2 cells, JIMT-1 and A549; while the ethereal extracts of the bark were cytotoxic for Hela, CaCo-2 and JIMT-1 cells with IC_{50} between 26 to 8 µg/ml. The aqueous extracts of the fruits of achachairu and ocoro did not show cytotoxicity for any of the cell lines. Additionally, molecules of the achachairu and ocoro extracts were isolated. The xanthone called 1 isolated from the achachairu was cytotoxic for Hela and JIMT-1 cell lines with IC_{50} of 31 µM and 10 µM respectively. Isoxantochimol isolated from ocoro was active against cancer cells CaCo-2, A549 (23.4 µM) and Hela. The aqueous and ethanol extracts of the tumbo inhibited the development of A549 cells, while the ethanol extracts of the fruit's shell and aqueous fruit are cytotoxic for HeLa cells at concentrations below 100 µg / ml. In the genotoxic evaluation, ocoro extracts did not form micronuclei in *Allium cepa* cells, but caused DNA breaks in human lymphocytes. The fruits of achachairu, ocoro and tumbo are not genotoxic and the ocoro fruit protects from breakage in the DNA and decreases the micronuclei frequency.

Key words: cytotoxic and genotoxic activity, *Passiflora tripartita* var. *mollisima* (tumbo), *Garcinia humilis* (achachairu), *Garcinia madruno* (ocoro)

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SIMPOSIO EPIGENÉTICA Y CÁNCER

COORDINACIÓN: Wilner Martínez, PhD

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INFLUENCE OF HISTONE ACETYLATION CHANGES IN THE REMOVAL OF UVC-INDUCED DAMAGE

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In mammalian cells, nucleotide excision repair system is constituted of two sub-pathways, global genomic repair (GGR) and transcription coupled repair (TCR). Deficiency of TCR pathway leads to Cockyane syndrome (CS) which is a rare human autosomal recessive disorder. Owing to the pivotal role of CSB gene in TCR, it's mutation causes severe repair and transcriptional defects in CSB patients. CSB protein belongs to the ATP chromatin remodeling complex, hence presumably an improper chromatin remodeling in CSB cells could be at the source of inefficient removal of pyrimidine dimers (CPDs) after UVC exposure in these patients. In this study, we evaluated the role of chromatin remodeling process on UVC induced CPDs and the ensuing effect on chromosomal aberrations in UV61 cells (TCR deficient) and its parental cell line, AA8 (TCR proficient). We observed that post 2h UVC irradiation, both cell lines underwent pronounced chromatin relaxation but was lower in CSB deficient UV61 cells. Since the deficiency in chromatin remodeling in CSB-mutated cells was accompanied by a decrease in the histone acetylation level, the histone deacetylase inhibitor trichostatin A (TSA) was employed to improve the removal of UVC-induced lesions by increasing the histone acetylation level. Contrary to expectations, TSA increased the induction of chromosomal aberrations and apoptotic cells along with amounts of CPDs after UVC-irradiation, indicating that changes in histone acetylation levels might contribute to the failure in the removal of UVC-induced lesions. Also, it has been shown earlier that the expression of genes regulated by CSB is affected by the increase in the acetylation level produced by TSA. Taken all together, we hypothesize that failure in the removal of UVC induced lesions in CSB-deficient cells can be caused by an imbalance in histone acetylation levels leading to chromatin conformation changes and hence interaction defects among repair proteins and DNA lesions.

Key words: histone acetylation, UVC, damage

EPIGENÉTICA DEL CÁNCER: DE LOS TUMORES A LA BIOPSIA LÍQUIDA

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En los últimos años se han producido grandes avances en la caracterización del epigenoma por medio del estudio a nivel global de los mecanismos epigenéticos. Estas modificaciones epigenéticas tienen un papel fundamental en la regulación de la expresión génica de las células. Sin embargo, hay determinadas situaciones que alteran estos mecanismos dando lugar al desarrollo de enfermedades como el cáncer. La metilación del DNA es el mecanismo epigenético mejor estudiado, mostrando una gran utilidad clínica como biomarcador del cáncer. Hasta el momento, este mecanismo ha sido mayoritariamente estudiado en muestras de tumores mediante el análisis del epigenoma o de genes individuales. Sin embargo, cada vez más estudios muestran la utilidad clínica de las diferentes marcas epigenéticas como biomarcadores en biopsia líquida, la cual permite estudiar de manera no invasiva el material tumoral circulante (DNA, células tumorales circulantes o CTCs, exosomas) liberado por los tumores a los diferentes fluidos biológicos. El estudio de los biomarcadores epigenéticos en biopsia líquida supone importantes ventajas sobre la biopsia tradicional, ya que puede aportar información relevante sobre la heterogeneidad tumoral y permite estudiar la evolución dinámica de los tumores a lo largo de la enfermedad de los pacientes. La metilación del DNA en biopsia líquida se ha estudiado principalmente mediante el análisis de genes individuales o paneles de genes. Sin embargo, recientemente se han empezado a usar herramientas epigenómicas que podrían permitir analizar los mecanismos epigenéticos directamente en las muestras de biopsia líquida. Esta nueva aproximación supone un gran avance para la epigenómica del cáncer favoreciendo así el descubrimiento de nuevos biomarcadores epigenéticos con utilidad clínica en oncología.

Palabras claves: Cáncer; Epigenómica; Metilación; Biomarcadores; Biopsia Líquida

GENOMIC AND EPIGENOMIC EPIDEMIOLOGIC

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The main focus of my research has been understanding the roles that genetic and epigenetic variation play on shaping complex diseases in human populations. My work is in genetic epidemiology and population genetics focused on the identification of genetic risk factors for breast cancer, melanoma, infertility and preterm birth in admixed populations like the Uruguayan. In fact, my research is centred in the effect/interaction of the hybrid structure of the populations on the genetic, epigenetic and environmental factors over a disease. Projects I have been involved with in this area assessed the influence of the admixed population in the hybrid genome structure of candidate genes and also how this hybrid structure influence the DNA methylation. Recently I began to analyze the complete sequence of candidate genes for breast cancer and melanoma, not only to find new variants, but also to understand how allele variants and the population admixture control the DNA methylation of these genes.

Key words: genomic- epigenomic- epidemiologic

EPIGENETIC ALTERATIONS IN HUMAN PAPILLOMAVIRUS ASSOCIATED CANCERS

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Approximately 15–20% of the 12.7 million incident cancer cases per year have a viral etiology. Epigenetic abnormalities in cancer involve aberrations in virtually every aspect of chromatin biology, including post-translational modifications of histone proteins, DNA methylation, chromatin remodeling, and non-coding RNAs (ncRNAs). Human papillomavirus (HPV) are small, double-stranded DNA virus members of the *Papillomaviridae* family. The mucosal HPVs are clinically classified as "high-risk" and "low-risk" based on the propensity for malignant progression. Infection with high-risk HPVs are associated with approximately 5% of all human cancers, in particular with cervical cancer, the fourth most common cancer in women worldwide. HPV infections are also associated with other anogenital cancers, including anal, vulvar, vaginal, and penile cancers, as well as head and neck cancers. In HPV-associated cancers initiation and progression are driven by the expression of the E6 and E7 oncogenes. High-risk mucosal HPV E6 and E7 oncoproteins, target p53 and retinoblastoma (pRB), respectively; these tumor suppressor pathways are also rendered dysfunctional by mutation in almost all human solid tumors. High-risk HPV E6 and E7 also interact with a number of other proteins, such as transcription factors, thus altering cellular gene expression. In addition to targeting specific transcriptional programs, the HPV E6 and E7 oncoproteins can globally alter the transcriptional competence of the infected cells by affecting epigenetic control mechanisms. Studies show that potential biomarkers like detection of oncoproteins E6/E7 could be used for early detection of cervical cancer. The objective is to present a review of HPV-induced changes in these epigenetic control mechanisms, including DNA methylation, histone modifications, chromatin remodeling proteins, ncRNAs and the results of Paraguayan studies about detection of HPV types and potential biomarkers for early detection of cervical cancer.

Key words: papillomavirus, cancer, epigenetic

SIMPOSIO CONTAMINANTES EMERGENTES, METALES PESADOS Y SALUD

COORDINACIÓN: Cassiana Montagner, PhD

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PESTICIDES AND EMERGING POLLUTANTS IN WATER AND BIOFILM: STRATEGIES FOR THE DETERMINATION AND EVALUATION OF TOXICOLOGICAL EFFECTS ON FISHES

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The determination of pesticides and emerging pollutants in the environment is very important to avoid health problems. In this sense, different techniques were evaluated for sample preparation. The rotating disk sorptive extraction (RDSE)[1] using a small amount polymeric sorbent was used for determination of 62 pesticides in water by ultra-high-performance liquid chromatography tandem mass spectrometry (UHPLC-MS/MS) with limit of detection (LOD) from 0.015-0.03 μg L^{-1}. In river water, atrazine, azoxystrobin, clomazone, difenoconazole, epoxiconazole, propoxur, simazine and tebuconazole were found from 0.06-0.35 μg L^{-1}. Using the bar adsorptive microextraction (BAμE)[2], an efficient method was validated for 13 emerging pollutants, representative of pharmaceuticals, hormones, plasticizers and flame retardants, in water by UHPLC-MS/MS at LODs from 0.012-0.6 μg L^{-1}. Real samples presented bisphenol A (0.08-0.66 μg L^{-1}) and paracetamol (0.14-4.2 μg L^{-1}). A solid phase extraction (SPE) method[3] was established for determination of 20 pharmaceuticals of different classes in water using UHPLC-MS/MS with LODs from 0.003-0.03 μg L^{-1}. Atenolol, carbamazepine and paracetamol were found in some samples. A multiclass method was established for the determination of 82 pesticides in biofilms using solvent extraction and UHPLC-MS/MS analysis. From the application of these methods, several compounds were found in real samples. These compounds were selected for toxicological studies at environmentally relevant concentrations, isolated and mixed, using fish species from the monitored areas.

Key words: pesticides, emerging pollutans, toxicology

ARSENIC METABOLISM AND DNA DAMAGE: ELIMINATION, GENOTOXICITY AND GENETIC SUSCEPTIBILITY IN BOLIVIAN INDIGENOUS WOMEN EXPOSED TO HIGH ARSENIC CONCENTRATIONS IN DRINKING WATER

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Exposure to arsenic (As) is a major problem in many parts of the world. In fact, it is estimated that more than 100 million people are exposed to arsenic, mainly through contamination of groundwater. Chronic arsenic exposure is associated with adverse effects on human health, such as cancer, cardiovascular diseases, neurological diseases and the rate of morbidity and mortality in the health of the exposed population is alarming. The capacity to metabolize arsenic differs between individuals and populations, and these variations matters for arsenic toxicity. There is evidence that hereditary factors modify the competence of arsenic elimination metabolism by modulating the ability of people to biotransform toxic inorganic arsenic (AsIII y AsV) in a less aggressive dimethylated form (DMA) in the cells of the human body. Arsenic has a strong genotoxic potential and is capable of causing DNA damage, such as aneuploidy; micronucleus formation, chromosomal aberrations, deletion mutations, sister chromatid exchanges and DNA-protein crosslinks. We recruited 200 women from 10 villages around Lake Poopó and 72 controls. Arsenic exposure was determined as the sum concentration of arsenic metabolites (inorganic arsenic; monomethylarsonic acid; MMA); and dimethylarsinic acid, DMA) in urine (U-As), measured by HPLC-HG-ICP-MS. Efficiency of arsenic metabolism was assessed by the relative fractions of the urinary metabolites. The women had a wide variation in U-As (range 12–407 µg/L, median 65 µg/L) and a markedly efficient metabolism of arsenic with low %MMA (median 7.7%, range: 2.2–18%) and high %DMA (80%, range: 54–91%) in urine. In relation to genotoxic damage results showed that there is DNA damage in a population by the Comet assay, significant difference between exposed and non-exposed groups were found (p=0.000); It was shown that women with genetic polymorphisms on GSTs (GSTM1 null) presented more genotoxic damage detected by the comet assay.

Key words: arsenic, DNA damage, drinking water, indigenous women

SIMPOSIO NUEVOS PARADIGMAS PARA LA EDUCACIÓN SUPERIOR DEL SIGLO XXI: LA COMPLEJA Y ENRIQUECEDORA ARTICULACIÓN ENTRE DOCENCIA, INVESTIGACIÓN Y COMPROMISO SOCIAL

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LA UNIVERSIDAD DE BUENOS AIRES Y EL ESCENARIO SOCIAL: EL DESAFÍO DE LAS PRÁCTICAS PROFESIONALES SITUADAS EN EL ÁREA DE LA SALUD

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La relación entre las instituciones educativas y sus comunidades, la vinculación entre educación y transformación de la realidad social, han sido y son temas recurrentes en la discusión pedagógica latinoamericana. La tradición extensionista de nuestras universidades constituye un rico patrimonio de experiencias que no siempre han sido valoradas en toda su dimensión educativa. Las prácticas que vinculan aprendizaje y servicio solidario permiten a los estudiantes aplicar lo aprendido en las aulas al servicio de la comunidad, y simultáneamente les permite adquirir nuevos conocimientos y poner en juego competencias en contextos reales, desarrollando prácticas valiosas tanto para la formación de una ciudadanía activa y participativa como para la inserción en el mundo del trabajo. El propósito de esta charla es resaltar el impacto de la aplicación del Aprendizaje-Servicio como disparador de nuevos conocimientos en el marco de la participación comunitaria, en proyectos desarrollados en instituciones de educación superior, tal como la Universidad de Buenos Aires. Brevemente, recorreremos las raíces internacionales y regionales de esta propuesta pedagógica y se presentarán algunas cuestiones conceptuales que hacen a su definición. Finalmente, se presentan los resultados de un caso que aplica este modelo de integración como una forma de aprendizaje situado, en un escenario real y al servicio de la comunidad.

Palabras claves: Instituciones educativas, Aprendizaje y servicio solidario, Propuesta pedagógica

EL SERVICIO SOCIAL EN LA UNIVERSIDAD NACIONAL AUTÓNOMA DE MÉXICO (UNAM)

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Fue en la Escuela Nacional de Medicina, donde en 1935 se iniciará el proyecto del Servicio Social gracias a la visión y al compromiso social del doctor Gustavo Baz Prada con el que se inició este pacto social con aquellos que necesitan del conocimiento que los alumnos y profesores de UNAM podrían brindar, por ello existe un reconocimiento que lleva su nombre. Este año el servicio social cumple 84 años, y fue la Universidad la que lo inició y con el tiempo se convirtió en una obligación reglamentaria de la educación superior para toda la nación. En noviembre de 2017 había registrados 5450 programas de servicio social de entidades de la UNAM a lo largo del país, dedicados a retribuirle a la sociedad lo que les ha dado. Nuestro Instituto cuenta en su estructura con 7 Unidades Periféricas y dos Unidades Foráneas en las Universidades de los Estados de Tlaxcala y de Veracrúz. En la Unidad de la Universidad de Tlaxcala existe la Estación la Malinche, que es un centro de investigación que integra el trabajo científico con el bienestar de la sociedad. La Unidad de Atención Integral a la Mujer cuenta con dos Programas: Niñas con Ciencia y Salud Integral que tienen como objetivo el promover la salud física y mental de las mujeres para construir una mejor calidad de vida. Se presentaron los proyectos que se han implementado en ambos programas y los resultados que se han tenido hasta el momento.

Palabras claves: Servicio Social, atención integral, salud física y mental

LAS ACTIVIDADES DE EXTENSIÓN COMO CAMINO PARA MEJORAR LA CALIDAD DE VIDA DE LAS COMUNIDADES

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Los Ava Guaraní constituyen una etnia Guaraní. Poseen una rica cultura en la que son esenciales la economía de reciprocidad y el liderazgo político como servicio. Se han visto obligados a abandonar sus tierras ancestrales por la expansión del agronegocio y engrosan los cinturones de pobreza en zonas urbanas. En el 2017 tomamos contacto con un grupo Ava Guaraní que vivía desde hacía 17 años en el vertedero Cateura, en condiciones de vida muy precarias. Luego de varios meses de atender sus necesidades más urgentes, expresaron la necesidad de tener tierra propia en la cual cultivar, estudiar, contar con viviendas apropiadas y criar animales domésticos para sacar a los niños del ambiente insalubre. Gracias al trabajo de varias organizaciones se compró 5 hectáreas en la ciudad de Itá. La Facultad de Ciencias de la Salud se sumó con el Proyecto de *Prevención, Promoción de la Salud y Atención Médica, en forma sostenida, para mejorar la calidad de vida de la comunidad Avá-Guaraní, que tiene como eje transversal la dignidad de las personas.* **1° etapa 2017**: Comprender la cultura y crear lazos de fraternidad. Se realizó un taller con la Coordinación Nacional de la Pastoral del Indígena, y se ofreció atención en la comunidad. Se construye el dispensario de Salud, con ladrillos hechos por los indígenas y gracias al aporte financiero de una Cooperativa. **2º Etapa 2018**: se instaló la escuela primaria en el mismo predio del dispensario con profesores Avá Guaraníes. Se realizaron 5 jornadas de atención con las carreras de medicina, enfermería y nutrición. La comunidad recibió el Premio de la Asociación Indigenista del Paraguay: por su unidad, laboriosidad, autogestión eficaz liderazgo vivido como servicio. Por trabajos de autogestión cuentan con agua potable, luz eléctrica, huerta comunitaria, fábrica de ladrillos y un grupo de empresarios construyó casas para las 29 familias. **3° Etapa 2019**: Educación para lograr un cambio "verdadero" con el MEC se realizó la construcción de la escuela. Felices de estar, finalmente, en el "Yvy Maraney", es decir, "la Tierra sin mal "que en su cultura significa, la tierra en la cual vivir el amor recíproco y preservar sus buenas costumbres". Este Proyecto pretende ser un "modelo" a seguir en el futuro en otras comunidades indígenas de todo el país, donde diferentes instituciones: Universidades, Cooperativas, Organizaciones Civiles, Estado y los mismos habitantes de la comunidad se unen en un proyecto común para mejorar la calidad de vida de estos compatriotas, logrando soluciones de "fondo".

