The College of Graduate Studies and the College of Medicine and Health Sciences Cordially Invite You to a

Master Thesis Defense

Entitled

THE POTENT AND SELECTIVE HISTAMINE H3 RECEPTOR ANTAGONIST E169 ALLEVIATES COGNITIVE DEFICITS AND MITIGATES DISTURBED PI3K/AKT/GSK-3B SIGNALING PATHWAY IN MK801-INDUCED AMNESIA IN MICE

by

Sabna Tagelsir Hassan Abdalla

Faculty Advisor

Prof. Bassem Shaban Sadek, Department of Pharmacology and Therapeutics

College of Medicine and Health Sciences

Date & Venue

At 1 PM

Tuesday, 15 November 2022

YANAH Theatre (2C010), CMHS

Abstract

The role of Histamine H3 receptors (H3Rs) in memory and the prospective of H3R antagonists in pharmacological control of neurodegenerative disorders, e.g., Alzheimer's disease (AD) is well-accepted. Therefore, the procognitive effects of acute systemic administration of H3R antagonist E169 (2.5-10 mg/kg, i.p.) on MK801-induced amnesia using the novel object recognition (NOR) paradigm in C57BL/6J mice were evaluated. E169 (5 mg) provided a significant memory-improving effect on MK801-induced short- and long-term memory impairments in NOR. The E169(5 mg)-provided effects were comparable to those observed with the phosphatidylinositol 3-kinase (PI3K) inhibitor LY294002 and were abrogated with the H3R agonist (R)-α-methylhistamine (RAMH). Also, results demonstrated that E169 ameliorated MK-801-induced memory deficits by antagonism of H3Rs and by modulation of the disturbing levels of PI3K, Akt and GSK-3β expressed proteins, signifying that E169 mitigated the Akt-mTOR signaling pathway in the hippocampus of tested mice. Moreover, the results observed revealed that E169 (2.5-10 mg/kg, i.p.) did not alter anxiety levels and locomotor activity of animals in open field test, demonstrating that performances improved following acute systemic administration with E169 in NORT are unrelated to changes in emotional responding or in spontaneous locomotor activity. In summary, these obtained results suggest the potential of H3R antagonists in simultaneously modulating disturbed brain neurotransmitters and imbalanced Akt-mTOR signaling pathway related to neurodegenerative disorders, e.g., AD.

Keywords: Alzheimer's Disease, H3R antagonists, MK801-induced amnesia mice, PI3K/AKT/GSK-3β signaling pathway, novel object recognition test, memory, cognition, neuroinflammation, neurodegeneration.