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NEUROCHEMISTRY AND NEUROPHARMACOLOGY

Protective roles of imidazolium salts in C. elegans models of neurodegeneration

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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 perform a screening and analyze their ability to improve oxidative stress resistance. We identified a derivate, 1-Mesithyl-3-(3-sulfonatopropyl)imidazolium (MSI), that enhances animal resistance to oxidative stress.
As a first approach to delineate its mechanism of action, we evaluated MSI ability to activate transcription factors involved in cytoprotective stress responses, such as the DAF-16/FOXO and SKN-1/Nrf2 pathways. We found that MSI stress protection was not dependent on DAF-16. Nevertheless, we discovered that GST-4 detoxifying enzyme, a downstream effector of SKN-1, is involved in MSI-mediated oxidative stress resistance.
Oxidative stress has been largely related to aging and neurodegeneration. To gain insight into MSI role in proteostasis, we evaluated mobility as an indicator of healthspan in Huntington's, Parkinson's and Alzheimer's disease models. We found that MSI ameliorates mobility rate decline in these proteotoxic models of neurodegenerative diseases. Surprisingly, our results show that MSI did not improve mean lifespan neith.er in wild-type worms nor in Alzheimer's disease animal models. Overall, our results show a scenario where healthspan seems to be uncoupled to lifespan. Additional research is needed to underpin the mechanism responsible for MSI's protective role.