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#### **ACCEPTED MANUSCRIPT**

# Neuroprotective effects of ginseng protein on PI3K/Akt signaling pathway in the hippocampus of D-galactose / AlCl<sub>3</sub> inducing rats model of Alzheimer's disease

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#### **ABSTRACT**

Ethnopharmacological relevance: Alzheimer's disease (AD) is a progressive neurodegenerative disease, with progressive memory loss, cognitive deterioration, and behavioral disorders. Ginseng (Panax ginseng C.A. Meyer) is widely used in China to treat various kinds of nervous system disorders. The study aimed to explore the therapeutic effect of ginseng protein (GP) on Alzheimer's disease and its correlation with the PI3K/Akt signaling pathway to understand the mechanism underlying the neuroprotective effect of ginseng.

Material and methods: The AD rat model was established by intraperitoneally injecting D-galactose [60 mg/(kg  $\cdot$  d)] followed by intragastrically administering AlCl $_3$  [40 mg/(kg  $\cdot$  d)] for 90 days. From day 60, the GP groups were intragastrically administered with GP 0.05 or 0.1 g/kg twice daily for 30 days. The ethology of rats was tested by Morris water maze test. The content of A $\beta_{1-42}$  and p-tau in the hippocampus of rats was detected by enzyme-linked immunosorbent assay. The expression of mRNAs and proteins of PI3K, Akt, phosphorylated Akt (p-Akt), Bcl-2, and Bax in the hippocampus was detected by real-time quantitative reverse transcription polymerase chain reaction and Western blot assay.

Results: GP was found to significantly improve the memory ability of AD rats and prolong the times of crossing the platform and the percentage of residence time in the original platform quadrant of spatial probe test. GP also reduced the content of  $A\beta_{1-42}$  and p-tau and improved the mRNA and protein expression of PI3K, p-Akt/Akt, and

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