Palabras claves: cultura, extensión, calidad de vida.

SIMPOSIO ÉTICA DE LA INVESTIGACIÓN

INFORMED CONSENT IN THE INVESTIGATIVE APPROACH WITH HUMAN BEINGS

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Compliance with the informed consent is the highest expression of respect for the dignity, autonomy and responsibility of the participants. In an investigation this must be requested before the start of any intervention with human beings and remains active until the end of the investigation it and even in some cases after its completion. It is also one of the main elements to be examined by the Committee of Ethics in Research (CRE), when analyzing a protocol. Its authorization depends on having all the necessary information regarding to the research and participation of the research subject, It should be easy to understand, appropriate to the culture and the language of the future participants, so that they can make an informed decision The way to obtain it is another component to be evaluated, especially when it involves populations considered vulnerable, in which case they require special protection. In those countries where there are CREs that follow-up and monitor the approved protocols, failure to comply with the stages to obtaining it may constitute grounds for suspension of an investigation. The CREs and the investigators are jointly responsible to the participants that the approved research is carried out in an ethical manner and that the human rights of the participants are being respected.

Key words: Committee of Ethics in Research, investigation, human rights

SIMPOSIO SALUD Y AMBIENTE: FACTORES AMBIENTALES Y GENOTOXICIDAD

COORDINACIÓN: María Eugenia Gonsebatt

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GENOTOXICIDAD Y CITOTOXICIDAD EN UN GRUPO DE NIÑOS DE UNA POBLACIÓN RURAL DE PARAGUAY

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Los niños por las características de su crecimiento y desarrollo constituyen una población con especial vulnerabilidad a los tóxicos ambientales y proteger su salud es una prioridad social, científica y emocional. El actual modelo agrícola productivo predominante que ocupa más de 5 millones hectáreas en Paraguay, se caracteriza por el uso intensivo de plaguicidas, expulsión de campesinos, efectos en el calentamiento global, la pérdida de la diversidad biológica y efectos dañinos potenciales en la salud humana. El monitoreo genotoxicológico en humanos es una herramienta útil para estimar riesgo genético de una exposición a una sustancia o a mezclas de productos químicos y se constituye en una medida de advertencia temprana para enfermedades genéticas y/o cáncer. La exposición crónica a plaguicidas debido a fumigación intensiva por cultivo de soja transgénica puede dañar el ADN y derivar en riesgo de cáncer, diabetes, enfermedades respiratorias, efectos reproductivos adversos, trastornos neurodegenerativos y neurodesarrollo. Se realizó un estudio para determinar la frecuencia de daño en el ADN a través del Ensayo Cometa y Test de micronúcleo en niños de zona rural que viven rodeados de soja transgénica y se comparó con niños cuyos padres realizan control biológico de plagas. El 100% de estas familias se dedican a la agricultura familiar diversificada de sustento y/o renta. Se concluye que en los niños expuestos a plaguicidas se observó mayor efecto genotóxico y citotóxico comparado con los niños no expuestos. Estas diferencias son estadísticamente significativas y no pueden ser explicadas por la influencia de otros factores.

Palabras Claves: Vulnerabilidad, Ensayo Cometa, Test de micronúcleo

TRANSPLACENTAL EXPOSURE TO AIR POLLUTION IN MEXICO CITY´S METROPOLITAN AREA

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Mexico City's Metropolitan Area (MCMA) inhabitants are exposed to emissions from over five million vehicles and stationary sources of air pollutants such as particulate matter (PM) and ozone. PM contains elemental carbon and organic carbon (OC) which includes polycyclic aromatic hydrocarbons (PAHs) many of which induce mutagenic and carcinogenic DNA adducts. We investigated the presence of bulky PAH-DNA adducts, plasma 8-iso-PGF2α (8-iso-prostaglandin F2α) and risk allele variants in neonates cord blood and their nonsmoking mothers' leucocytes from families that were living in a highly polluted area during 2014–2015. The presence of adducts was significantly associated with PM levels, mainly during the last trimester of gestation in both neonates and mothers, while the last month of pregnancy was significant for the association between ozone levels and maternal plasma 8-iso-PGF2α. Fetal CYP1B1*3 risk allele was associated with increased adduct levels in neonates while the presence of the maternal allele significantly reduced the levels of fetal adducts. Maternal NQO1*2 was associated with lower maternal levels of adducts. Our results suggest the need to reduce actual PM limits in MCMA.

Key words: Mutagenic, carcinogenic, polycyclic aromatic hydrocarbons

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OCCUPATIONAL EXPOSURE TO PESTICIDES IN BOLIVIAN FARMERS: ASSOCIATIONS BETWEEN BIOMARKERS OF EXPOSURE, EFFECT AND SUSCEPTIBILITY

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Although the use of pesticides reinforces the productivity of the harvest, humans also pay a price for the benefits, translated into effects on health. The toxicological evidence of the mutagenic and carcinogenic action of several pesticides and the occupational or accidental exposure of large human populations to these compounds has focused the attention of many cytogenetic studies. In Bolivia a high percentage of the population is engaged in agriculture and uses different pesticides for the production of their crops, where the management of these products is empirical, without personal protective equipment. The aim of this study was to assess the correlation between exposure, genotoxic effects and genetic susceptibility of pesticides in Bolivian farmers exposed. A Cross sectional study was performed in three agricultural communities among 297 exposed pesticide farmers. Pesticide exposure was determined by questionnaire, urine samples were analyzed for urinary pesticide metabolites (UPMs) and blood samples for comet assay and GSTT1, GSTM1 polymorphisms. Results of these study showed that UPM measurements indicate high levels of exposure to clorpyrifos, pyretroids and 2,4 D. Comparing the three communities studied we saw that individuals from one community had higher levels of DNA strand breaks and MN frequencies in blood lymphocytes respect to the others (p=0.001–0.002). The influence of the genetic GSTs polymorphisms showed that GST positive genotype for either GSTM1 or GSTT1 displayed higher levels of both strand breaks and MN frequencies.

Key words: Pesticides, susceptibility, cytogenetic

Financial support: SIDA (Swedish International Development Cooperation Agency) and Genetic Institute-UMSA.

HEALTH EFFECTS AND EXPOSURE SCENARIO TO THE MAIN INORGANIC CONTAMINANTS IN DRINKING WATER: ARSENIC AND FLUORIDE

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The co-occurrence of arsenic and fluoride in groundwater due to geogenic sources is relatively common in several regions in Latin America and globally. Thus, the concurrent human exposures to arsenic or and fluoride affects to millions of people. The WHO has established a maximum recommended limit of 10 µg/L for arsenic and 0.5 to 1 mg/L for fluoride in drinking water. In contrast, the current Mexican regulations establish 25 µg/L for arsenic and 1.5 mg/L for fluoride. Arsenic accumulates mainly in the skin, causing cutaneous alteration; changes in pigmentation and hyperkeratosis are the best described and characterized toxic signs of chronic exposure to arsenic, mostly in the adult population. Other adverse effects are genetic damage, impaired learning and memory abilities, neuropathies, cardiovascular alterations, endocrine dysfunctions, and immunosuppression. Worldwide, excessive fluoride ingestion has been associated with dental and skeletal fluorosis and nonskeletal adverse effects, such as neurocognitive alterations, thyroid dysfunction, kidney injury, and cardiovascular alterations. Use of biomonitoring data in population studies is an indispensable tool to identify or characterize external exposure sources or validate external exposure estimates, and for studying differential toxicokinetic properties of arsenic and fluoride. The assessment of the exposure of arsenic and fluoride in drinking water accompanied by biomonitoring studies gives us a better response and a greater evaluation of health risk from exposure to these pollutants.

Key words: Inorganic contaminants, biomonitoring, Arsenic, Fluoride

SIMPOSIO DAÑO GENÉTICO ASOCIADO A ESTRÉS OXIDATIVO

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THE ROLE OF MELATONIN IN DNA DAMAGE AND OXIDATIVE STRESS CAUSED BY AGING

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Aging, a multifactorial phenomenon, correlates with decreased physiological and cellular functions and ability for stress response and increased incidence of various degenerative diseases, characteristic of aging. Studies on melatonin (N-acetyl-5-methoxytryptamine), a potent natural antioxidant secreted by the mammalian pineal gland, including humans, is gaining attention. Melatonin, the main pineal hormone, is synthesized from tryptophan predominantly at night. With aging, nocturnal melatonin production decreases in various animal species, including humans, thus questioning the role of melatonin in aging. We evaluated the effects of melatonin chronic consumption on genotoxic and mutagenic parameters of old Swiss mice. Here, 240 albino 3-month-old Swiss male mice were divided in eight groups, viz., animals consuming melatonin from 3, 6, 12, and 18 months to 21 months, groups G1, G3, G4, and G6, respectively; animals starting melatonin consumption at 3 or 12 months until natural death, groups G2 and G5, respectively; and animals receiving only water with 0.04% ethanol until 21 months or natural death, G7 and G8, respectively. After 21 months, animals were euthanized for blood collection and organ dissection. Our results demonstrated that melatonin prolonged the animal life span. Relative to genomic instability, melatonin, at tested dose, independently of initiation age, was effective in reducing DNA damage caused by aging, presenting antigenotoxic and antimutagenic activities. The group receiving melatonin for 18 months had high APE1 and OGG1, and DNA repair system enzyme levels. Conclusively, our results showed that melatonin presents an efficient antioxidant mechanism aiding in modulating genetic and physiological alterations due to aging.

Key words: Melatonin, oxidative stress, antioxidant

OXIDATIVE STRESS, DNA DAMAGE AND CANCER

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Oxidative stress is defined as an imbalance between production of free radicals and reactive metabolites, so-called oxidants or reactive oxygen species (ROS), and their elimination by protective mechanisms, such as antioxidants. This imbalance leads to significative DNA damage then may induce somatic mutations and, finally, neoplastic transformation. ROS are involved in a wide spectrum of diseases, including aging, chronic inflammation, degenerative disease and carcinogenesis. DNA repair is the protective mechanism of response to the oxidative stress and in particular Base excision repair (BER) is the main pathway to repair oxidized DNA lesions in all cells, highly conserved from *E. coli* to humans. Moreover, adequate enzymatic activity by superoxide dismutase, catalase and glutathione peroxidase is required to reduce the ROS in the cell plays a role in order to avoid DNA lesions and genome instability. The understanding of molecular mechanisms leading the regulation of oxidative stress in the cell could open new therapeutic opportunities in cancer.

Key words: Cancer, reactive oxygen species, antioxidants

DNA OXIDATIVE DAMAGE DETECTION IN PRE-CLINICAL MODELS

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The alkaloid lobeline derived from *Lobelia inflata* has shown high affinity for nicotinic acetylcholine receptors and has been studied due to its potential use in treatment of alcoholism and drug abuse. This study aimed to evaluate the mutagenic and genotoxic effects of lobeline, to assess its modulation of ethanol-induced toxicological effects and to evaluate its possible anticonvulsant and neuroprotective activities. The mutagenicity was assessed using *Salmonella*/microsome assay and micronucleus test in bone marrow while the genotoxicity was assessed using comet assay in several tissues, including hippocampus and cerebral cortex of mice. In addition, biochemical and oxidative stress parameters were used to support the findings, since the formation of free radicals is involved in the ethanol toxicity and during the processes of seizures. Lobeline was not able to induce gene or chromosomal mutations and the absence of genetic toxicity was maintained even when it was associated with ethanol. DNA damage induced by hydrogen peroxide were decreased in blood, hippocampus, and cerebral cortex from mice treated with lobeline. There was an increase in the latency to the first seizure and decrease in the percentage of seizures in a pilocarpine-induced seizure model, suggesting anticonvulsant effects. These findings may be mediated by antioxidant-like mechanisms of lobeline.

Key words: mutagenic, genotoxic, *Salmonella*/microsome

Support: ULBRA, CNPq, CAPES, and FAPERGS

GENOTOXICITY AND OXIDATIVE STRESS INDUCED BY PESTICIDES*

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In everyday life, people living in rural areas are exposed to many environmental risks associated with agriculture productivity that include pesticides. The concern regarding the risks to human health by exposure to pesticides has increased significantly. The effects of long-term exposure to low doses of pesticides are often difficult to assess, since associated signs and symptoms may not manifest clinically. During the last decade our research group has demonstrated influence of pesticides on DNA damage, telomere length and global methylation profile in rural workers. Results from our studies with workers occupationally exposed to mixture of pesticides at tobacco, soybean and grape fields showed significantly DNA damage increase, evaluated using alkaline Comet assay and Micronucleus test (lymphocytes and buccal cells), as well as influence on shorter telomere and global DNA hypomethylation. Several inorganic elements such as Na, S, P, Cl and K, usually found in pesticides formulations, have significantly elevated plasma levels in farmers than controls. The content of inorganic elements was measured using the particle-induced X-ray emission (PIXE) technique. The results suggest that long term occupational pesticide exposure in rural workers is associated with increased genetic instability and epigenetic alterations, mainly by stress oxidative mechanisms.

Key words: Pesticides, hypomethylation, micronucleus test, comet test

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SIMPOSIO ESPECIES NATIVAS COMO INDICADORES DE EFECTOS GENOTÓXICOS

COORDINACIÓN: Fernanda Simoniello

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EVALUACIÓN DEL DAÑO OXIDATIVO Y EN EL ADN EN *Cnesterodon decemmaculatus* GENERADO POR LA ESCORRENTÍA DE PESTICIDAS PROVENIENTE DE UN LOTE EXPERIMENTAL DE MAÍZ, TRIGO Y SOJA

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La contaminación difusa producida por agroquímicos en ambientes urbanos, periurbanos y rurales constituye una preocupación para nuestra sociedad. El objetivo de este trabajo fue evaluar el daño oxidativo y genotóxico causado por las escorrentías de plaguicidas en el pez *Cnesterodon decemmaculatus* (Jenyns, 1842), un organismo de amplia distribución en América del Sur. Los bioensayos se realizaron utilizando limnocorrales situados en un sistema natural superficial de agua que recibe los residuos de lotes bajo producción agrícola con rotación de cultivos, incluyendo maíz, trigo y soja. Se evaluó la actividad de la enzima antioxidante Catalasa, la peroxidación lipídica y el índice de daño al ADN utilizando el Ensayo Cometa en células branquiales de ejemplares controles y expuestos. Los especímenes fueron retirados del limnocorral 72 hs después de un evento de lluvia con escorrentía sobre el tajamar. Durante este periodo se realizaron análisis de agua considerando residuos de plaguicidas, pH y temperatura. Los resultados mostraron diferencias estadísticamente significativas ($p< 0,05$) en el daño oxidativo y genotóxico sobre el epitelio branquial de los individuos expuestos a las escorrentías, en comparación con el control previamente determinado. Estos resultados muestran la utilidad de esta especie como centinela de contaminación por las mezclas de las escorrentías y la sensibilidad de los biomarcadores utilizados. Además, ponen de manifiesto la necesidad de comprender, prevenir y corregir los conflictos ambientales implementando medidas de mitigación y protección del ambiente asociado a las prácticas agrícolas para contribuir a la sostenibilidad y recuperación socio-agroambiental.

Palabras claves: Genotóxico, daño oxidativo,ensayo cometa

USO DE MACRÓFITAS ACUÁTICAS EN ESTUDIOS DE GENOTOXICIDAD, CASI UNA DEUDA PENDIENTE

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La genotoxicidad de contaminantes ambientales tradicionalmente ha sido estudiada en especies vegetales terrestres (ej. *Allium cepa*), y más aún en modelos animales (ej. ensayo de micronúcleos en peces). Sin embargo, cuando el objetivo es analizar potenciales efectos genotóxicos de contaminantes en ecosistemas acuáticos, resulta más pertinente seleccionar especies acuáticas como las macrófitas del género Myriophyllum. Particularmente para el estudio de plaguicidas de uso actual, nuestro grupo de investigación ha elegido a *Myriophyllum quitense* y a la margarita *Bidens laevis*, una flotante y la otra palustre respectivamente. Para seleccionarlas, hemos analizado el poder germinativo de las semillas y/o la propagación vegetativa que permita obtener plantas en laboratorio, así como sus características citológicas (ej. número y tamaño cromosómico, índice mitótico) para evaluar parámetros de genotoxicidad. A partir de experimentos de laboratorio con exposiciones a concentraciones de plaguicidas de relevancia ambiental hemos demostrado el incremento de la frecuencia de aberraciones cromosómicas en anafase- telofase (ACAT) en *B. laevis* expuesta al insecticida organoclorado endosulfán, al insecticida neonicotinoide imidacloprid, al fungicida estrobilurínico azoxistrobina y al triazólico tebuconazol. En *M. quitense* expuesta experimentalmente a azoxistrobina hemos detectado un incremento de la fragmentación del ADN mediante el ensayo "Cometa". Hemos comparado la sensibilidad de ambas especies respecto a las plantas modelo, resultando las acuáticas altamente sensibles, tanto a los plaguicidas como a sustancias de reconocida mutagenicidad. Concluimos que estas especies constituyen una alternativa adecuada para complementar los estudios de genotoxicidad ambiental.

