

Dietary genistein in ameliorating glucose-induced β -amyloid toxicity, oxidative stress, aging, and lipid metabolism impairment.

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Alzheimer's disease (AD) has been considered a type of diabetic encephalopathy due to numerous similar etiologic contributing factors involved in their pathogenesis. The specific mechanism of diabetic encephalopathy remains underexplored, so drug and functional food development is still a challenge. This present study aimed first to investigate the potential harmful effects of glucose enrichment on neurotoxicity, apoptosis, oxidative stress, and impaired lipid metabolism. Moreover, it explored the effective dietary polyphenol genistein and potential molecular mechanisms through network pharmacology and in vivo experiments. It has been found that high glucose feeding in worms induces body size impairment, acceleration of aging, formation of amyloid β and ROS, and impairment of lipid metabolism, among other effects. Genistein intervention not only prolonged the lifespan but also mitigated AD-like symptoms in *C. elegans*, as demonstrated by thioflavin S staining, the H2DCFDA assay, and MDA determination, among other methods. Further results from network pharmacology, RT-qPCR, and lipidomic analysis revealed that the anti-aging, antioxidative, and neuroprotective effects of genistein involve the regulation of sphingolipids, glycerophospholipids, and glycerolipids, which are likely mediated through the PI3K-AKT signaling pathways. Conclusion: Modulating the PI3K/Akt pathway and lipid metabolism plays a critical role in mitigating A β -induced toxicity and oxidative stress induced by glucose enrichment. These findings provide novel insights into the role of dietary polyphenols in preventing diabetic cognitive impairment and aging.

Biography

WANG Jingwen received her undergraduate education at the Guangdong University of Technology (China), and obtained her MSc degree in the University of Leeds, U.K. She is now PhD candidate from Beijing Normal-Hong Kong Baptist University. Current research interest is to use nematode *C. elegans* of neurodegenerative diseases to elucidate the underlying molecular mechanisms and relationship among regulating oxidative stress, amyloid β aggregation, aging, fat metabolism, and Alzheimer's disease. I seek to address the following questions: (1) What are the potential harmful effects of glucose enrichment on neurotoxicity, oxidative stress, impaired lipid metabolism, and AD-like symptoms? (2) Pharmacology of dietary polyphenols.

Received: April 20, 2025; **Accepted:** April 21, 2025 ; **Published:** May 27, 2025