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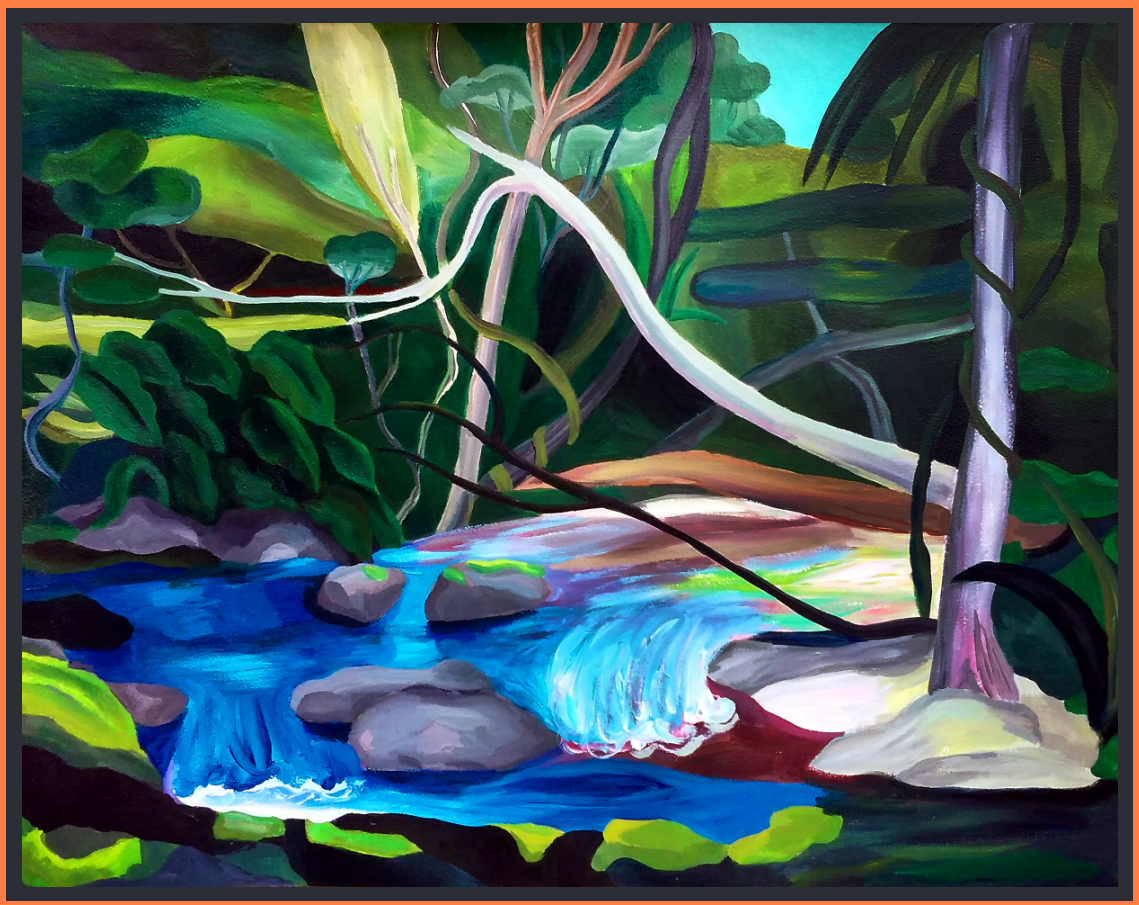

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25.9 %). Conclusion Antitumor and antimetastatic activity of luteolin enhance upon coordination.

477. 178. **EXPLORING NEUROPROTECTIVE EFFECTS OF STEVIOSIDE, A GLYCOSIDE DERIVED FROM *STEVIA REBAUDIANA*: *IN VITRO* AND *IN VIVO* STUDIES**

Pastore Valentina, Colettis Natalia, De Tezanos Pinto Felicitas, Marcos Alejandra, Marcucci Carolina, Rademacher Marina, Marder Mariel.
Instituto de Química y Fisicoquímica Biológicas Prof. Dr. Alejandro C. Paladini (IQUIFIB, UBA-CONICET). Facultad de Farmacia y Bioquímica, UBA. Junín 956, (1113) CABA, Argentina

Epilepsy is a chronic neurological disorder characterized by recurring seizures, with neuronal hyperexcitability and oxidative damage from free radicals being key factors in its development. Current antiepileptic drugs control seizures in 70% of cases, while 30% are treatment-resistant. In Latin America and the Caribbean, 68.2% of countries use natural resources for seizures. Medicinal natural products and structural modification of active compounds are sought for high-impact public health disorders. Several preclinical and clinical studies suggest the use of stevia (*Stevia rebaudiana* B.) and its derivatives with therapeutic and pharmacological applications, as they exhibit a variety of biological activities. Here, we evaluate the neuroprotective activity of a stevia derivative, stevioside (STV). We worked *in vitro* with human neuroblastoma cells (SH-SY5Y), which were treated under 4 conditions: A) STV (1-100 μM, 24 h); B) PTZ, a cytotoxic convulsant compound (20 mM, 24 h); C) H_2O_2 (1 mM, 48 h); D) STV (30 and 100 μM, 24 h) plus B or C. It was observed that STV is not cytotoxic up to 100 μM. Furthermore, pretreatment of cells with STV prior to PTZ and H_2O_2 treatments reversed both the damage caused by PTZ and oxidative damage from H_2O_2, suggesting that STV is a promising agent capable of preventing oxidative stress inherent to seizure episodes. On the other hand, in *in vivo* assays in male Swiss mice, following National Institute of Health (NIH) protocols, STV at 100 mg/kg, i.p., provided 75% protection of mice treated with PTZ (85 mg/kg, s.c.) at 4 hours after administration. Additionally, mice brains were homogenated and antioxidant assays were performed. STV showed a decrease in TBARs formation (P<0,0001) and an increase in endogenous antioxidant agents, GSH (P<0,01), compared to the PTZ group. Therefore, STV appears to be a potential anticonvulsant agent whose mechanism of action could be associated with the inhibition of reactive oxygen species production.