Palabras claves: Macrófitas acuáticas, *Myriophyllum quitense, Bidens laevis,*

USE OF AQUATIC MACROPHYTES IN GENOTOXICITY STUDIES, ALMOST A PENDING ASIGNEMENT

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The genotoxicity of environmental contaminants have been traditionally studied in terrestrial plants (e.g. *Allium cepa*), and much more in animal models (e.g. micronuclei assay in fishes). However, when the objective is to analyze potential genotoxic effects ood contaminants in aquatic ecosystems, it is more proper to select aquatic species like the ones from the genera Myriophyllum. Particularly for the study of current use pesticides our research group has selected *Myriophyllum quitense* and the marigold *Bidens laevis*, a floating and a wetland species, respectively. For that selection, in order to assess biomarkers of genotoxicity, the capacity of germination and/ or the vegetative propagation that allows obtaining seedlings for bioassays, as well as cytological characteristics (e.g. the number and size of the chromosomes, the mitotic index) were evaluated. The results of laboratory studies using environmentally relevant concentrations of several compounds have shown the increase of the frequency of anaphase- telophase chromosomal aberrations (CAAT) in *B. laevis* exposed to the organochlorine insecticide endosulfan, the neonicotinoid imidacloprid, the strobilurinic fungicide azoxistrobina and the triazolic tebuconazol. In M. quitense experimentally exposed to azoxystrobin an increase of DNA fragmentation through the "Comet" assay was detected. Once we have compared the sensitivity of these species with respect to the model plants, high sensitivity to pesticides as well as to recognized- mutagenic compounds were found. In conclusion, these species constitutes a suitable alternative to complement studies of environmental genotoxicity.

Key words: Aquatic macrophyte, *Myriophyllum quitense, Bidens laevis,*

MODIFICATION IN GENE EXPRESSION PATTERN AS BIOMARKERS OF PESTICIDE EXPOSURE IN NATIVE REPTILE SPECIES

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Habitat loss and fragmentation produced by agricultural expansion, as well as pesticides exposure and its mixtures become a great concern for many reptile species in South America. During the last decade, through different studies we demonstrated the effect produced by pesticides on genotoxicity, oxidative stress, immunotoxicity, enzymatic and developmental alterations in embryos, yearlings and adults of native reptile species. The tremendous progress obtained in the last years in the field of molecular biology and bioinformatics enables the development of a new family of biomarkers, based in the analysis of the transcription of genes related to cellular stress that can be used to detect the exposure to xenobiotics, acting as early warning sensors. The aim of this new research line is to identify gene molecular markers and relate their expression levels to other conventional toxicological assays already validated and applied as routine markers by our research group, in order to improve our understanding of the molecular processes underlying pesticide toxicological effects. Up to the moment, these kinds of biomarkers have not been studied in any crocodilian species worldwide. We carried out studies on the expression level of antioxidant enzyme genes in caimans subchronically exposed to pesticide formulations and its mixtures, demonstrating its alteration even when enzymatic activity was not modified. We also conducted a transcriptomic study through RNAseq (Illumina) in juveniles exposed to pesticide formulations, identifying gene groups and functional pathways affected by these compounds in blood cells. These new data allow us to identify new genes sensible to xenobiotic exposure that can be applied in future studies and contribute to the protection of natural populations of wild species environmentally exposed.

Key words: Crocodilians; toxicogenomics; deregulated genes

SIMPOSIO NUTRICIÓN Y EPIGENÉTICA, GENOTOXICIDAD Y ANTIGENOTOXICIDAD

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BRAZIL NUT CONSUMPTION REDUCES DNA DAMAGE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS PROBABLY THROUGH CHANGES IN OXIDATIVE STATUS

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Type 2 diabetes mellitus (T2DM) is a metabolic disease, occurring largely due to lifestyle changes. There is a strong link between T2DM and oxidative stress, that leads to damage to lipids, proteins and DNA. Dietary interventions are essential for the treatment and prevention of T2DM-related complications. Knowing that Brazil nut (*Bertholletia excelsa, H.B.K.*) is the richest source of selenium in nature, and this mineral presents several health benefits, including improve of redox cellular status and maintenance of genomic stability, the aim of this study was to assess the effects of consumption of selenium through Brazil nut on biochemical and oxidative stress parameters, as well as genomic instability in T2DM patients. We evaluated 74 patients with T2DM, registered in the Integrated Clinics of University of Southern Santa Catarina. Participants consumed one Brazil nut a day (that provides 210 μg of selenium) for six months. Blood and exfoliated buccal cells samples were collected at the beginning and at the end of treatment. The glycemic profile (fasting glucose, insulin, glycated hemoglobin, HOMA-IR, HOMA-β and QUICKI), lipid profile (total cholesterol, HDL-, LDL- and non-HDL-cholesterol, triglycerides, and Castelli Index I), renal (creatinine and urea), hepatic (AST, ALT and GGT), oxidative stress (DCF, MDA, nitrites, total thiols, protein carbonylation, GSH, GPx and CAT), DNA damage (comet assay and micronucleus) and selenium were evaluated. The data relative to biochemical parameters presents an increased in fasting glucose levels, HDL- and LDL-cholesterol, and GGT levels. On the other hand, insulin levels and triglycerides/HDL-cholesterol ratio were decreased. Six-month Brazil nut consumption proved to be enough to significantly increase selenium and GSH levels, and GPx and CAT activity, improving the antioxidant system of patients. In relation to oxidant production, DCF and nitrites levels were decreased. Besides, was observed an increase in total thiols, and a decrease in protein carbonyl and MDA levels, suggesting a reduction of proteins and lipids oxidized. Relative to genomic instability, the levels of basal and oxidative DNA damage in T2DM patients were significantly decreased after Brazil nut consumption, as well as the frequency of micronuclei and nuclear buds. Taken together, our results indicate that Brazil nut consumption could be an ally to module the genomic instability in T2DM patients, probably through changes in redox balance.

Key words: Type 2 diabetes mellitus, *Bertholletia excelsa*, oxidative stress

DIETARY IRON INTAKE AND RISK OF CANCER

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Diet is considered a potentially modifiable risk factor for several cancers and it was analyzed in Uruguayan studies along 25 years. The Uruguayan average diet is meat-based, with the World's highest per capita beef intake. Red and processed meat have been implicated in carcinogenesis due to some of their components (own or added ones) as fats, cholesterol, heterocyclic amines, nitrosodimethylamine, iron, etc. Iron is essential for many biological processes, however, too much or too little iron can derive into pathological consequences. Iron balance is achieved by careful control of its intake and recycling. Both heme (in red meat, fish, poultry) and non-heme (in plant foods, also in meat) dietary iron are mostly present as Fe3+ (oxidized state). Heme-iron consists of 2/3 of the average person's iron intake in developed countries. In particular, iron intake is associated to aspects related to carcinogenesis, such as the formation of endogenous N-nitroso compounds, and the increase of oxidative stress. Iron overload induces free radical formation, lipid peroxidation, DNA and protein damages. In addition, higher body iron represented by higher iron and ferritin levels may be associated with cancer risk. We have explored the proportions of dietary iron according to its sources and subtypes, and also their epidemiologic associations with breast, colorectal and lung cancer risk. These recent studies reported epidemiologic evidence of an animal/plant ratio as well as a heme/non-heme ratio of dietary iron in support of a direct association to the disease. To our knowledge, these are the first epidemiologic studies on dietary iron types and cancer risk, and the main results will be herewith summarized and communicated.

Key words: Cancer, oxidative stress, epidemiologic

EXTRA-HEPATHIC CYTOCHROME P450 AND IT'S IMPORTANCE IN XENOBIOTICS METABOLISM

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Cytochromes P450 (CYP) are a family of enzymes that are responsible for the biotransformation of organic compounds through their oxidation. Within its multiple substrates are xenobiotic compounds, including drugs, which when are oxidized acquire an electrophilic character that promotes their elimination from the organism. Therefore, it is not uncommon for CYPs to be found mainly in the liver. However, CYPs are also present in other organs such as the intestine, heart, lung and brain. In the brain, CYPs participate in the metabolism of various drugs such as isoniazid and endogenous compounds such as arachidonic acid. We have described how isoniazid is metabolized by CYP2E1 in cerebellar neurons and how this metabolism produces ROS that can cause neuronal damage when antioxidant mechanisms are not adequate. In addition, we have also studied the negative regulation through inflammation of CYP2J3 and CYP2C11, responsible for the metabolism of arachidonic acid and the production of anti-inflammatory metabolites in astrocytes. These studies are highly relevant given the increasing correlation that has arisen between oxidative stress and chronic inflammation with the development of neurodegenerative diseases such as Alzheimer's and Parkinson's.

Key words: Cytochromes P450, neurodegenerative, xenobiotic compounds

JORNADA DE JÓVENES INVESTIGADORES

EVALUATION OF DNA DAMAGE AND OXIDATIVE DNA DAMAGE IN MOTHERS OF NEWBORNS BABIES WITH CONGENITAL ANOMALIES FROM SANTA FE, ARGENTINA

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Maternal exposure during pregnancy to chemicals, alcohol, tobacco, and some infections, may increase the risk of having a newborn affected by congenital anomalies (CA). The aim of this study was to evaluate genotoxicity in mothers of newborn with and without CA (cases and controls, respectively). A face to face questionnaire allowed to obtain information on demographic data and individual lifestyle were performed. Comet assay was applied in peripheral blood samples to determinate DNA damage (Comet) and oxidative DNA damage with Endonuclease III enzyme (Endo and Endo sites: Endo subtraction Comet) in 173 woman (25.2 ± 5.8 years old). No significant DNA damage was observed between case and control groups for three variables: Comet (p=0.7), Endo (p=0.3) and ENDO sites (p=0.3). In Control group, fruit and vegetables intake and physical activity during pregnancy indicated less DNA damage and oxidative DNA damage (Comet p=0.05; Endo p=0.03 and Comet p=0.04; ENDO sites p=0.009, respectively). In Controls, active or passive smoking, and alcohol drinking habit during pregnancy showed slightly higher DNA damage, but not statistically significant (p>0.05). In Case group, no significant differences were observed considering these habits. The results obtained for mothers of newborns with CA were useful to improve the characterization of individual risk and encourage us to continue working to understand the mechanisms involved in this particular group.

Key words: congenital anomalies, newborn anomalies, DNA damage

CITOTOXICY AND SENSITIZATION TO CISPLATIN BY VIOLACEIN IN BLADDER CANCER CELL LINES

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Violacein, a pigment produced by many bacterial strains, has antiproliferative activity in many cell lines. The aim of this work was to study the ability of Violacein to sensitize T24 and 253J bladder cancer cell lines against Cisplatin (CDDP). CDDP is a chemotherapy agent commonly used for bladder cancer therapy. Unfortunately, it is toxic and produce many side effects. In addition, cells use to development CDDP-resistance; thus, the search for new drugs is continuously working. We studied: the antiproliferative activity of Violacein by the Rezasurin; its genotoxicity by cytokinesis blocking micronucleous and comet assays; the effect of Violacein in the cell cycle by flow cytometry; the effect in the apoptotic death by using Annexin V; and the effect in cell migration by the wound healing assay. The results showed that Violacein is an antiproliferative effect against both bladder cancer cell lines and does not show genotoxic effect. This pigment already sensitizes these cell lines to CDDP due that allowed to reduce the concentration of CDDP but maintaining a similar antiproliferative effect. Violacein shows a strong effect in cell cycle, changes the patron effect of CDDP (augmentation of sub G1 area), shows an apoptotic effect, increases CDDP apoptotic death, and reduces the cell migration in wound healing assays. These are promising results that encourage us to continue the analysis of Violacein as anticancer or sensitizer to CDDP drug in bladder cancer.

Key words: violacein, anticancer, bladder cancer, cisplatin

EXPRESSION PATTERN OF ANTIOXIDANT ENZYMES GENES IN *Caiman latirostris* HATCHLINGS EXPOSED TO PESTICIDE MIXTURES

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Pesticide exposure of *Caiman latirostris* natural populations is of great concern, considering the effects we reported previously on genotoxicity and oxidative stress. Recently, a new family of biomarkers was developed for the analysis of gene expression related to cellular stress, which can be used as early warning sensors of xenobiotics exposure. The aim of this study was to validate *cat* and *sod* genes involved in the antioxidant response and quantify their expression levels in peripheral blood of *C. latirostris* after embryonic exposure to pesticide mixtures of Cypermethrin, Chlorpyrifos and Glyphosate based formulations. Treatments were: vehicle control treated with ethanol; one group exposed to the mixture of the three formulations (Mx3: CYP -0.12 % + CPF-0.8% + RU-2%) and three groups exposed to the binary mixtures of them (M1: RU + CYP; M2: CPF + CYP; M3: CPF + RU). The concentrations applied for each compound corresponded to that recommend for soy crops and applied on the nest material in contact with the eggs. After hatching, total RNA was isolated from blood through a protocol adapted for *C. latirostris* by our research group. Results showed a statistically significant increase in expression level of *cat* for M3 and of *sod* for M1 and M3, compared to control ($p<0.05$), even when we found no differences in the activity of these enzymes. The application of new highly sensitive biomarkers allows us to obtain reliable and complement information, giving us a better outlook of the possible short-and long-term consequences for *C. latirostris* natural populations.

Key words: Catalase; Superoxide dismutase; expression levels

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ELECTROSPUN PVA-DACARBAZINE NANOFIBERS: NOVEL NANO BRAIN-IMPLANT FOR TREATMENT OF GLIOBLASTOMA

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Malignant glioblastoma (GBM) treatment consists in resection surgery followed by radiotherapy and chemotherapy (CT). Despite its several implications, such as systematic toxicity and low efficacy, CT continues to be used for GBM therapy. Eventually, practically every tumor recurs. Recurrent GBM are less responsive to CT than the original tumor and they are extremely invasive. Owing to that GBM can recur and invade functional brain areas, the second surgical resection is risked. Due to the non-effective treatment for recurrent GBM, the patients' overall survival is between 12 and 15 months of initial diagnosis. Autopsy studies suggest that recurrent GBM are mainly local and appear within 2 centimeters of the initial tumor site. Therefore, localized and controlled CT straight into the tumor site provides an alternative DDS for GBM treatment. Aiming to overcome the blood brain barrier (BBB) limitations, one of the most promising approaches is the use of drug delivery systems (DDS) to treat the cancer cells in loco. The CT drug, dacarbazine (DTIC), is a well-tolerated imidazotetrazine derivate with established efficacy in recurrent GBM. However, DTIC presents some severe limitations. This CT drug is instable and has poor solubility also, DTIC is usually administered intravenously and this route is painful and usually the patients become non-compliant. To improve the treatment efficacy with DTIC, directly DDS that can be administered during the surgery. This approach can significantly reduce the systemic side effects and can prevent tumor recurrence. Due to its biocompatibility, polymeric DDS are one of the most encouraging approaches to use in several tumors treatment. Since it exhibits low toxicity and controlled release properties, this system is suitable choice in delivery of DTIC. Our research group focus is the study of polyvinyl alcohol (PVA). PVA is an interesting option to design nanoproducts, since this polymer presents low cytotoxic and is biodegradable. In this study, DTIC polymeric nanofibers (NF) were successfully prepared, characterized and its anticancer efficacy was determined. This system demonstrated a high drug loading of $83.9 \pm 6.5\%$, good stability and mechanical properties and continuous release profile for DTIC over 5 days with improved drug release in tumor pH. This suggested that the performance of the DTIC NFs is appropriate for GBM management and it is a promising approach to achieve a sustained drug delivery for GBM therapy. Additionally, DTIC NF showed an increased cellular uptake mostly after 24 hours of treatment and a continuous uptake until 48 hours. This controlled release prolonged the uptake of GBM improving DTIC antitumor effects. DTIC NF significantly decreased the cell viability in both pHs, 7.4 and 6.8, and it was statistical different ($p>0.05$) from DTIC solution in the pH 6.8 media, decreasing the viability more than the DTIC solution after 5 days, indicating that the NFs improved the efficacy

of DTIC after a prolonged exposure. Moreover, in order to analyze DTIC activity, this study evaluated γH2AX formation, due to its foci represents the effective DNA damage activity of DTIC in the cells. Confocal microscopy showed significantly more γH2AX foci percentage in cells treated with DTIC NF compared to NC and DTIC after 1 and 5 days of treatment. This damage was accompanied by an increase in apoptosis. Cells treated with DTIC NFs presented a higher apoptosis and late apoptosis percentages (19.9 and 32.8%, respectively) when compared to DTIC by itself (15.8 and 14.2%, respectively), after 5 days. Additionally, when compared to the negative control, DTIC NF presented 7-fold increase in the apoptosis and 3.1-fold increase in the late apoptosis, while DTIC presented 2.1-fold and 3-fold increase, respectively. Thus, data from DNA damage and cell death indicate that the NF facilitated drug uptake and enhanced accumulation of DTIC into the GBM cells improving its genotoxic and cytotoxic effects. In conclusion, DTIC NF brain-implant could be a promising drug delivery system for GBM therapy.

Key words: Electrospinning, Dacarbazine, Nanofibers, Polyvinyl alcohol, Glioblastoma.

