Dendrobium nobile Lindl. alkaloids-mediated protection against Aβ25-35-induced synaptic deficits is dependent on activation of Wnt/β-catenin pathway in rats and in cells

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Abstract

Abstract: Synaptic degeneration, associated mitochondrial dysfunction and accumulation of amyloid-β peptide are considered as the important manifestation which leads to cognitive impairment and memory loss in Alzheimer's disease (AD)-affected brain. Avoiding the early characteristic symptoms of AD, such as synapse loss, seems to be a promising approach to prevent AD. Dendrobium nobile Lindl. alkaloids (DNLA), an active alkaloid component extracted from Chinese medicinal herb Dendrobium nobile, has a wide range of pharmacological functions including prolonging life, anti-dementia and anti-hyperglycemia effects. However, the activity of DNLA on synaptic protection and the underlying mechanism is yet unexplored. Herein, this study attempted to investigate the protective effects of DNLA on synaptic damage in Aβ25-35 toxin-induced rat AD model in vivo and vitro. A rat AD model was established via a single Aβ25-35 injection (10 μg) into the bilateral hippocampal. DNLA (40 mg/kg/d; 80 mg/kg/d) was intragastrically administrated 7d prior to the Aβ injection, and the administration was continued for 28 days. The effect of DNLA on spatial learning and memory, synaptic morphology, synapse-related proteins levels and Wnt signaling components GSK3β and β-catenin phosphorylation were evaluate. In vitro studies, mitochondrial function and amyloidogenesis of APP were examined. An inhibitor of Wnt pathway Dickkopf-related protein-1 (Dkk-1) was used to determine whether the DNLA-mediated synaptic protection against Aβ25-35 (20 μM) was blocked. DNLA reduced Aβ-mediated toxicity, increased the number of synapses, elevated the postsynaptic density thickness and expression of synapse-related proteins synapsin and PSD95 in hippocampus of rats, and restored dendritic morphology and mitochondrial function, along with an inhibition of amyloidogenesis of APP, leading to the improvement of behavior abnormalities and synaptic deficits induced by bilateral hippocampal injection of Aβ25-35. Furthermore, treatment with DNLA suppressed Aβ-mediated GSK3β activity and the β-catenin phosphorylation. Inhibition of the Wnt-catenin pathway using Dkk-1 partially blocked the effect of DNLA on the expression of Aβ1-42 and PSD95 in culture cells. Taken together, these findings indicated that DNLA could promote the rescue of Aβ-mediated synaptic and mitochondrial pathology in a manner requiring activation of Wnt/β-catenin signaling pathway, demonstrating that DNLA has a protective potential against AD.

Image

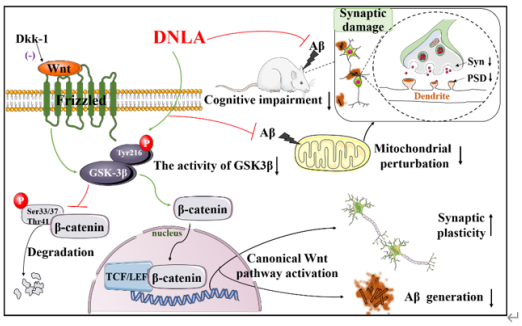


Fig. 8 A schematic representation elucidating the proposed mechanisms that DLNA protects against $A\beta_{25\text{-}35}$-induced synaptic injury.

Recent Publications (minimum 5)

Wei Zhang; Qin Wu; Yan-liu Lu; Qi-hai Gong; Feng Zhang; Jing-shan Shi*. Protective effects of Dendrobium nobile Lindl. alkaloids on amyloid beta (25–35)-induced neuronal injury, Neural Regeneration Research, 2017, 12(7):1131-1136.



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Biography (150 word limit)

Dr. Wei Zhang studied pharmacology at the Zunyi Medical University, China and graduated as MS in 2013. She then joined the research group of Prof. Jingshan Shi at the key laboratory of basic pharmacology of ministry of education and joint international research laboratory of ethnomedicine of ministry of education. She received her PhD degree in 2018 at medical college in the Guizhou University . She has published 4 research articles in a reputed journal.

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