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Bis(ethylmaltolato)oxidovanadium (IV) significantly attenuated the pathological hallmarks of Alzheimer's disease in the triple transgenic model mouse

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Abstract

Vanadium compounds have been reported to mimic the anti-diabetes effects of insulin in rodent models, but their effects on Alzheimer's disease (AD) have rarely been explored. Bis(ethylmaltolato)oxovanadium (IV) (BEOV)has pleasant malt-aromad and exhibits insulin-like function with low toxicity and good hypoglycemic effect. In this paper, BEOV was found to improve contextual memory and spatial learning in two types of transgenic AD model mice (3×Tg-AD and APP/PS1). Italso improved glucose metabolism in the AD brains, as evidenced by ^{18}F-labeled fluoro-deoxyglucose positron emission tomography (^{18}F-FDG-PET) scanning. Protection of neuronal synapsesby BEOV was detected by transmission electron microscopy.The dendritic spines of pyramidal neuron in neocortex were detected by *in vivo* two-photon imaging of AD-YFP mice (the offspring of 3×Tg-AD and YFP mice).Treatment with BEOV significantly increased the numbers of total dendritic spines, mushroom spines and thin spines in AD-YFP mice, indicating the protective effect of BEOV on cortical neurons and dendritic spines.Meanwhile, significant inhibition of BEOV on β-amyloid (Aβ) plaques and neuronal impairment in the cortex and hippocampus of fluorescent AD mice were visualized three-dimensionally by applying optical clearing technology to brain slicesbeforeconfocal laser scanning microscopy. Mechanism study showed that BEOV increased the expression of peroxisome proliferator-activated receptorγ (PPARγ) to block the amyloidogenesis cascade, thus attenuating Aβ-induced insulin resistance in two transgenic AD models. BEOV also reduced protein tyrosine phosphatase 1B (PTP1B) expression to promote insulin sensitivity and subsequently reducing tau hyperphosphorylation in those AD models.Collectively, the present study provided a proof-of-concept evidence and showed for the first time thatBEOV has the potential as a novel treatment for AD.

Keywords—*Alzheimer's disease (AD); bis(ethylmaltolato)oxidovanadium (IV) (BEOV); β-amyloid (Aβ); peroxisome proliferator-activated receptorγ(PPARγ);*

Biography:

Qiong Liu has completed her PhD in 1998 from the Roskilde University in Denmark and postdoctoral studies from the Karolinska Institute in Sweden in 2000. From 2000 to 2005, she worked as an associate professor in the Department of Chemistry in the Huazhong University of Science & Technology, China. From 2005 till now, she has been working as a professor in the Colle of Life Sciences & Oceanography in the Shenzhen University in China. She has been devoted to the researches of biological trace elements and their application in biomedicine for a long time.Currently she is studying biomarkers for early clinical diagnosis of Alzheimer's and drug precursors for intervention of this disease. She has published around 100 papers in the academic journals, participated in writing the chapters of 5 books and applied for 8 Chinese patients for invention.

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