PON POLYMORPHISMS AND ITS CORRELATION WITH DNA DAMAGE IN BOLIVIAN FARMERS EXPOSED TO PESTICIDES*

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The human serum paraoxonase 1 gene shows a simple nucleotide polymorphism located in Q192R that has the potential to be determinant in the variable toxicity response to organophosphorus pesticides in farmers. The aim of this study is to evaluate the relationship between PON1Q192R polymorphism and the micronucleus frequency in farmers who are occupationally exposed to pesticides in Cochabamba and La Paz -Bolivia. Demographic and occupational data were collected through a questionnaire applied to 205 exposed subjects. The genotype of paraoxonase 1 Q192R was detected by PCR-RFLP and genotoxic damage was evaluated by the MN test in binucleated cells. All statistical analyzes were performed with the SPPS / 22 statistical program. In the genotype PON1 Q192R, genotype frequencies of the Wild Type QQ allele 49.7%, heterozygous mutant QR 16.6%, homozygous mutant RR 33.6% and allelic frequencies Q 0.580 and R 0.419. The genotypic frequencies are in Hardy- Weinberg equilibrium. The correlation between the genotypes of PON1-192 and genetic damage, the following frequencies: MN QQ + QR 3.9 ± 3.4 and RR 3.6 ± 2.8. The difference between QQ + QR and RR was p = 0.883. In conclusion, the most frequent genotype in the studied population was the QQ genotype, followed by QR and RR. The frequency of the Q192R polymorphism in farmers exposed to pesticides was identified. The RR genotype is associated with a lower frequency of micronuclei in comparisson with other genotypes.

Key words: PON1Q192R, Pon polimorphisms, DNA damage, pesticides

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GENOTOXICITY OF TRICLOSAN IN AN *IN VITRO* MODEL AND ITS PREVENTION BY DIETARY PRODUCTS*

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Triclosan (5-chloro-2-(2,4-dichlorophenoxy)phenol, TCS) is a synthetic antibacterial agent employed as an active ingredient or preservative in toothpastes, cosmetics, soaps and numerous other personal care items. The American FDA banned its use in specific wash products based on strong evidence of its hormonal disrupting effects and hepatotoxicity. Rocket and watercress (Brassicaceae family) have demonstrated their ability to prevent genotoxic damage both *in vitro* and *in vivo*. Therefore, the aim of the present study was to assess TCS's putative cytotoxicity and genotoxicity *in vitro* and to determine whether rocket and watercress juice were able to prevent this damage. We exposed CHO-K1 cultures for 24 hours to different concentrations of TCS ranging between 50 and 4000µM, with previous incubation with rocket (30mg/ml) or watercress (33mg/ml) juice for DNA protection experiments. Cell viability and genotoxicity were evaluated through MTT, and the alkaline Comet and Cytome assays, respectively. Results evidenced cytotoxicity in concentrations of TCS over 1000µM ($p<0.05$). Moreover, exposure to TCS in concentrations over 500µM resulted in significant DNA damage as evidenced by the Comet assay ($p<0.05$) in a dose-dependent manner ($r=0.70$, $p=0.0027$). The Cytome assay demonstrated a decrease in nuclear division index and an increase in the frequency of nucleoplasmic bridges and nuclear buds, these effects being dose-dependent and significant for 700µM TCS ($p<0.001$, $p<0.05$, and $p<0.05$, respectively). Pre-treatment with rocket or watercress juice exhibited no significant modifications in TCS's toxicity ($p>0.05$). In conclusion, our results suggest that TCS may be cytotoxic, cytostatic and genotoxic under these experimental conditions, but our Brassicaceae had no success in preventing this damage.

Key words: Triclosan, cytome assay, alkaline Comet, Brassicaceae

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ENVIRONMENTAL SAFETY EVALUATION OF A NEW PRODUCT BASED ON CASHEW NUT SHELL LIQUID (CNSL) FOR CONTROL OF *Aedes aegypti* (DIPTERA: CULICIDAE)

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The development of new insecticides and/or strategies to control *Aedes aegypti* are an important issue to public health. Technical Cashew Nut Shell Liquid (TCNSL) is byproduct rich lipid phenols with insecticidal activity. Our objective was produce TCNSL emulsions to control *Ae. Aegypti* and evaluate environmental safety by toxic-genetic tests in non-target species. Sodium sulfonate synthesis of TCNSL (TCNSLSNa) was performed, followed by the emulsion obtaining the product TCNSL+TCNSLSNa. It´s larvicidal activity was verified using *Ae. aegypti* larvae of third instar. The toxicity tests were performed using aquatic organisms from three different trophic levels and genotoxicity using *Salmonella*/microsomal assays and nuclear alterations/micronucleus in *Oreochromis niloticus*. The TCNSL+TCNSLSNa presented larvicidal activity in *Ae. aegypti* with LC50 of 15.8 mg L^{-1}. Regarding toxicity, *Daphnia similis* was more sensitive test-organism, followed by *Pseudokirchneriella subcapitata* and *O. niloticus*. The *Salmonella*/microsome assay showed that the emulsion was mutagenic at concentrations of 200 and 2000 mg L^{-1}. The emulsion was non genotoxic to *O. niloticus*. Although the product has shown toxicity to aquatic organisms at concentrations below the LC50 obtained for the larvicidal effect, toxic concentrations of the product are unlikely to be found in the aquatic environment due to their environmental dispersion, dilution and degradation. Despite the product was effective in controlling the larvae and presented multifunctionality, it showed mutagenic activity and could not be registered for intended use in Brazil. It is therefore important that modifications are proposed in the product aiming at the elimination of mutagenicity and, if possible, the toxicity to aquatic organisms.

Key words: cashew nut shell liquid, *Aedes aegypti, toxicit, salmonella microsomal*

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IS HORCHATA A DRINK WITH FUTURE?

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"Horchata" is an herbal mixture infusion consumed in Southern Ecuador, the main herbs of which it has different biological activities like analgesic, anti-inflammatory, diuretic, and can prevent carcinogenesis. We evaluated the cytotoxicity, apoptotic, and chemopreventive effect of this infusion. Nine different varieties of Horchata were prepared in the traditional way and then freeze-dried. The cytotoxic activity was evaluated on some cell lines D-384, PC-3, MCF-7, RKO, A-549, CHO-K1, and human peripheral blood lymphocytes via a MTS assay. The pro-apoptotic effects were evaluated with Anexin V/Propidium Iodide and western blot of Bax, Bcl-2, TP53, and TP73. Induction and reduction of ROS were assessed by fluorimetry. Genotoxic and chemopreventive effects were evaluated with a comet assay and micronuclei on binucleated cells. Results showed the five Horchatas had cytotoxic effects against D-384 while not affecting normal cells; these induce cell death by apoptosis modulated by p53/p73. In CHO-K1 cells, the Horchatas decrease the damage induced by H_2O_2 and Mitomycin C measured in the comet and micronucleus assay respectively. Four Horchatas (H1, H2, H7 and H9) act as bio anti-mutant agents, evidenced by comet assay post treatment H1, H2 and H7 reduced the genotoxicity (cyclosporine induced), and H9 had an anti-mutagenic effect in pretreatment. As conclusions the IC_{50} range in D-384 was 41 to 122 μg/mL; in the other hand we show that the results in CHO-K1 and lymphocytes are same, not show a cytotoxic effect. It would to highlight the Horchatas present anti-genotoxic properties, which may be related to the antioxidant capacity.

Key words: Horchata, antimutagenic, anti genotoxic

RT-QPCR VALIDATION FOR DETECTION AND QUANTIFICATION OF LEUKEMIA-ASSOCIATED FUSION GENES

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Some Fusion Genes (FG) constitute hallmarks that characterize variants of Leukemia and are employed for diagnosis, prognosis and monitoring because they reveal the cause of the neoplasia in the patient, predict the risk depending on the genes involved and can be monitored during and after the treatment. For this reason, the objective of this study is to develop an in-house validated method, RT-qPCR, to detect FG involved in different types of Leukemia. The analytical procedure consisted in the sampling of bone marrow or peripheral blood and RNA extraction by Ficoll density gradient and organic extraction. The analytical method consisted in the reverse transcription with SuperScript III kit and qPCR with Quantitect Probe Kit. Both analytical stages were tested by a modular validation approach. The control for the analytical procedure was quantitation on Qubit (~1000 ng/µL) and detection of the endogenous control ABL on qPCR, detected in 85% of the samples. For the analytical method we worked in a working range of 10 – 10^6 copies and, on average, the slopes presented a value of -3.33 demonstrating its high sensitivity, an effectiveness of 99.49% and an r^2=0.98. Also, the method demonstrated to be 100% selective, precise ($\%RSD_R$ = 17.49%, $\%RSD_r$=2.15%) and expressed a LOD=189.72 copies and a LOQ=367.98 copies. Based on the results, it is demonstrated that the method fits for purpose. Also, we detected some FG in the 20% of the patients concluding that the validation results positively influence the detection and quantification and therefore, the decision-making process for the treatment**.**

Key words: Fusion Gene, validation, Leukemia, qPCR, reverse-transcription.

Financial support: IDH Fund

ALCOHOL AND STRESS INDUCED NUCLEAR DAMAGE IN HIPPOCAMPAL ASTROCYTES

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Alcohol consumption and high stress levels represent a serious problem for subjects and society. Alcohol impairs the synapses of neural circuits with cognitive, behavioral and/or psychiatric consequences. Both alcohol and psychological stress produce oxidative stress, which can induce DNA damage. Employing hippocampal homogenates from Sprague Dawley rats, primary cultures of astrocytes were implemented. The cultures were treated with ethanol (EtOH, 200 mM) and/or corticosterone (CTS, 1 μM, stress response effector in rodents) to characterize DNA damage and the glial response to acute exposure (1h) either simultaneously or independently to both noxas. The cultures were fixed in 4% PFA and sites of primary DNA damage (foci- γH2AX) were immunodetected using GFAP (cell line marker), DAPI (nuclear counterstain) and confocal LASER microscopy. In parallel, a set of cultures were prepared for scanning electron microscopy (SEM) analysis. The data were analyzed with the R statistical program, applying Shapiro-Wilk test, Levene, Kuskal-Wallis, and Wilcoxon-Holm post-hoc (= 5%). EtOH or CTS treated cells show frequencies of foci- γH2AX per nucleus higher than controls ($p < 0.00001$, $p = 0.001$, respectively). Likewise, nuclear size was smaller, foci- γH2AX frequency was higher, and fluorescence intensity decreased in cultures treated with EtOH+CTS compared to those exposed only to CTS or EtOH (both $p < 0.00001$). This could indicate an elevated genetic and nuclear damage induced mainly by combined exposure to both agents. At the morphological level, stress vesicles were visualized by SEM on the nuclear surface.

Key words: alcohol, stress, hippocampal astrocytes

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PÓSTERS

NEW COMPOUNDS DERIVED FROM COBALT CHLORIDE WITH ANTIMICROBIAL ACTIVITY AND ABSENCE OF MUTAGENICITY AND CYTOTOXICITY

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The increase in infections due to the resistance of microorganisms, as well as the limited therapeutic options to treat them have led to the search for new antimicrobials with better mechanisms of action and low toxicity. In this sense, this objective work evaluates the antifungal, cytotoxic and mutagenic activity of two new cobalt chloride complexes with Br and Cl ligands. The antimicrobial activity of the complexes was evaluated by the broth microdilution technique against Gram positive and negative bacteria and yeasts. Cytotoxicity was evaluated by the method based on the reduction of MTS against HeLa, SiHa and Vero cell lines. The mutagenic potential was assessed by the Ames test using the Salmonella Typhimurium TA97a and TA100 lines with and without exogenous metabolism system. Both complexes presented promising antimicrobial activity for yeasts, being more effective against Candida glabrata presenting a minimum inhibitory concentration of 7.81 μg / mL (Br) and 15.62 μg / mL (Cl), for the bacteria the complexes did not present promising results. The concentrations of 5000 and 1500 μg / mL of both complexes showed cytotoxicity characteristics against all cell lines tested. The complex with the Br binding also showed a mutagenic potential against the TA100 line with no metabolic activation at the concentration of 5000 μg / mL. However, the concentrations obtained in the antimicrobial activity are lower than these, causing no interference. Thus, since the concentrations of the complexes that showed antimicrobial activity were not cytotoxic and mutagenic, they can be used in antifungal therapy due to its promising activity.

Key words: cobalt chloride, antimicrobial, antifungal, cytotoxic, mutagenic

GENOTOXIC EFFECT OF THE RHIZOMES OF *Kyllinga vaginata* AND *Scleria distans* IN RADICAL CELLS OF *Allium cepa*

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The *Kyllinga vaginata* and *Scleria distans* species, marketed under the name of *"kapi'i kati"* in Paraguay, are medicinal plants used as phytotherapeutic, being the rhizomes, barks and leaves the parts used for their consumption, however its genotoxic action it's not known. In order to evaluate the genotoxic effect of these plants, using the *Allium test*, radical meristematic cells of *Allium cepa* radical apex were exposed to different concentrations of the aqueous extract of *K. vaginata* and *S. distans* (0.06%, 0.11% and 0.22%) accounting for 2000 cells per concentration. The results obtained were analyzed by means of the T test (95% confidence) and these showed that the extract of the rhizomes of *K. vaginata* and *S. distans*, have produced significant anomalies at concentrations of 0.11% and 0.22% ($P < 0.05$). A higher percentage of telophase cells were also observed at the concentration of 0.11% ($P < 0.05$); As for the cytotoxic damage, sticky and advanced chromosomes were observed. With these results, no significant genetic damage has been identified, but there has been damage at the cytotoxic level.

Key words*: Kyllinga vaginata, Scleria distans, Allium* test

STUDY OF THE POTENTIAL ANTITUMORAL PROPERTIES OF *Eugenia uniflora* LEAVES

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Historically, natural products are used by different cultures worldwide to benefit health and approximately 80% of the world population relies on natural products and/or Traditional Medicine for their primary health care. Interestingly, many native plants usually consumed in rural areas have being insufficiently studied for these health properties. One of such is *Eugenia uniflora L.* from the Myrtaceae family, popularly known as Pitanga. This plant is widely spread in Uruguay, southern Brazil and northeast Argentina. Besides the polyphenol-containing fruit, the essential oil (EO) extracted from Pitanga leaves shows antifungal, antibacterial, cytotoxic and antiparasitic properties. In our laboratory, we have evidenced a dose dependent antiproliferative effect of Pitanga EO. Based on the hypothesis that EO of *E. uniflora* has anticarcinogenic properties, we have determined the chemical composition of the EO prepared from the Pitanga VIII-7 plant, clonally selected as representative of the population of Pitangas of Uruguay (GPS: 31°22'S57°56'O). To assess the biological effects of Pitanga EO, *in vivo* studies of toxicity and bowel epithelium cytotoxicity were performed in Spague-Dawley rats. The composition analysis by gas chromatography-mass spectrometry evidenced 51 terpenes being sesquiterpenes the most abundant compounds: 3-Hidroxi-trans-Calameneno (41.04%), delta-Cadineno (18.73%) and tau-Muurolol (12.72%). *In vivo* studies with different EO concentrations showed no animal or digestive toxicity. Anatomopathological studies are under way to determine digestive track alterations at the microscopic level. The previously identified antiproliferative properties of the compounds and the lack of toxicity lead us to propose the EO of Pitanga leaves as a potential quimiopreventive agent of colon cancer.

Key words: antitumoral, *Eugenia uniflora L,* colon cancer, quimiopreventive

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ANALYSIS OF DNA PURINE NUCLEOBASES NITRATION AT PHYSIOLOGICAL pH*

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Exposure to chemical and physical agents that increase intracellular levels of reactive oxygen (ROS) and nitrogen (RNS) species, may lead to DNA damage. If this damage is not properly repaired, lethality, mutagenesis and/or genomic instability may occur, effects known to be fundamental in the initiation and promotion of carcinogenesis. Oxidative DNA damage and its repair is subject of extensive qualitative and quantitative study, however, less it is known about nitration DNA damage. In addition, limited information is available on nitration reaction rates of DNA bases, particularly under physiological conditions. Since the formation, persistence, and degradation of nitrated DNA lesions may determine their processing by cellular DNA repair mechanisms, it is fundamental to gain more knowledge about the reactions of RNS with nucleotide bases as well as their kinetics. We studied the formation of 8-Nitroguanine (8-NitroGua) by the reaction of peroxynitrite anion as a nitration agent with Guanine (Gua) nucleobase using a SX20 stopped-flow rapid-mixing apparatus. The mixing time was ~1 ms. Time courses for Gua and (ONOO-) reaction in phosphate buffer (pH 7.40) were recorded at 0.15 and 1 s at different temperatures (10- 40°C). Kinetics plots showed three formation components of different slope and no spontaneous denitration of 8-NitroGua was observed after 120 min. Analysis of 8-NitroGua kinetics reveals the feasibility of occurrence of 8-NitroGua in cells becoming a potential source of genomic damage. Nitration studies of Adenine are underway.

Key words: RNS, DNA Purine nitration

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TOXIC-GENETIC EVALUATION OF THE MIXTURE OF CASHEW NUT SHELL LIQUID PLUS CASTOR OIL THAT HAVE AN EFFICIENT LARVICIDE EFFECT TO *Aedes aegypti**

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Dengue, chikungunya and Zika virus are epidemics in Brazil that are transmitted by mosquitoes, such as *Aedes aegypti*. The product with surfactant properties based on castor oil liquid associated with castor oil (TaLCC-20) has a proven larvicidal effect for *Ae. aegypti* at a concentration of 5 mg/L. However, in addition to proving its efficiency, it is necessary to evaluate the product safety from a toxicological point of view. Our objective was to evaluate the toxic-genetic potential of TaLCC-20 using *Oreochromis niloticus*. The acute toxicity (96h) of TaLCC-20 for the fish was determined using test concentrations ranging from 10 to 25 mg/L and was expressed in median lethal concentration (LC50). For evaluation of genotoxicity the fish were exposed to concentrations of 1.5; 4.0 and 7.5 mg/L, corresponding to 10; 25 and 50% of the LC50 obtained previously. To analyze nuclear alterations/micronuclei, caudal fin venipuncture was performed 72h after exposure. The LC50 determined for TaLCC-20 using *O. niloticus* was 15.3 mg/L. Nuclear alterations were observed only at the highest concentration tested (7.5 mg/L). In the evaluation of micronuclei, absence of genotoxicity was observed for all the tested concentrations. Acute toxicity of TaLCC-20 to fish is not expected in real usage conditions since the determined LC50 is higher than the concentration required to obtain the larvicidal effect (5 mg/L). However, due to the low genotoxicity of TalCC-20 observed, an in-depth evaluation with other models for genotoxicity assessment should be conducted, since in Brazil the registration of insecticides with genotoxic properties is prohibited.

