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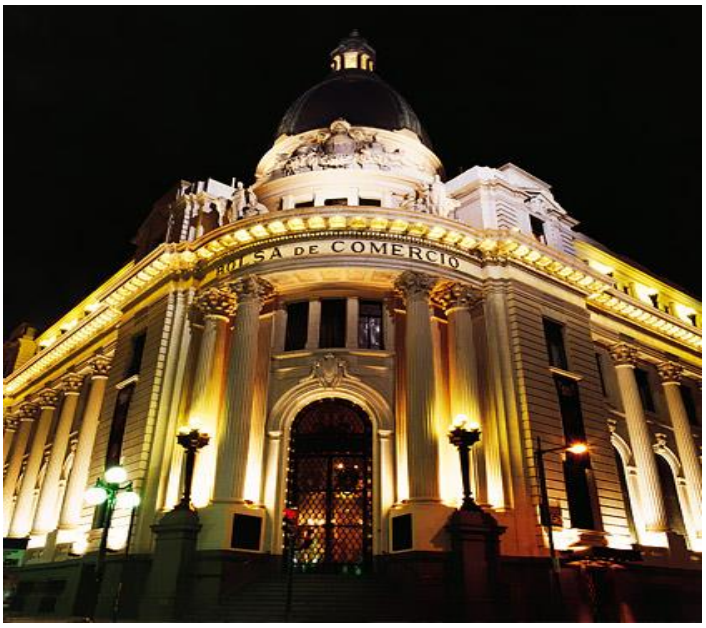
Bolsa de Comercio de Rosario

Rosario, Argentina



Bolsa de Comercio de Rosario

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3- Protective roles of imidazolium salts in *C. elegans* models of stress and neurodegeneration

Natalia Andersen[1,3], Tania Veuthey[1,3], Milagros Fariña[1,3], Gustavo Silbestri[2,4], Diego Rayes[1,3] and María José De Rosa[1,3]

1.INIBIBB. CCT-CONICET. 2.INQUISUR. CCT-CONICET. 3.Departamento de Biología, Bioquímica y Farmacia, UNS. 4.Departamento de Química, UNS

In this study, we aim to evaluate the role of imidazolium salts as antioxidant and anti-aging agents. We synthesized imidazolium salts and use the nematode *C. elegans* to performed a screening to analyze their ability to improve oxidative stress (OS) resistance. We identified a derivate, 1-Mesithyl-3-(3-sulfonatopropyl)imidazolium (MSI), that enhances animal resistance to OS. To delineate MSI roles, we split this work into two goals: i) to evaluate MSI role in neurodegenerative models, and, ii) to describe the mechanism of action underlying its protective effects.

There is a theory that links OS to aging and neurodegeneration. To evaluate MSI neuroprotection, we used *C. elegans* models of neurodegenerative diseases. As an Alzheimer disease (AD) model, we used a strain that expresses Aβ1-42 in muscle and shows age-dependent protein aggregation and paralysis. Our results show that MSI delays paralysis in this strain. Since mean lifespan is preserved in wild-type worms exposed to MSI, anti-aging effects of MSI in AD model seems to be dependent on its antiproteotoxic role. To gain further insight into its role in other neurotoxic models, we evaluate mobility as an indicator of healthspan in Huntington disease (HD) and Parkinson disease (PD) models. We found that MSI ameliorates mobility rate decline in these proteotoxic models of neurodegenerative diseases.

As a first approach to delineate its mechanism of action, we evaluated MSI ability to activate DAF-16 (FOXO in vertebrates), a transcription factor relevant for cytoprotective defense mechanisms. We found that MSI stress protection was not dependent on DAF-16. Therefore, other transcription factors (such as SKN-1 (Nrf-2 in vertebrates), HSF-1), could be involved in MSI protection.

Additional research is needed to underpin the mechanism responsible for MSI's protective role and to confirm if these effects can be extrapolated to other neurodegenerative scenarios.