Lithium Benzoate Exerts Neuroprotective Effect by Improving Mitochondrial Function, Attenuating Reactive Oxygen Species (ROS), and Protecting Cognition and Memory in an Animal Model of Alzheimer's Disease

ABSTRACT

BACKGROUND: Alzheimer's disease (AD) is a multifactorial neurodegenerative disease affecting many cellular pathways, including protein aggregation, mitochondrial dysfunction, oxidative stress (OS), and neuroinflammation. Currently, no effective treatment for AD exists.

OBJECTIVE: We aim to determine the effect of Lithium benzoate (LiBen) in protecting neurons form $A\beta$ or other neurotoxin insults.

METHODS: Primary rat cortical neurons were co-treated with neurotoxins and LiBen were used to examine its effect in cell viability, ROS clearance, and mitochondria functions by MTT, CellRox fluorescence staining and seahorse assay. Then, Barnes maze and prepulse inhibition test were performed in APP/PS1 mice received chronic LiBen treatment for assessing its effect of cognitive protection. Oral bioavailability of LiBen was also assessed by pharmacokinetic study in rat plasma.

RESULTS: In this study, we discovered that LiBen can attenuate cellular ROS level, improve mitochondrial function, increase cell viability against multiple different insults

of mitochondrial dysfunction, Aβ accumulation and neuroinflammation, and promote neurogenesis. We demonstrated that LiBen has advantages over lithium or sodium benzoate alone as LiBen displays superior neuroprotective efficacy and oral bioavailability than the other two agents when being applied either alone or in combination. Furthermore, chronic administration of LiBen showed protection for cognition as well as spatial memory and reduced the senile plaque deposition in brains of AD animal models.

CONCLUSIONS: LiBen stands as a promising therapeutic agent for delaying the progression and improve the cognition of AD.