478. 281. **GERANIOL PROTECTS AGAINST OXIDATIVE STRESS AND PROTEOTOXICITY IN C. ELEGANS PARKINSON'S DISEASE MODELS**

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2-Departamento de Biología, Bioquímica y Farmacia (UNS)

Due to the escalating life expectancy, the prevalence of age-related disorders like neurodegenerative diseases (ND) has surged. Oxidative stress (OS) has emerged as a key accelerator in ND progression. In Parkinson's disease (PD), for instance, compromised free radical scavenging capacity has been linked to worsened α-synuclein aggregation and proteotoxic damage. Geraniol (GER), a plant-derived essential oil, has recognized antioxidant properties. Considering that OS contributes to ND progression, compounds with antioxidant activity have been postulated as potential therapeutic agents. Leveraging the suitability of *Caenorhabditis elegans* as a model organism in biomedical research due to its genetic homology with mammals, including cytoprotective proteins, we aim to assess GER's biological efficacy in a *C. elegans* PD model and delve into the underlying molecular mechanisms. Our results first confirmed the in vivo antioxidant activity of GER. We cultured wild-type animals with GER and then exposed them to Juglone (oxidative agent). Locomotion was employed as a survival proxy using the Worm MicroTracker device. Strikingly, GER exhibited a significant increase in animal survival under OS conditions (P=<0.001). To unravel the precise mechanism driving GER's protective effects, we analyzed null mutants within key molecular pathways associated with OS response. Intriguingly, our preliminary findings showed that either DAF16/FOXO, HSF1 or SKN1/NRF2 are involved in mediating GER's protective effect. Given the link between OS and PD, we also evaluated the GER´s impact within a *C. elegans* PD model. We found that GER improves the impaired-locomotion phenotype of this model (P = 0,011). So far, these results indicate a potential antiproteotoxic effect of GER in C. elegans PD models. To comprehensively dissect GER's effects, we propose an integrative approach involving genetic analyses, advanced microscopy techniques, and behavioral assessments.

479. 315. **PROPRANOLOL ATTENUATED A CONTEXTUAL FEAR MEMORY AFTER FEAR GENERALIZATION IN MALE AND FEMALE MICE**

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Destabilization-reconsolidation, a retrieval-dependent process, allows for the modification of established memories, which is why this phenomenon has been considered an opportunity for attenuating the negative features of pathological memories. Memory attenuated in this way suggests an effective therapeutic strategy to provide long-term relief. However, very aversive memories are often resistant to this process. Here, after the induction of a resistant fear memory in mice using robust fear conditioning, we examined whether it is possible to render it susceptible to pharmacological disruption according to the degree of generalized fear. For this, based on the perceptual similarity between the associated context (CA) and non-associated contexts (CB, CC, and CD) to the aversive event, we established an ordered gradient of generalized fear (freezing and risk assessment). We observed that as the exposure context became less similar to CA, the conditioned response decreased (CA-CB vs CC-CD, p<0.05). Next, in conditioned mice, we injected propranolol, a known reconsolidation interferent, after exposure to the different contexts. In males, propranolol treatment resulted in a decreased fear response following exposure to CA or CB, but not CC or CD, compared to the control group (p<0.05). In females, the decrease in fear response due to propranolol was observed after exposure to CC, but not to the other contexts, compared to the control group (p<0.05). Taken together, these results indicate the possibility of indirectly manipulating a robust contextual fear memory by controlling the level of generalization during recall, highlighting that it is not necessary to expose animals to context conditioning as is commonly done. From a clinical standpoint, this would be of considerable relevance since, following this strategy, the treatment of psychiatric disorders associated with traumatic memory formation would be more effective and less stressful.

480. 319. **EXOGENOUS KETONE BODIES MODULATION OF GABAERGIC SIGNALING IN *C. elegans***

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Mutations in PTEN (a negative regulator of the PI3K pathway) are associated with neurodevelopmental disorders, epilepsy, and schizophrenia. Several reports suggest that an increase in the excitation/inhibition (E/I) ratio in the brain is a hallmark of these disorders. The *C. elegans* Neuro-Muscular system, where both excitatory (ACh) and inhibitory (GABA) neurons innervate muscles, provides a suitable model for studying E/I balance. Combining pharmacological and behavior assays, we found that *daf-18* (*C. elegans* ortholog for PTEN) mutants are hypersensitive to cholinergic drugs, suggesting a deficit in GABAergic signaling. *daf-18* mutants are deficient in eliciting complex movements such as the "omega turn", a sharp turn in which the GABAergic inhibition on dorsal muscles plays a critical role. Moreover, using microscopy techniques, we observed that