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Oral administration of Gintonin attenuates cholinergic impairments by scopolamine, amyloid-β protein, and mouse model of Alzheimer's disease: Involvement of Lysophosphatidic Acid (LPA) receptor

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Gintonin is a novel ginseng-derived lysophosphatidic acid (LPA) receptor ligand. Oral administration of gintonin ameliorates learning and memory dysfunctions in Alzheimer's disease (AD) animal models. The brain cholinergic system plays a key role in cognitive functions. The brains of AD patients show a reduction in acetylcholine concentration caused by cholinergic system impairments. However, little is known about the role of LPA in the cholinergic system. In this study, we used gintonin to investigate the effect of LPA receptor activation on the cholinergic system *in vitro* and *in vivo* using AD animal models. Gintonin induced [Ca2+]i transient in cultured mouse hippocampal neural progenitor cells (NPCs). Gintonin-mediated [Ca2+]i transients were linked to stimulation of acetylcholine release through LPA receptor activation. Oral administration of gintonin (25, 50, or 100 mg/kg/day, 3 weeks) significantly attenuated scopolamine-induced memory impairment. Oral administration of gintonin (25 or 50 mg/kg, 2 weeks) also significantly attenuated amyloid-β protein (Aβ)-induced cholinergic dysfunctions, such as decreased acetylcholine concentration, decreased choline acetyltransferase (ChAT) activity and immunoreactivity, and increased acetylcholine esterase (AChE) activity. In a transgenic AD mouse model, long-term oral administration of gintonin (25 or 50 mg/kg, 3 months) also attenuated AD-related cholinergic impairments, such as decreased acetylcholine concentration, decreased ChAT activity and immunoreactivity, and increased AChE activity. In this study, we showed that activation of G protein-coupled LPA receptors by gintonin is coupled to the regulation of cholinergic functions. Furthermore, this study showed that gintonin could be a novel agent for the restoration of cholinergic system damages due to Aβ and could be utilized for AD prevention or therapy.

Biography

Hyeon-Joong Kim has completed his bachelor's degree from Konkuk University and got a veterinary medical license at the age of 24 years. He studies at Konkuk University College of Veterinary Medicine as a PhD candidate from 2011. He is the writer of Science Webzine, Science-on, and he has published 6 papers in reputed journals.

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