Key words: toxic genetic**,** TaLCC-20, *Oreochromis niloticus*

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MUTAGENIC EFFECTS OF THE SOCIAL WASP VENOM *Polybia sericea* (HYMENOPTERA: VESPIDAE)

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Animal's poisons are made up of a complex mixture of bioactive agents, thus becoming a source of studies for application in the pharmaceutical industry. This complex mixture may include proteins that decrease/ inhibit its mutagenic potential. In this sense, the objective of the study was to evaluate the mutagenicity of the venom of *Polyps sericea* in the presence and absence of the protease inhibitor using the Ames test. The concentrations of 5; 15; 50; 150 and 500 μg/plate of venom with and without the protease inhibitor were used against the strains of *Salmonella* Typhimurium TA98 and TA100 in the presence and absence of exogenous metabolism. The revertant colonies were analyzed and the mutagenicity index determined. The concentration of 150 μg/plate without the protease inhibitor significantly increased the number of the revertant colonies and showed a mutagenicity index > 2, demonstrating a mutagenic potential against the TA98 strain in the presence of exogenous metabolism. The results showed that in determined concentrations of the venom has the potential indirect to cause displacement of the reading frame, which did not occur in the presence of the protease inhibitor, suggesting that some protein present in the venom may lead to the degradation of substances that damage the DNA present in the venom.

Key words: mutagenic effect, *Polybia sericea- wasp venom*

MUTAGENIC POTENTIAL IN VITRO AND IN VIVO OF THE AQUEOUS EXTRACT OF *Aleurites moluccana* SEEDS POPULARLY USED FOR WEIGHT LOSS

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Aleurites moluccana, has a seed popularly known as "noz da Índia" that is ingested for weight loss, however, there are no scientific studies that assure this consumption. The objective of this work was to evaluate the in vitro and in vivo mutagenic potential of the aqueous extract of the *Aleurites moluccana* seeds (EASAM) by the Ames test and the micronucleus test, respectively. In the Ames test the concentrations of 50; 150; 500; 1500 and 5000 µg/plate were used against the strains of *Salmonella* Typhimurium TA97a, TA98, TA100 and TA1535 with and without metabolic activation. In the Ames test, for the assay without metabolic activation, concentrations of 1500 and 5000 µg/plate had a mutagenic potential against the TA97 strain and the concentrations of 50, 150, 500 and 1500 µg/plate to the TA100 strain, in the metabolic activation assay, the concentrations of 50 and 5000 µg/plate presented a mutagenic potential against the TA100 strain and the concentrations of 50, 150 and 1500 µg/plate to the strain TA1535. In the micronucleus test, females treated with 25 mg/kg of extract also presented mutagenic potential. It is concluded that EASAM presents mutagenic potential in vitro and in vivo under the evaluated conditions, evidencing the risk of its consumption and alerting the population to the consumption of natural products based only on popular knowledge.

Key words: mutagenic potential, *Aleurites moluccana,* Ames test

MUTAGENIC EFFECTS OF *Aristolochia triangulares* (*CHAM*. ET SCHL.) BY THE AMES *SALMONELLA* TEST

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*Aristolochia triang*ulares popularly known as "cipó-mil-homens" have been used in popular medicine like antirheumatic, contraceptive agent, diaphoretic, diuretic, antiseptic, emenagogue, antidote, and abortifacient. Despite of large use in the popular medicine, the information about mutagenicity effect is unknow. Hence, the aim of the present study was to investigate the mutagenic activity of the butanol and acetate fractions and infusion from *Aristolochia triangulares*. The mutagenic potential was evaluated by the *Salmonella*/microsome assay with and without metabolic activation using two strains of *Salmonella* Typhimurium TA98 and TA100. The results showed mutagenic activity in strain TA100 without metabolic activation, in the acetate fraction at the concentrations of 1500 and 5000 μg/plate. However, in test with metabolic activation, only at the concentration 5000 μg/plate, while the infusion presented at concentrations of 500, 1500 and 5000 μg/plate. In strain TA98, the assay without metabolic activation, the butanolic fraction had potential at the concentration of 500 μg/plate and cytotoxicity at the concentrations of 1500 and 5000 μg/plate, and for the acetate fraction, all concentrations in the assay with and without activation showed mutagenic potential. These results demonstrated the mutagenic potential of *A. triangulares*, highlightings the importance of screening of species used in popular medicine provide a better understanding of the mechanisms by which this specie act in DNA damage.

Key words: AMES test, popular medicine, mutagenicity.

MUTAGENIC AND CITOTOXIC POTENTIAL OF THE LEAVES AND BARK OF *Ocotea minarum**

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Ocotea minarum (Nees & Mart) is a medium-sized tree popularly known as 'canelinha' or 'canela-vassoura' which has been used in popular and traditional medicine for the treatment of various diseases. Some research has already proven the antimicrobial and antioxidant activity of leaves and bark of this species, but there are no studies that guarantee its pharmacological safety. In this sense, this study aimed to evaluate the mutagenic and cytotoxic potential of the infusion of leaves and bark of *Ocotea minarum*. The mutagenic potential was assessed by the Salmonella/Microsome assay using the strains of *Samonella* Typhimurium TA97a, TA98, TA100, TA1535 and TA102 in the presence and absence of the exogenous metabolism system. Cell viability was evaluated by the MTS reduction method against the HeLa (cervix adenocarcinoma cell line), Vero (Kidney epithelial cells extracted from an African green monkey, *Cercopithecus aethiops*) and SiHa (human cervical cancer cells). In both assays infusions were tested at concentrations of 50 to 5000 µg/mL. The results showed that the infusion of leaves and bark of *O. minaarum* did not present potential to induce mutations of the type of substitution of base pairs and displacement of the reading frame in the presence and absence of exogenous metabolism system, nor did they present cytotoxic effects compared to the cell lines and concentrations evaluated. In this sense, the infusion of *O. minarum* is a safe alternative as the mutagenic potential can be used by popular medicine and as a source of raw material for the development of new drugs.

Key words: *Ocotea minarum*, Salmonella/Microsome, cytotoxic, mutagenic,

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IN VITRO GENOTOXIC AND CYTOTOXIC EFFECT OF *Smallanthus sonchifolius* INFUSION*

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Yacon (*Smallanthus sonchifolius*) is a perennial herb native to South America which leaves are used in the preparation of medicinal infusions. The aims of this study were to characterize the phytochemical compounds of a yacon's infusion and to evaluate its cytotoxicity and genotoxicity *in vitro*. Dichloromethane, ethyl acetate and residual aqueous extracts were obtained of a 2%w/v infusion and analyzed by TLC. The MTT assay was performed to evaluate the cytotoxicity; while the comet assay and cytokinesis-block micronucleus (CBMN) cytome assay were carried out to evaluate the genotoxicity of the infusion. CHO-K1 cell line was employed for both assays. A range of doses (530-25µg/mL) was used for the MTT, whereas for the genotoxicity tests the doses were 66.7, 44.5, 33.3 and 26.7µg/mL, considering human consumption. TLC analysis allowed the detection of phenolic and hydroxycinnamic acids, flavonoids and sesquiterpene lactones in the extracts. The CC50 was 144.5µg/mL by MTT assay. The results of the comet assay showed an increase in the DNA damage for the 66.7 and 44.5µg/mL doses compared to the negative control. Furthermore, a significant increase ($p < 0.05$) in the frequency of nucleoplasmatic bridges was observed for all treatments. On the other hand, we detected a significant increase in micronuclei and nuclear buds at the highest concentration. These results showed a cytotoxic and genotoxic behavior induced at doses lower than traditional human intake of yacon infusion, under these experimental conditions.

Key words: *Smallanthus sonchifolius*, genotoxicity, cytotoxic

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EFECTOS DE LOS EXTRACTOS ACUOSO Y ETANÓLICO DE *Ambrosia tenuifolia* Spreng EN EL DESARROLLO EMBRIONARIO DE *Danio rerio*

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Las plantas medicinales, de amplio uso en el país, carecen en general de estudios científicos que sustenten tales usos, por lo que se hace necesario estudiar su efecto sobre la fisiología general, alguna patología específica que podría ocasionar o también sus posibles efectos secundarios. La altamisarã, *Ambrosia tenuifolia,* hierba perenne de la familia Asteraceae, se utiliza popularmente como abortiva, antipirética, digestiva y contra el dolor de cabeza, siendo útil la parte aérea de la planta. El objetivo de este trabajo fue determinar el efecto letal del extracto acuoso y etanólico de altamisarã en embriones de pez cebra tratados con diferentes concentraciones. Se realizaron observaciones a partir de las 24 horas post fecundación hasta las 96 horas post fecundación bajo el microscopio teniendo en cuenta la coagulación. Se demostró que el extracto presenta efecto letal en el desarrollo embrionario de *Danio rerio,* agravándose el mismo con el aumento de la concentración utilizada.

Palabras clave: *Ambrosia tenuifolia, Danio rerio,* embriotoxicidad

GENOTOXICITY AND ANTIGENOTOXICITY OF ETHEREAL EXTRACTS AND FRUITS FROM *Garcinia madruno*

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Garcinia madruno (Kunth) Hammel is a tropical tree with great potential as a source of natural products with biological activity. Many studies have reported the antioxidant, antibacterial and antitumoral potential of its extracts and molecules. We assessed the genotoxicity and antigenotoxicity of ethereal bark, stem, and epicarp extracts from this tree and the juice (aqueous extract) from its fruit, commonly called "ocoró" and consumed in Bolivia. We applied the mutagenicity Ames test, the Comet Assay in peripheral blood lymphocytes and the micronuclei test in Allium cepa, evaluating doses from 6.25 to 100 µg/ml. The results showed that the bark, stem, leaves and epicarp extracts did not exhibit mutagenic or clastogenic activity and were able to reduce genotoxicity of mitomycin C and hydrogen peroxide in the Ames test and micronuclei test respectively. Bark extracts caused simple and double DNA strand breaks as measured by comet assay in doses higher than 6.25 µg/ml, however the juice had no genotoxic effect in lymphocytes and showed antigenotoxic properties, reducing H_2O_2 oxidative damage up to 53 %. The antigenotoxic capacity of these extracts was explained by a phytochemical analysis that reported high concentrations of phenolic compounds, especially flavonoids, xanthones and benzofenones that are known for their antioxidative activity. Overall this species has many compounds that can be studied as nutritional supplements or phytofarmaceutical products to prevent cancer, and the fruit has antioxidant potential that can be exploited.

Key words: *Garcinia madruno*, Ames test, Comet test

STUDY OF *Matricaria chamomilla* L. BY ACUTE TOXICITY TEST WITH ZEBRAFISH EMBRYOS (*Danio rerio* Buchanan-Hamilton, 1822)

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Chamomile (*Matricaria chamomilla* L.) is popularly used as a digestive, anti-inflammatory, anticolic, among other uses. Pregnant women could use medicinal plants without knowing the potential effects for both the woman and the embryo or the fetus. The objective of this work was to study the toxic effect of the infusion of the *M. chamomilla* flower by means of the acute toxicity test with zebrafish embryos (*Danio rerio*). Eggs of 6 hpf (hours post fertilization) and four dilutions of an infusion prepared with 7.538 g in 180 mL of distilled water (0.25%, 0.5%, 1.00% and 2.00%) were used, as positive control was 3,4-dichloroaniline in concentration of 4 mg/L, and a standardized medium for embryo development was used as negative control and diluent. The results were analyzed by means of the analysis of the unidirectional variance and the Bonferroni test, the significance level was set at 0.95 ($p< 0.05$). Among the groups exposed to the infusion, the highest percentage registered in coagulation at 24 hpf was the concentration of 1.00% (13.33%) and 48 hpf of the concentration of 2.00% (23.33%). None of the groups exposed to the dilutions of the infusion presented significant difference with the negative control. 100% of the eggs to the positive control coagulated at 24 hpf. The infusion of *M. chamomilla* does not present acute toxicity in *D. rerio* embryos for the parameter evaluated.

Key words: acute toxicity, *Danio rerio,* embryotoxicity, infusion, *Matricaria chamomilla*.

ANTIOXIDANT ACTIVITY OF *Mangifera indica* L. EXTRACT USING THE METHOD OF CAPTURE OF FREE RADICAL DPPH

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The medicinal properties of *Mangifera indica* species are well known and is used mainly to treat intestinal conditions such as anthelmintic and antiparasitic. However, its activities as an antioxidant are unknown, so it was proposed as main objective of this investigation to analyze the antioxidant activity of ethanolic extract of flowers of *M. indica*, by means of the method of free radical 2,2-Diphenyl-1- Picrilhidrazilo (DPPH·) capture. For this, 40, 80, 200, 400, 560 µg of *M. indica* extract were used in the assay, using as solvent Ethanol 96°. As an antioxidant reference compound, Ascorbic Acid (8, 12, 16, 20, 24 µg) was used. The data were obtained by the reading at 517 nm in a spectrophotometer, evidencing antioxidant activities 15 times higher compared to the reference standard. The IC_{50} of the extract was 338.2 ± 0.5 µg (r = 0.999) compared to the IC_{50} 22.1 ± 0.03 µg (r = 0.999) of Ascorbic Acid. These results indicate that the *M. indica* flowers ethanolic extract in addition to having anthelminthic action, is a good antioxidant, adding preventive medicinal value to this specie.

Key words: mango, flowers, antioxidant, free radicals.

ANÁLISIS CITOTÓXICO Y GENOTÓXICO DEL EXTRACTO ETANÓLICO DE *Polygonum punctatum* ELLIOT. (KA´A TÁI)

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Polygonum punctatum Elliot. conocido en Paraguay como Ka´a tái es utilizada en medicina popular como antihemorroidales, como cataplasmas para curar heridas y úlceras; como rubefacientes y diuréticos. Las partes aéreas de esta planta presentan actividad antimicrobiana y antifùngica. Se evaluó el efecto mutagénico del extracto etanólico de *Polygonum punctatum* Elliot., mediante el test de micronúcleos en células de la médula ósea de roedores a dos concentraciones 10 mg/Kg y 5 mg/Kg, utilizando como control positivo ciclofosfamida y negativo PBS, como también la actividad citotóxica del extracto sobre células de macrófagos peritoneales de ratones in-vitro a concentraciones de 100, 50 y 25 µg/mL. El análisis estadístico mostró que, a estas concentraciones de evaluación, el extracto no induce un aumento significativo de micronúcleos en las células de los ratones. En el ensayo de citotoxicidad todos los porcentajes de células vivas son valores altos comparados con el control negativo a una concentración de 100 µg/mL el extracto presentó un porcentaje de células vivas de 94% comparando con el control negativo que fue de 100%, el cual indica la baja toxicidad del extracto evaluado, también se pudo observar un comportamiento similar en las concentraciones de 50 y 25 µg/mL con 84 y 91% de células vivas. De esta manera se amplían los conocimientos acerca del potencial terapéutico que posee dicha planta medicinal y contribuye a la búsqueda y desarrollo continuo en el área de la biofarmacéutica.

Palabras claves: Macrófagos peritoneales, extracto, in vitro, *Polygonum punctatum.*

GENOTOXIC EVALUATION OF *Urera baccifera* L. ETHANOLIC EXTRACT IN *Drosophila melanogaster*

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Urera baccifera is a plant used as a medicinal, widely distributed throughout the Americas. It is used as infusions and decocts due the numerous properties attributed to it such as anti-inflammatory, antidiabetic, analgesic and hypotensive. However, genotoxic capacity is unknown, this research has as main objective to determine the genotoxic activity of *U. baccifera* ethanolic extract using SMART bioassay in *Drosophila melanogaster.* For this, an experimental pure analytical with completely randomized block design study was carried out , where third instar larvae of *D. melanogaster* were treated with different concentrations of extract (0.1, 1 and 10 $mg.mL^{-1}$) for 72 hours, as negative control distilled water was used and as mutagenic agent Cyclophosphamide 2.61 $mg.mL^{-1}$. Data obtained were analyzed statistically by Kastenbaum-Bowman Test $\alpha=\beta= 0.05$, where the types of phenotypic markers frequently observed and analyzed were the small single spots (SSP) and large single spots (LSG) with non significant difference. These results indicate that none of the concentrations of the ethanolic extract used for treatments have not mutagenic activities in *D. melanogaster*.

