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K⁺ channel blocker-induced neurodegenerative model: Pharmaco-immunomodulation effect of an antioxidant drug

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Channelopathies due to the brain ion channel dysfunction is considered to be an important mechanism involved in various neurodegenerative diseases such as epilepsy. In this study, a neurodegenerative model was developed using KTX a neuroexcitotoxic agent that blocks specifically Kv1 channels in the CNS, to explore the pathogenesis of excitotoxicity in neurodegenerative disorders. The detection of the KTX was analyzed by immunofluorescence in various brain areas, neuroinflammatory parameters (i.e. levels of NO, MDA, GSH, catalase, proinflammatory cytokines IL-6 and TNF α), NF+ κ B expression and tissue analysis of neurodegenerative alterations were evaluated with or without pretreatment using an antioxidant (astaxantin). Results showed that KTX was detected only in cerebral cortex area after 1 day due to its binding to the specific receptors. It induced an activation of inflammatory cascade characterized by an increase of IL-6, TNF α , NO, MDA levels and NF- κ B expression associated to a decrease of GSH level in cerebral cortex and hippocampus after 15 days. The neuroinflammation is associated with seizure and cerebral alterations in cortex observed at 1 and 15 days and in the hippocampus only at 15 days. The use of an antioxidant prior to the KTX exerts a preventive effect not only on the neuroinflammation but also on altered tissues and the BBB disruption. This model could be a useful tool to study neuronal degeneration, as well as to better understand the mechanisms underlying neurodegenerative diseases and to improve and design new therapeutic strategies.

Biography

Fatima Laraba-Djebari is Teacher-Researcher at the Faculty of Biological Sciences of USTHB. She completed her Doctorate in Cellular Biology and Microbiology in 1994 from Marseille University and Biochemistry in 1995 from USTHB. She is Head of team on Biomolecules of interest and Immunotherapy. After being Head of Department of Cellular and Molecular Biology, she serves as Dean of Faculty at USTHB. Her main topics focused on Biochemistry-Immunology and Pharmacology in Toxinology She is invited as reviewer by several editors and is author of two chapters in Handbook and more than 60 papers (Web of Science, Scopus, NCBI).

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