Key words: *D. melanogaster*, *Urera baccifera*, genotoxic

DICENTRIC CHROMOSOME ASSAY BY THE TRIAGE METHODOLOGY: A POTENTIAL TOOL IN LARGE SCALE RADIOLOGICAL ACCIDENTS

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The dicentrics and centric rings assay allows to estimate the absorbed dose in people exposed to ionizing radiation from venous blood samples. In accidents with multiple victims, there are methodologies that lead to increase the speed of response. One of them is the scoring of dicentrics chromosomes with triage criteria (reduction of the number of cells analyzed), which makes it possible to reduce analysis time. The aim of this approach is the classification of the victims in dose ranges of clinical importance. The validation of this methodology was carried out through the participation of the biological dosimetry laboratory (LDB) of the Nuclear Regulatory Authority in three intercomparison exercises: two of them organized by the Ministry of Health of Canada (international) whose objective was the determination of the absorbed dose at 10 dose points with an X-ray source, in the range of 0 to 5 Gy; and one regional exercise organized by the LDB in which 2 dose points were evaluated with an Ir-192 source in a range of 0 to 0.5 Gy. The results showed a better fit for doses lower than 2.5 Gy, with a tendency to overestimate for higher doses. However, for doses close to the limit of detection, larger uncertainty was observed in the dosimetry estimation. These findings demonstrate that the analysis of 50 metaphases provides enough information to perform a classification of victims in dose ranges for medical decision, allowing the use of this methodology in cytogenetic biodosimetry laboratories networks for mutual assistance.

Key words: Ionizing radiation, biological dosimetry, Nuclear Regulatory Authority

DNA DAMAGE IN PROFESSIONALS OCCUPATIONALLY EXPOSED TO ANESTHETICS IN VETERINARY HOSPITAL

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Introduction: Inhaled anesthetics have been used for several decades in human and veterinary operating rooms (ORs). Consequently, OR professionals may be at risk due to occupational exposure to waste anesthetic gases (WAGs). The potential health effects of continuous exposure to WAGs in individuals in ORs remain controversial. However, in relation to professionals working in veterinary hospitals, there is limited literature regarding possible genotoxic effects. Objectives: Thus, the current study evaluated the genotoxic potential of exposure to WAGs in professionals who worked in veterinary ORs. Methods: This study was approved by the local ethics committee, and seventy-seven subjects were included in the study and were allocated into two groups, as follows: 40 professionals mainly exposed to isoflurane and to a lesser degree to sevoflurane anesthetics for at least one year from the School of Veterinary Medicine and Animal Science of São Paulo State University, Brazil (exposed group) and 37 volunteers not exposed to WAGs (control group). All participants provided written informed consent. Fasten blood samples were collected and peripheral blood lymphocytes were isolated to evaluate DNA damage detected by the alkaline comet assay (tail intensity). Results: There was no difference between the groups in relation to the demographic data, and no significant change was observed between groups in relation to DNA damage ($p>0.05$). Conclusion: Under the study conditions, our findings suggest that occupational exposure to the WAGs isoflurane and sevoflurane may not induce DNA damage in professionals who work in veterinary ORs.

Key words: DNA damage, anesthetic, WAGs, Ors, isoflurane, sevoflurane

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GENOTOXIC EFFECTS OF THE ANESTHETICS BENZOCAINE, EUGENOL AND *Lippia alba* ESSENTIAL OIL TO TWO FISH SPECIES*

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Synthetic or natural anesthetics are indispensable in experimental procedures and fish handling in aquaculture, as they avoid animals physical damage and stress. The use of natural products such as *Lippia alba* essential oil (EO) may be an alternative to replace these synthetic compounds. However, it is necessary to carry out genotoxicity evaluation of these anesthetics. Our objective was to evaluate the genotoxic effect of three anesthetics using *Astyanax lacustris* and *Oreochromis niloticus*. The fish were exposed to six treatments, two with commercial anesthetics (Benzocaine and Eugenol), one with *L. alba* EO and the controls, negative (without treatment), vehicle (Ethanol PA), and positive (Cyclophosphamide). The fish were exposed to anesthetics and controls in bath for 10 minutes and they were transferred to individual aquariums without anesthetics or controls for further analysis. Venipuncture in the caudal vein was performed 72 hours after exposure. For genotoxicity assessment, nuclear alterations and micronucleus were analyzed in blood smears, and DNA damage by the comet assay. Eugenol presented genotoxicity to the both species. Benzocaine and Eugenol increase the DNA damage verified by the comet assay in both species. No genotoxicity effects were verified for animals exposed to *Lippia alba* EO. Thus, we concluded that *L. alba* EO becomes a viable alternative to commercial anesthetics, since it does not genotoxic, therefore it becomes a safe and adequate product to anesthetize fish in handling procedures.

Key words: genotoxic effects, benzocaine, Eugenol, *lippia alba*

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SYSTEMIC INFLAMMATION AND DNA DAMAGE DETECTED IN SURGICAL PATIENTS ANESTHETIZED WITH DESFLURANE*

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Anesthetics may influence the inflammatory response by altering cytokine profile and the expression of genes responsible for the production of inflammatory mediators, which can lead to DNA damage. Desflurane is the newest volatile halogenated anesthetic to be introduced in clinical practice, and little is known regarding possible genetic and inflammatory effects of this agent. Since inflammation and genotoxicity are linked events, it is important to evaluate these effects in anesthetized patients. This study evaluated inflammatory cytokines and their gene expression along with DNA damage in surgical patients anesthetized with desflurane. A total of 16 adult patients who underwent minimally invasive otorhinological surgeries under desflurane anesthesia was assessed before anesthesia and after the surgical procedure. The comet assay was applied to assess DNA lesions, while the cytokines IL-1β, IL-6, IL-8, IL-10, IL-17A and TNF-α were evaluated in serum by flow cytometry. In addition, the altered cytokines were also evaluated by gene expression by quantitative real-time polymerase chain reaction (qPCR). Results: A genotoxic effect was observed (P=0.027), and pro-inflammatory IL-6 and IL-8 levels were significantly increased after surgery (P=0.001 and P=0.02, respectively), whereas the levels of the other cytokines did not significantly change. IL-6 and IL-8 gene expression was unaltered (P>0.05). Anesthetic maintenance with the modern agent desflurane during minor surgeries led to genotoxic and inflammatory effects without altering the expression of inflammation related- genes the day after surgery in healthy patients. Thus, desflurane genotoxicity is linked to inflammatory response.

Key words: Systemic inflammation, DNA damage- desflurane

***Financial support**: FAPESP, CNPq and CAPES

EVALUATE OF METALS IN FISH SCALES WITH LOW IMPACT TECHNIQUES TO CONSERVATION OF FISHING STOCKS*

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The analysis of metals in fish is an important environmental monitoring tool as the scales are directly exposed to a variety of toxic agents and contaminants. The objective of this study was to evaluate the efficiency of Laser-Induced Breakdown Spectroscopy (LIBS) to detect the presence of bioaccumulated Fe and Pb in scales of *Prochilodus lineatus*, and to compare the results from this technique with those obtained using the conventional atomic absorption spectrometry technique. The study used fish collected in the Amambai River, Upper Paraná River, Brazil. The LIBS technique detected the presence of Fe and Pb in *P. lineatus* scales on different regions. The Atomic Absorption Spectrometry were measured in triplicate. *P. lineatus* scales presented two Fe peaks in the regions 260.27 and 261.36 nm, and two Pb peaks (260.77 and 260.94 nm) at different regions on the outer side of the scales. Pb was not detected using atomic absorption spectrometry in either species because the concentration of this element was below the limit of detection of this technique. Using atomic absorption spectrometry, we verified Fe concentration in scales. The LIBS technique was efficient in detecting Fe and Pb in scales of the one species analyzed, proving to be a promising tool for environmental monitoring. Also, when applied to fish scales, it does not require animal sacrifice for collection of biological material. The results show that fish scales can be used as environmental bioindicators to evaluate potential risk for the ichthyofauna and, consequently, for the humans that consume these fishes.

Key words: *Prochilodus lineatus*, bioindicators, hierro, plomo

***Acknowledgment:** CAPES, FUNDECT and UEMS.

BIOACCUMULATION OF IRON IN SCALES OF *P. lineatus*

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Scales can accumulate contaminants, acting as a chemical fingerprint of the environmental pollution events to which the fish has been exposed. The objective of this study is to evaluate concentration of iron in fish scales in comparison to the results to bioaccumulation in muscle and liver of *P. lineatus*. This study was developed using fish collected in the Amambai River, Upper Paraná River, Brazil. Concentration of Fe in scales, muscle and liver of *P. lineatus* were analyzed using Atomic Absorption Spectrometry and measured in triplicate at the main atomic wavelength for the multielement determination of Fe (0.2-4.0 mg L^{-1}). To compare the data, we use a non-parametric Kruskal-Wallis test. We identified that the bioaccumulation of iron in the scales of *P. linetaus* presented the same concentration in comparison to the muscle and the liver ($p=0.22$). Scales in fish are considered to be excellent environmental bioindicators and are widely used to evaluate the health and condition of aquatic ecosystems, are directly exposed to a variety of toxic agents and contaminants. Also, when applied to fish scales, it does not require animal sacrifice for collection of biological material. The results show that fish scales can be used as environmental bioindicators to evaluate potential risk for the ichthyofau.

Key words: *Prochilodus lineatus*, aquatic ecosystems, bioaccumulation

RELATIONSHIP BETWEEN EXPOSURE TO ARSENIC AND LIPID PEROXIDATION IN INHABITANTS OF THE PERUVIAN ANDES*

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In Peru there is a widespread contamination by arsenic in water for human consumption that in many cases exceeds the limit established by the WHO. The generation of reactive oxygen species (ROS) is associated with the metabolism of arsenic and its toxic effects. The objective of this study was to investigate the relationship between arsenic exposure and serum lipid peroxidation levels as an indicator of oxidative stress in an Andean population in Peru. Prior a signed informed consent, blood and urine samples were collected from residents of 2 districts of the province of Jauja located at 3430 m above sea level. Sixty-six villagers from the Molinos district participated as an exposed group (47 µg / L of As in drinking water) and thirty-three from the Apata district as a control group (5 µg / L of As in drinking water). The concentration of arsenic in the first urine was determined using atomic absorption spectrometry by generation of hydrides (HG-AAS), the concentration of urine wascorrected by creatinine determination by the Jaffe method, the concentration of TBARS was analyzed in serum using the colorimetric method proposed by Buege. The inhabitants of Molinos showed higher levels of As in urine> 20 µg / g creatinine and the serum TBARS levels in Molinos population was significantly higher than the Apata group and correlated directly with the levels of As in urine. Thus, As exposure in drinking water is generating oxidative stress of the studied population.

Key words: Arsenic, reactive oxygen species

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EVALUATION OF GENOTOXIC RISK AND HEALTH STATUS IN A GROUP OF VOLUNTEERS AFTER SUPPLEMENTATION WITH A NOVEL ORAL FORMULATION OF COENZYME Q10

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The deficiency of Coenzyme Q10 (CoQ10) is a rare disease associated with various pathologies. The treatment is the supplementation of up to 50mg/kg/day; therefore, it is necessary to develop a safe pharmaceutical form containing high doses of CoQ10. The aim of this study was to evaluate the genotoxic safety of CoQ10 supplementation in a novel matrix (oleogel), in addition to determine the plasma concentration of coenzyme, other antioxidants and glutathione. A dose of 1000mg/day of CoQ10 contained in an oleogel was administered to 10 healthy volunteers for 14 days. Non-simultaneously, the same dose in a commercial form (capsule) was supplied to the participants. The genotoxicity was evaluated by the cytome assay in peripheral blood lymphocytes. The plasma concentrations of the oxidative parameters were quantified by HPLC. Furthermore, the general health status of the participants was monitored through the determination of biochemical parameters. The results did not show a significant difference (p>0.05) between the frequencies of the genotoxicity biomarkers (micronuclei, buds or nucleoplasmic bridges) after supplementation with oleogels or capsules. In addition, a significant increase (p<0.05) in the plasma concentration of CoQ10 was observed after both supplementations, being significantly higher with oleogels. The increases in vitamin C as well as in the oxidized and reduced glutathione levels were not different between the pharmaceutical forms, while a greater increase in vitamin E was observed after consumption of capsules. Regarding the biochemical parameters, they remained within the expected reference ranges. In conclusion, the consumption of the innovative oral formulation (oleogel) did not represent a genotoxic risk and showed a higher plasma concentration of the coenzyme compared to the capsule.

Key words: Coenzyme Q10, vitamin C, vitamin E

DNA DAMAGE AND DEVELOPMENT OF PTERYGIUM PRODUCED BY SOLAR RADIATION IN WOMEN OF LAKE POOPÓ-BOLIVIA EXPOSED TO ARSENIC. PRELIMINARY REPORT

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Despite extensive research on the toxicity of arsenic to humans, possible synergies between metals and ultraviolet solar radiation, and their deleterious effects on human health have had little epidemiologic investigation. Experimental studies have shown that arsenic acts as a co-carcinogen to induce oxidative damage to DNA and impair the mechanism of damage repair induced by UV-R. Communities around Lake Poopó in Bolivia living in a region that receives the most solar radiation in the world (8,5kWh/m^2), but they are also exposed at high levels of inorganic arsenic through drinking water (46 to 130 µg /L). The aim of this study was to evaluate the effect of Arsenic exposure and solar radiation on the development of genetic damage and eye effects in women in the Lake Poopó areas. Urinary arsenic was measured by HPLC-HG-ICP-MS and the genetic damage was assessed by the comet assay. The study included 78 adult women, a high prevalence of pterygium (40%) was found correlated with prolonged sun exposure, total arsenic concentration in urine, years of residence, and percentage of genetic damage was observed. In conclusion, exposure to arsenic is an additional risk factor for the development of ocular and genetic damage in the study population, but future studies are needed to confirm this risk association.

Key words: Arsenic, solar radiation, UV-R

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GENOTOXIC INDEX IN FISH IN TWO SUB-BASIN IN THE SOUTHERN PANTANAL - BRAZIL*

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The fish genotoxicity index is an important environmental monitoring tool. This work aimed to evaluate the Genotoxicity Index of *Leporinus friderici* and *Prochilodus lineatus* in two sub-basins of the Southern Pantanal. We analyzed 2000 erythrocytes per slide, resulting in a total of 4000 cells for each individual. The Genotoxicity Index (GI), was calculated as the total number of altered cells divided by total cells observed. To evaluate the GI between the sub-basins we used a t-test (α=0.05). In total, 13 individuals of *P. lineatus* were analyzed in the Negro River sub-basin and 14 in the Apa River sub-basin. For the *L. friderici* species, 21 individuals were analyzed in the Negro River sub-basin and 4 in the Apa sub-basin. We identified six types of nuclear alterations: Notched nuclei, Nuclear budding, Vacuolated nuclei, Nuclear pyknosis, Binucleated cell and Lobed nuclei. The most frequent alteration in fish erythrocytes in the sub-basins were followed by Lobed nuclei. In the Apa River sub-basin it presented higher frequencies of nuclear alterations for *P. lineatus* ($p<0.001$) and for *L. friderici* species ($p=0.018$), in comparison to the sub-basin of Negro River. The analyzed species presented indicative of genotoxic potential, and in larger proportions in the sub-basin of the Apa River, demonstrating that in the aquatic environment there is presence of contaminants that are affecting the integrity of the DNA of the fish, needing complementary studies.

Key words: Genotoxicity, *Leporinus friderici*, *Prochilodus lineatus*

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GENOTOXIC POTENTIAL IN STREAMS FISHES OF HEADWATERS IN SOUTHERN PANTANAL OF MATO GROSSO DO SUL*

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The metals of natural fonts and antrhropogenics are continualy lanced in rivers are serious threats because of their toxicity, and that can cause an disequilibrium in the aquatic biota. With the objective of evaluated the environmental genotoxic concentrations of Nickel, Chrome and Lead cause in *Prochilodus lineatus* and *Leporinus friderici* in headwaters rivers of southern Pantanal, the samplings were realized between 2017 and 2018. In rivers of Upper Basin Paraguay. The concentrations of metals were mensurated by Flame Atomic Absorption Spectrophotometry. The genotoxocity assay were evaluated with erythrocytes. The dates weres collect by Multiple principal correspondence analysis. The nine copies of *L. friderici* and eight of *P. lineatus* presented diferents concentrations of Ni, Cr and Pb, being identified the following dameges: invaginação nuclear, binucleated cell , lobed nuclei, vacuolated nuclei, vacuolated nuclear pycnosis, vacuolated cytoplasm and micronuclei assay. How grower is the concentration of Cr, Ni, and Pb ($p=0.024$) in the mucle fish, higher were the genotoxic damages, contrasting the lobed nuclei. The frequency of lobed nuclei can lead to aneuploidy and the micronuclei generation. Being that the Pb, even in low concentrations is toxic to the aquatic biote. Probably, the presence of those metals can be related with the farming activities, and accordingly that ciliary cover are reduce, carrying contaminants at the river course. Therefore, this study can serve as a basis for future research and constitutes an important source of environmental diagnosis.

Key words: Genotoxic, *Leporinus friderici*, *Prochilodus lineatus*

***Acknowledgment:** FUNDECT and UEMS.

CELLULAR ALTERATIONS OF THE MOUTH EPITHELIUM IN WORKERS OCCUPATIONALLY EXPOSED IN HEMODYNAMICS AND NUCLEAR MEDICINE*

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Hemodynamics and Nuclear Medicine are studies where ionizing radiation is used, the first one allows to obtain radiological images by the transmission of X-rays from a fluoroscopic equipment, and the second acquires the images by detecting the radiation emitted from the patient. Although there is a variability of factors that induce genetic damage, exposure to radiation is one of them. The objective of the present investigation was to evaluate the frequency of cellular alterations in the buccal mucosa epithelium, in hemodynamics and Nuclear Medicine, in comparison with a control group, using the micronucleus test. The methodology consisted of scraping the buccal mucosa depositing the sample in the porta objects, the leaves were fixed with the farmer, and finally they were stained with the solution saturated with methylene blue. The normal cells for the control group are 73.86%, while for the group exposed in hemodynamics 70.52% are normal, 16.84% represent 8 cellular alterations and the group exposed in Nuclear Medicine states that the 68 , 2% are normal cells and 22.7% belong to 10 types of cellular alterations. For the group exposed in hemodynamics, the cells with cariolysis (CAR) and binucleated (BN), showed statistical significance in the media, while, for the group assigned to Nuclear Medicine, the cells: micronucleated (MN), hyperchromatic (HC), karyorexics (CA) and condensed chromatin (CR). Lobed (CL), pyknotic (CPIC), trinucleate (TN) and apoptosis (AP) cells do not mean significant statistics in the means.

Key words: Nuclear Medicine, biomonitoring, cellular alterations.

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BASAL FREQUENCIES OF MICRONUCLEI IN THREE FISH SPECIES FROM COASTAL AND FRESHWATER ECOSYSTEMS OF ARGENTINA

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Aquatic ecosystems are impacted by different types of anthropogenic pressures. Hence, to evaluate health status of organisms in these habitats becomes important. The objective of the present work is to analyze the frequency of micronuclei (MN) and other nuclear abnormalities (NA) in different fish species representative of coastal and freshwater ecosystems. This work is included in a major project that attempts to evaluate in a temporal scale the anthropogenic pollution of Mar del Plata city coast and the Mar Chiquita coastal lagoon basin in Argentina. The following species were selected as biomonitors: *Oligosarcus jenynsii* from Nahuel Ruca lagoon, *Odontesthes argentinensis* from Mar Chiquita coastal lagoon, and *Gobiosoma hemigymnSum* from Mar del Plata's harbour. Blood samples were obtained in summer 2018 from mentioned species and blood smears were prepared, fixed in methanol and stained with Giemsa 15% for their observation by microscopy at 1000X. Obtained results showed basal frequencies (mean± s.d.) for *O. jenynsii* of 1.35± 0.58 and 6.75± 5.05, for *O. argentinensis* of 1.07± 1.54 and 5.29± 1.58, and for *G. hemigymnum* of 2.97± 1.49 and 149.81± 29.78 for MN and AN, respectively. These are the first data obtained from the first sampling period, and they will be completed after five years of project by analyzing correlations of these biomarkers of genotoxicity with fisico- chemical characteristics of the water as well as measurement of pollutants.

Key words: Aquatic ecosystems, *Oligosarcus jenynsii,Odontesthes argentinensis, Gobiosoma hemigymnSum*

BIOMONITORING BUCAL CELLS OF WORKERS EXPOSED TO IONIZING RADIATIONS IN ASSISTANCE CENTERS OF ASUNCION-PARAGUAY IN 2017*

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Diagnostic radiology facilitates the diagnosis of diseases, however, the induction of micronuclei was discovered after exposure to radiation, since then the appearance of micronuclei under normal and pathological conditions has been described. The objective of this work was to evaluate the frequency difference of micronucleus in cells of the buccal epithelium between people not exposed to ionizing radiation and exposed workers of the conventional radiology area. The methodology consisted in evaluating two groups: one control (which allowed obtaining normal parameters of genetic alterations in buccal epithelial cells) and another one exposed to ionizing radiation in the conventional radiology area. To obtain samples of epithelial cells, the scraping of the buccal mucosa was carried out, subsequently, the smear was made on a sterile slide, fixed with Farmer and stained with Giemsa. In the control group, 0.78% corresponded to micronucleated cells, binucleated cells and cells with a nucleus in karyonosis. While for the exposed group, 9.36% corresponds to seven types of alterations; micronucleated cells, binucleated cells, cells with lobulated nuclei, cells with carriorresis, cells with apoptosis, hyperchromatic cells and trinucleated cells. Statistical analysis revealed that individuals exposed to ionizing radiation in the Conventional Radiology area have more micronucleated cells in averages than non-exposed individuals. In addition, it has been found that the average micronucleus is significantly higher in the exposed population because of the worker's chronic exposure to ionizing radiation acts as a mutagenic agent.

Key words: biomonitoring, genotoxicity, ionizing radiation.

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EVALUATE OF METALS IN FISH SCALES WITH LOW IMPACT TECHNIQUES TO CONSERVATION OF FISHING STOCKS*

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The analysis of metals in fish is an important environmental monitoring tool as the scales are directly exposed to a variety of toxic agents and contaminants. The objective of this study was to evaluate the efficiency of Laser-Induced Breakdown Spectroscopy (LIBS) to detect the presence of bioaccumulated Fe and Pb in scales of *Prochilodus lineatus*, and to compare the results from this technique with those obtained using the conventional atomic absorption spectrometry technique. The study used fish collected in the Amambai River, Upper Paraná River, Brazil. The LIBS technique detected the presence of Fe and Pb in *P. lineatus* scales on different regions. The Atomic Absorption Spectrometry were measured in triplicate. *P. lineatus* scales presented two Fe peaks in the regions 260.27 and 261.36 nm, and two Pb peaks (260.77 and 260.94 nm) at different regions on the outer side of the scales. Pb was not detected using atomic absorption spectrometry in either species because the concentration of this element was below the limit of detection of this technique. Using atomic absorption spectrometry, we verified Fe concentration in scales. The LIBS technique was efficient in detecting Fe and Pb in scales of the one species analyzed, proving to be a promising tool for environmental monitoring. Also, when applied to fish scales, it does not require animal sacrifice for collection of biological material. The results show that fish scales can be used as environmental bioindicators to evaluate potential risk for the ichthyofauna and, consequently, for the humans that consume these fishes.

Key words: metal, fish scale, conservation

***Acknowledgment:** CAPES, FUNDECT and UEMS.

BIOACCUMULATION OF IRON IN SCALES OF *P. lineatus**

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Scales can accumulate contaminants, acting as a chemical fingerprint of the environmental pollution events to which the fish has been exposed. The objective of this study is to evaluate concentration of iron in fish scales in comparison to the results to bioaccumulation in muscle and liver of *P. lineatus*. This study was developed using fish collected in the Amambai River, Upper Paraná River, Brazil. Concentration of Fe in scales, muscle and liver of *P. lineatus* were analyzed using Atomic Absorption Spectrometry and measured in triplicate at the main atomic wavelength for the multielement determination of Fe (0.2-4.0 mg L^{-1}). To compare the data, we use a non-parametric Kruskal-Wallis test. We identified that the bioaccumulation of iron in the scales of *P. linetaus* presented the same concentration in comparison to the muscle and the liver ($p=0.22$). Scales in fish are considered to be excellent environmental bioindicators and are widely used to evaluate the health and condition of aquatic ecosystems, are directly exposed to a variety of toxic agents and contaminants. Also, when applied to fish scales, it does not require animal sacrifice for collection of biological material. The results show that fish scales can be used as environmental bioindicators to evaluate potential risk for the ichthyofauna.

Key words: *Prochilodus lineatus*, bioaccumulation, aquatic ecosystems

***Acknowledgment:** CAPES, FUNDECT and UEMS.

MOLECULAR DETECTION OF CLONALITY IN T CELLS IN PARAGUAYAN PATIENTS DIAGNOSED WITH LYMPHOID NEOPLASMS*

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In the process of maturation of T lymphocytes, the T cell receptor (TCR) reorganizes the gene segments, giving rise to a new and unique configuration of DNA. In T lymphoid neoplasms (TLN), clonal proliferation occurs from a single T cell. T-cell lymphomas are often difficult to diagnose by morphology and immuno-histochemistry. The neoplastic T-cell infiltrates can be polymorphous and are sometimes difficult to separate from benign T cells by immunohistochemistry. Demonstrating an aberrant immunophenotype is often not possible, even with flow cytometry. For these reasons, the molecular methods are important for demonstrate the presence of a clonal T-cell population**.** The aim of this study was the detection of cell clonality by means of molecular techniques (PCR) in patients diagnosed with lymphoid neoplasms. DNA was isolated from 64 paraffin samples of patients with presumptive diagnosis of NLT. The T cell receptor gene was amplified by qualitative PCR. The products were revealed by high resolution electrophoresis with polyacrylamide. 64 patients were studied. 14/64 (22%) with presumptive diagnosis of mycosis fungoides, 25/64 (39%) were suspected of T cell lymphoma, 7/64 with pseudolymphomas and 18/64(28%) were other TLN. Clonality was detected in 33/64 patients (52%) confirming the diagnosis of T cell Lymphoma**.** The clonality of T lymphocytes was detected by molecular biology with a good agreement between the molecular results and those obtained by; morphological study, immunohistochemical and immunophenotype. Highlighting some cases in which the clinic was inconclusive and the molecular study contributed to the diagnostic accuracy.

Key words: clonality, T cells, lymphoid neoplasms

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STANDARDIZATION OF FLUORESCENCE IN SITU HYBRIDIZATION TECHNIQUE (FISH) FOR THE DETECTION OF CHROMOSOMAL MICRODELETIONS

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The fluorescence *in situ* hybridization technique (FISH) involves the hybridization of a probe (DNA segment) labeled with fluorophores to a chromosomal target *in situ*, it's widely used for the visualization, identification and study of chromosomes, especially to detect numerical or structural anomalies. The aim of this investigation was to standardize the FISH technique in cytogenetics laboratory of Instituto Investigaciones en Ciencias de la Salud (IICS) for the detection of chromosomal microdeletions, in the project funded by the Conacyt (14-INV-456). As a result of the first stage of the pilot plan, six determinations were made using the Vysis® commercial probe protocol for the critical region of Prader-Willi/ Angelman syndrome (15q11-q13) on which the adaptations and modifications that led to the standardization; subsequently, peripheral blood samples were taken from 17 patients with clinical suspicion for chromosomal microdeletion, nine for the SRY gene (Yp11.3), three for Prader-Willi syndrome (15q11-q13), two for William's syndrome (7q11.23) , one for Di George syndrome (22q11.2) and two for the 1p36 microdeletion syndrome. Hybridization signals were observed with fluorescence microscopy using specific filters for Dapi, Green and Orange spectra. One hundred cells were analyzed for each sample, taking photographic records. The standardization and incorporation of the FISH technique was achieved, vital to improve the quality of the healthcare service, offering patients an analysis of greater specificity that can contribute to a certainty diagnosis.

Key words: Molecular cytogenetics, hybridization *in situ*, microdeletions.

EVALUATION OF MUTAGENIC EFFECT OF YPACARAÍ LAKE EFFLUENT BY ALLIUM TEST

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Ypacaraí Lake, located in the Cordillera Department, suffers from contamination problems decades ago. The beaches are full of toxic algae of wastewater, industrial waste and garbage, this research work was carried out to analyze the mutagenic level of Lake Ypacaraí in *Allium cepa* roots grown in contaminated water taken from three different points, San Bernardino, Middle Lake and Coast of Aregua Beach. To evaluate the mutagenic damage, 3000 cells were counted, the mitotic and phase index for each sample was made and the types of anomalies were identified and counted. In station 1 San Bernardino, the mitotic index was 36.8%, 25.7% in prophase, 9.3% in metaphase, 0.4% in anaphase and 1.07% in telophase, 0.4% c-metaphases, 0.2% advanced chromosomes, 0.1% lagged chromosomes, 0.3% chromosomal bridge, 0.03% Rings, 0.03% Sticky Chromosomes and 0.03% micronucleus. In station 2 Middle Lake Ypacaraí, the mitotic index was 8.4%, 2.6% in prophase, 1.6% in metaphase, 0.8% in anaphase and 1.7% in telophase. We observed 0.7% of c-metaphases, 1.5% of advanced chromosomes, 0.1% of lagged chromosomes, 0.2% chromosomal bridge and 0.1% of Binucleated cells. In station 3 Aregua, the mitotic index was 1.5%, that of phases was 4.2%, of prophase, 2.5%, of metaphases, 2.4% of anaphases and 4.07% of telophase. We observed 0.8% of c-metaphases, 1.6% of advanced chromosomes, 0.6% of lagged chromosomes, 0.9% with chromosomal bridge, 0.09% Sticky chromosomes and 0.2% of Binucleated cells. With these results it is concluded that Ypacaraí lake presents high cytotoxicity indexes.

Key words: Mutagenic, Ypacaraí Lake, meristematic cells

TERATOGENIC EFFECTS OF VANCOMYCIN ON THE EMBRYONIC DEVELOPMENT OF *Gallus gallus domesticus*

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Vancomycin is an antibiotic widely used against infectious diseases, categorized as a teratogenic drug by the FDA (Food and Drug Administration), however, so far has not shown any conclusive information about the adverse effects that could occur in animals and humans. For it, the main objective of this research was to determine the teratogenic effects of vancomycin at different concentrations on the embryonic development of *Gallus gallus domesticus*. For this, a stock solution of 25 $mg.mL^{-1}$ of Vancomycin was made, and from this, dilutions were obtained for doses of 15 and 5 $mg.mL^{-1}$; and 0.9% saline was used as a control group. A total of 20 fertile eggs were treated by exposure to 0.2 mL of different doses (25, 15 and 5 $mg.mL^{-1}$) for 10 days during the embryonic development; treatments were performed for five repetitions. The data were analyzed using the KrusKal-Wallis test and Dunn's *post-hoc* test, in which significant differences were observed ($p < 0.05$) in the length of the extremities of the right and left wings, right tarsi and left, aborted embryos and malformations such as eviscerations, weight reduction and size of embryos at higher doses were also found. The results suggest that vancomycin has teratogenic effects on the development of *G. gallus domesticus* embryos, being the doses of 15 and 25 $mg.mL^{-1}$ those that had greater effect on morpho-anatomical development of embryos.

Key words: malformations, embryos, birds, vancomycin, antibiotic.

DNA DAMAGE INDUCED BY EXPOSURE TO PESTICIDES IN CHILDREN OF RURAL AREAS IN PARAGUAY

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Chronic exposure to pesticides can damage DNA and lead to cancer, diabetes, respiratory diseases, neurodegenerative and neurodevelopment disorders. To determine the frequency of DNA damage through the Comet assay and Micronucleus test in two populations of children. We formed two groups of children from 5 to 10 years old. For each child we studied 2000 cells for the micronucleus test and 200 cells for the comet assay. The exposed group (n = 43), born and currently living in a community dedicated to family agriculture and surrounded by transgenic soybean crops and the Control Group (n = 41) born and living in a community dedicated to family agriculture with biological control of pests. The comparison between exposed and control children revealed statistically significant differences in all biomarkers studied for the measurement of genetic damage-cell death and DNA damage: the median of micronucleus was higher in the exposed group (6 vs 1) ($p < 0.001$). Binucleated cells (2.9 vs. 0.5; $p < 0.001$) Broken eggs (5.5 vs 1.0, $p < 0.001$) Karyorrhexis (6.7 vs 0.5, $p < 0.001$) Kariolysis (14.0 vs 1.0, $p < 0.001$) Pyknosis (7.4 vs 1.2, $p < 0.001$); Condensed Chromatin (25.5 vs 7.0, $p < 0.001$). The Comet Assay exposed vs not Exposed: Tail Length (59.1 vs 37.2); Tail Moment (32.8 vs. 14.4); Tail Moment Olive (15.5 vs 6); % DNA Tail (45, 2.1 vs 27.6) % DNA Head (54.8 vs 72.4). In children exposed to pesticides, we observed a greater genotoxic and cytotoxic effect compared to non-exposed children.

Key words: Biomonitoring; Buccal micronucleus cytome assay; Children; Comet assay; DNA; Pesticides.

ANTIGENOTOXIC PROTECTIVE EFFECT OF VITAMIN E AND OF β-CAROTENE EVALUATED BY THE COMET ASSAY AND THE MICRONUCLEUS TEST IN FEMALE RECYCLERS EXPOSED TO CONTAMINANTS OF THE CATEURA LANDFILL IN ASUNCIÓN PARAGUAY

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The garbage that arrives daily at the landfill is classified and separated by recyclers called "hooks", who are exposed to a complex mixture of pollutants that according to previous studies have genotoxic and cytotoxic activity. The objective of this research was to evaluate the anti genotoxic protective effect of vitamin E and β carotene in women who recycle garbage who live and work in the landfill. For this purpose, they followed a 4-month treatment with daily vitamin E and β carotene supplements and a complementary diet was suggested. The level of damage was evaluated at the beginning and at the end of the treatment, using the bioassays of the comet and the micronucleus test as biomarkers of damage in the genetic material. It was observed that the% of DNA in the comet's tail decreased by 64% after of the treatment with vitamins and the nutritional plan proposed for each participant and therefore there is a significant difference ($p < 0.05$ according to the Wilcoxon tests, and the ANOVA analysis and the student F and t tests. Likewise, they were observed also, significant differences between the frequencies of MN and the other cell abnormalities before and after treatment with Vitamin E and β-carotene, for ANOVA tests with a $p < 0.05$.

Key words: Antigenotoxic, vitamin E, β caroteno, landfill

LIPIDIC PEROXIDATION IN WORKERS EXPOSED TO LEAD IN "CERCADO DE LIMA" PRINTING PRESSES. LIMA-PERU

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Lead is a heavy metal present in the environment as a pollutant that at moderate levels of chronic exposure generate biochemical and functional changes. Despite not having a unique mechanism of toxicity, it has been shown that lipid peroxidation plays a fundamental role. The objective of this study is to find the relationship between blood lead levels and lipid peroxidation measured by levels of TBARS (thiobarbituric acid reactive substances) as an indicator of oxidative stress in workers of the "Cercado de Lima" printing press. Forty subjects between the exposed and the control group participated in the study, who filled out a survey and signed the informed consent, then 5mL of venous blood were extracted in metal-free heparin tubes, which were kept in a cold chain for later analysis. The quantification of lead was performed by the atomic absorption with graphite oven while the concentration of TBARS was obtained by the formation of the MDA adduct with thiobarbituric acid (TBA) readed by Uv-Visible spectrophotometry. The exposed group was confirmed by workers with 45 years old average who worked in the printing press for more than 9 years. The concentrations of lead in blood in the workers of the press did not exceed the exposure values established by the WHO (40 $ug.dL^{-1}$), however, our results showed a significant direct relationship ($p < 0.01$) between the concentration of lead and the TBARS concentration in those workers with blood lead levels above 5 $ug.dL^{-1}$.

Key words: Lipidic peroxidation, Uv-Visible spectrophotometry, thiobarbituric acid reactive substances

PHYTOREMEDIATION OF EFFLUENTS FROM TANNERIES TREATED WITH *Echicornia crassipes* EVALUATED BY THE MICRONUCLEUS TEST IN *Danio rerio* ERYTHROCYTES

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The contamination of water courses by heavy metals is a problem that threatens ecosystems and human health.The use of aquatic plants for the removal of residual pollutants from both urban and industrial origin, is an advantageous technology due to its low cost and relative ease of construction. Floating macrophytes have enormous potential to accumulate heavy metals in their tissues that they have taken from the environment where they are found, so they have been used for bioremediation mechanisms. This research was proposed to evaluate using the micronucleus technique in *Danio rerio*, the genotoxicity of effluents from tanneries treated with *Echicornia crassipes* as a mechanism of phytoremediation. For this purpose, scale tests were first performed to measure the absorption capacity of cr III of the selected plant and physical chemical parameters were measured such as: chemical oxygen demand or (COD), total phosphorus (P), N-Ammoniacal (N-NH4), NTK (N), sulfides (S2-) and chromium. The genotoxicity of the wastewater resulting from phytoremediation was evaluated using the micronucleus technique in *Danio rerio* erythrocytes before treatment with the plant and after treatment with E cressipes. It was observed that the plant removed more than 50% of Cr III from the effluent, and the other chemical physical parameters had a removal percentage of 23, 15, 10, 22, 93 for COD, P, N-NH4, NTK and sulfides, respectively, also finding that the frequency of MN in Danio erythrocytes decreased significantly by 60% after treatment with E cressipes.

Key words: phytoremediation, *Echicornia crassipes, Danio rerio, tanneries*

EXPOSURE TO ARSENIC IN DRINK WATER AND ITS ASSOCIATION WITH OXIDATIVE DAMAGE TO DNA IN RURAL POPULATIONS OF SANTA FE, ARGENTINA

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The presence of arsenic (As) in the environment is a high frequency event, detected in a different country among which is Argentina. The As was classified by the IARC as a carcinogenic agent for humans based on epidemiological studies that relate its ingestion and the development of cancer. The groundwater of the province of Santa Fe, Argentina, naturally contains As in different concentrations. The objective was to carry out an ecological study to evaluate the association between the levels of As in drinking water and the oxidative damage to DNA in seven rural populations belonging to three departments of the province of Santa Fe (n = 308). Concentration means found in the groundwater expressed in µg / L were for Providencia: 163; Humboldt: 106; Presidente Roca: 59.4; Santa Clara de Saguier: 59.79; Lehmann: 60.5; Nelson: 32 and Laguna Paiva: 43. A structured interview showed that 44% of the inhabitants declared to consume safe water, 25% consume underground water and the rest only consume safe water to drink but not to cooking food. These results are associated with those obtained from the urinary excretion of As (µg/g creatininuria). This categorization allowed to evaluate the results of oxidative damage to the DNA by Comet assay modified with the addition of Endonuclease III, showing statistically significant differences between two exposed groups evaluated through Endo Sites (54.9 ± 4.8 and 53 , 5 ± 5.3) with respect to the group that does not consume water with As (38.9 ± 3.3). The communication of results to volunteers, to the rest of rural populations and to health authorities of the province can collaborate with risk management.

Key words: Arsenic, oxidative damage to DNA

CURSOS DURANTE EL CONGRESO

BASIC CONCEPTS ON BIOLOGICAL DOSIMETRY

Lecturer

Wilner Martínez-López,PhD

Biodosimetry Service .Academic Unit on Radiation Protection (UARP), Instituto de Investigaciones Biológicas Clemente Estable (IIBCE) - Faculty of Medicine - Universidad de la República (UdelaR) Montevideo - Uruguay

Course Program

Thursday 25

•The basic nature of radiation
•Biological effects of ionizing radiation
•DNA damage and repair
•What is a Biodosimetry?
•Absorbed dose
•Endpoints for biological dosimetry
•Dicentric assay
•Retrospective dosimetry

Friday 26

•Premature chromosome condensation (PCC) analysis
•Cytokinesis block micronucleus (CBMN) assay
•Dose effect calibration curve
•Applied statistics for biological dosimetry
•Automatic analysis of chromosomal assays
•Molecular biomarkers for ionizing radiation
•Biodosimetry in mass casualty events
•Biological Dosimetry role in radiological accidents occurred in Latin America
•(Mariana Cabitto, Nuclear Regulatory Authority - ARN, Buenos Aires, Argentina)

CURSO DE RADIO PROTECCIÓN

Disertantes

MsC Fredy Gómez, Lic. Analiz López & Lic.Yamila Rodriguez

Laboratorio de Ciencias Radiológicas e imagenología - Facultad de Ciencias Exactas y Naturales - Universidad Nacional de Asunción

Programa del curso

Capítulo 1: Principios de Protección Radiológica

Capítulo 2: Magnitudes dosimétricas.

Capítulo 3: Efectos Biológicos.

Capítulo 4: Clasificación de efectos biológicos.

Capítulo 5: Accidentes en Radiodiagnóstico.

CURSO DE MUTAGENESIS

Disertantes:
Marta Carballo, PhD, Marcela Lopez Nigro, PhD & Fabián Martínez Perafán, doctorando
Citogenética Humana y Genética Toxicológica) (CIGETOX), Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC), Dto Bioquímica Clínica, FFyB-UBA

Programa

1. **Toxicogenética.** Impacto de las alteraciones genéticas Mutagénesis. Teratogénesis. Carcinogénesis. Biomarcadores. Evaluación de daño inducido o espontáneo. Biomonitoreo mediante bioindicadores de exposición, susceptibilidad y efecto. Niveles de Evaluación de daño genético. Ensayos de corto (STT) plazo para la evaluación de daño. Batería mínima de STT.
2. **Test de Micronúcleo (MN).** Mecanismo de formación de micronúcleos. El test de MN como indicador de aneugenicidad y clastogenicidad, adaptaciones. Utilidad. Ventajas y desventajas. Criterios de identificación. Aplicación *in vitro* e *in vivo*. Método de bloqueo de la citocinesis. Ensayo CITOMA. Significado. Aplicación en distintos modelos experimentales y matrices. Monitoreo de poblaciones expuestas y en ensayos con fines regulatorios.
3. **Test de Cometa o Electroforesis en gel de una sola Célula.** Fundamentos de la técnica. Tipos de Daños evaluados mediante el Ensayo Cometa. Metodología y Controles. Análisis de Resultados: análisis visual vs software. Sensibilidad y especificidad. Cinética de reparación. Modificación del Ensayo Cometa por el uso de enzimas de restricción. Aplicaciones.

TALLER DE MENTORING

Facilitadoras

Ofelia Olivero[1] & Marta Carballo[2]

[1]Center for Cancer Training, National Cancer Institute. United States
[2]Citogenética Humana y Genética Toxicológica) (CIGETOX), Instituto de Fisiopatología y Bioquímica Clínica (INFIBIOC).Dto Bioquímica Clínica, FFyB-UBA

El taller de Mentoring dictado por las profesoras Doctoras Ofelia Olivero y Marta Carvallo ofreció a los participantes a conocer los fundamentos de la Mentoría. En el mismo se describieron los objetivos, los roles del mentor y del mentee, así como las ventajas del mismo para el desarrollo de mentores calificados que puedan replicar lo aprendido en sus diferentes instituciones de origen.

Mentoring es una de las técnicas más novedosas para el desarrollo de las competencias personales y profesionales. Consiste en la transmisión de conocimientos y experiencias por parte de un mentor a un mentee (estudiante). El mentor o tutor es la persona que invierte parte de su tiempo y esfuerzo en formar a otra, a quien se le transmite experiencia y conocimientos por medio de un aprendizaje colaborativo. De este modo, el mentor es un guía que ayuda al mentee, que lo asesora, estimula e instruye con el objetivo de impulsar su evolución personal y profesional desarrollando todo su potencial. El mentor ayuda a su discípulo a tomar decisiones, alcanzar sus metas y a superar sus retos, reforzando la capacidad de análisis.

Además, todos los buenos mentores deben estar dispuestos, donde puedan, a brindar oportunidades de aprendizaje, incluida la posibilidad de aprender del fracaso. Tanto los mentores como los aprendices deben apreciar el valor de celebrar el éxito y de la crítica constructiva. Y ninguno de los dos debería ver la relación como un boleto a prestigiosas invitaciones para hablar, o para impulsar publicaciones de alto impacto. En todo momento, la relación debe ser de confianza y respeto mutuo, y de comunicación abierta y transparente.

El mentee asume la responsabilidad de ¨dirigir¨ su propio desarrollo definiendo sus objetivos y estableciendo un marco de diálogo efectivo con su mentor que le permita compartir sus inquietudes, retos y aspiraciones por medio de un acuerdo fijado entre ambos, estableciéndose parámetros y límites para el mismo. Del cumplimiento de este proceso derivará una relación fluida y significativa para ambos

Las ventajas que el mentoring proporciona son infinitas, ya que no solo promueven el crecimiento personal y profesional del mentee, sino que garantizan una continua renovación y transmisión de los conocimientos para el desarrollo de las capacidades individuales. Sus efectos pueden ser notables y duraderos con la capacidad de transformar grupos de individuos y comunidades científicas.

S. P. G
Sociedad Paraguaya de Genética

I JORNADA DE LA SOCIEDAD PARAGUAYA DE GENÉTICA

Los temas desarrollados durante la Primera Jornada fueron

Minicurso dictado por la Ing. Agr. Crisanta Rodas Cardozo: **Aspectos a considerar en la Evaluación de Riesgo, Uso Actual, Potencial de los OGM y nuevas tecnologías.**

Simposis dados:

* Genética Forense en el Paraguay a cargo del MSc. Iván Mongelos Franco.

* Registro de defectos congénitos en el Paraguay a cargo de la Dra. Marta Elvira Ascurra de Duarte.

* Uso de datos genéticos aplicados a estudios de biodiversidad a cargo del Dr. Francisco Adolfo Brusquetti Estrada.

* La genética vegetal: avances y desafíos en Paraguay a cargo de la MSc. Claudia Diana Pereira Sühsner.

* Introducción y detección de la translocación 7DL.7Ag al germoplasma local de trigo a cargo de la MSc. Lourdes María Cardozo Tellez.

* Marcadores moleculares y sus usos en genética de poblaciones a cargo de la Lic. Cynthia Rivarola.

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A la Dra. María Magdalena Mayor, Decana de la Facultad de Ciencias de la Salud de la Universidad Católica Nuestra Señora de la Asunción

Al Prof. Lic. Nicolás Guefos, MAE, Decano de la Facultad de Ciencias Exactas y Naturales de la Universidad Nacional de Asunción

Al Dr. Francisco Santacruz, Director de Investigación de la Facultad de Ciencias de la Salud de la Universidad Católica Nuestra Señora de la Asunción

A Paul White, PhD, International Association of Environmental Mutagenesis and Genomics Societies

A la empresa:

A Mauricio Ruiz Maciel de la empresa Nineteen solutions

A los señores Hernán Ramírez y Luis Schmeda de la empresa CEDIAL

A la Sociedad Científica de estudiantes de Medicina de la Facultad de Ciencias de la Salud de la Universidad Católica Nuestra Señora de la Asunción

GUÍA PARA LOS AUTORES

Reportes Científicos de la FACEN, es una revista de acceso libre y gratuito y es la publicación científica oficial de la Facultad de Ciencias Exactas y Naturales de la Universidad Nacional de Asunción. Es emitida semestralmente y publica **Artículos originales**, **Artículos de revisión**, **Tópicos actuales**, **Reportes de casos**, **Comunicaciones cortas** y **Correspondencia**, en las áreas de Biología, Química, Física, Matemática Pura, Matemática Estadística, Geología, Biotecnología y Tecnología de Producción. Los principales criterios para la selección de los artículos son la solidez científica y la originalidad del tema. Los trabajos y opiniones publicados en la revista son de exclusiva responsabilidad de los autores. El idioma oficial de la revista es el español, pero se aceptan trabajos en inglés y en portugués. No existe costo de publicación para los autores.

El trabajo será enviado en formato electrónico a la dirección email de la revista (reportescientificos@gmail.com), consistiendo en archivos de texto, archivos de planilla electrónica y archivos de imagen. **El archivo principal de texto debe contener únicamente texto, sin ilustraciones ni tablas embebidas**, sino únicamente las respectivas citas a las mismas en el texto (numeradas secuencialmente). **Las tablas e ilustraciones deberán ser remitidos en formato digital en archivos independientes.** Los respectivos archivos deberán indicar en su nombre a qué número de tabla o ilustración corresponden.

El archivo de texto debe ser producido con Microsoft Word® u otro editor de texto perfectamente compatible. El texto deberá estar en letra Times New Roman, tamaño 11. Todo trabajo llevará en su primera página los siguientes elementos: **a)** el **Título** en español e inglés, **b)** la lista de **Autores** con nombre y apellido, **c)** la **Afiliación** laboral de cada autor, **d)** un **Resumen** de un máximo de 250 palabras en español, **e)** un máximo de 7 **Palabras clave** en español, f) un **Abstract** en inglés, correspondiente a la versión en español y g) un máximo de 7 **Key words** en inglés, correspondientes a la versión en español. **En caso de trabajos en Portugués** se añaden Título, Resumo y Palavras chave en dicho idioma. El resumen sólo podrá obviarse en el caso de Editoriales, Comunicaciones cortas y Correspondencias presentadas como tales. El cuerpo principal del texto podrá contener, según el contexto del trabajo, las secciones de **1) Introducción**, **2) Materiales y métodos (o sólo uno de ellos de acuerdo al caso)**, **3) Resultados**, **4) Discusión**, **5) Conclusión**, **6) Agradecimientos** y **7) Literatura citada**. Tales secciones podrán sufrir fusión o no existir, de acuerdo a la metodología de trabajo o enfoque dados por el autor, así como al tipo de escrito (Artículo original, Comunicación corta, etc.) como haya sido presentado por autor o como lo decida el comité editorial. **Los pies de figuras y tablas** deberán ir al final del texto, a continuación de la sección de literatura citada.

Las citas bibliográficas deberán seguir las normas APA. Según estas normas, el año va entre paréntesis y se destacan el autor y año en las citas en texto: "Según González (1999)" o "El método es reciente (González, 1999)". Para la lista en la sección de Literatura citada la secuencia lógica y formato es de "Autor. (Año). Título. Publicador, Volumen(Número): Páginas.", poniéndose siempre primero el apellido de cada autor, seguido de sus correspondientes iniciales y separados por comas, con el útimo autor separado por un signo de ampersant. Se aplicará cursivas respectivamente en el título si se trata de un libro o tesis, o en el publicador si se trata de un artículo. Se ilustra en los siguientes ejemplos:

González, A.P. (1999). *Métodos de análisis crítico.* Asunción: Editorial Nueva. 120 pp.

González, A.P., Martínez, G.T. & Robledo, H.A. (1999). Análisis de la producción científica del pais. *Revista de Filosofía Científica*, 45(2): 56-61.

Las tablas y cuadros deberán presentarse en archivos de Microsoft Excell® u otro programa perfectamente compatible, aunque en muchos casos se acptan también tablas embebidas en archivo de Microsoft Word®, siempre que sea en archivo separado del de texto. **Las ilustraciones (graficos, imágenes, fotos, dibujos, mapas, esquemas o láminas completas) deberán presentarse cada una en un archivo aparte**, en formato JPG o TIF, generados en Adobe Photoshop u otro programa de procesamiento de imágenes. Deberá cuidarse que posean buen enfoque, claridad y contraste, que tengan una resolución mínima de 300 dpi y máxima de 1000 dpi y teniendo en cuenta que su anchura máxima en la revista será de 16 cm.

El proceso de evaluación incluye una primera revisión por el Comité Editorial para determinar si el artículo corresponde a la línea editorial y si cumple con los criterios generales de publicación. Una vez que el artículo se considere pertinente, se someterá a por lo menos dos revisores especialistas en el tema, de cuya opinión depende la aceptación definitiva del artículo. Si existiera una contradicción en la opinión de ambos especialistas, se someterá al Comité editorial o en caso contrario se solicitará una tercera opinión de un tercer especialista. El dictamen podrá ser aceptado, rechazado o condicionado, que será comunicado por escrito al autor principal en un plazo no mayor de tres meses de la recepción del material original. Si el dictamen es condicionado, el autor deberá remitir la nueva versión impresa y en formato digital en el plazo que se le indique que no podrá exceder de los 30 días posteriores a la recepción de la comunicación.

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MEMORIAS DEL XI CONGRESO LATINOAMERICANO DE MUTAGÉNESIS, CARCINOGÉNESIS Y TERATOGÉNESIS AMBIENTAL

"Salud Global, Genes y Sociedad"

I Primera Jornada Paraguaya de Genética

25, 26 y 27 de abril, 2019
Asunción, Paraguay