Oral Administration of Gintonin Attenuates Cholinergic Impairments by Scopolamine, Amyloid-β Protein, and Mouse Model of Alzheimer’s disease: Involvement of Lysophosphatidic Acid (LPA) Receptors


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Alzheimer’s disease (AD) is the most common age-associated neurodegenerative disease. The formation of senile plaques and neurofibrillary tangles are well characterized in AD neuropathy. Senile plaques contain amyloid-β protein (Aβ). Ginseng extracts increased acetylcholine release and enhanced cognitive performance in human and AD patients. However, little is known about the active ingredient of ginseng and its signaling mechanisms. We showed that gintonin contains a novel G protein-coupled lysophosphatidic acid (LPA) receptor ligand, gintonin. Gintonin-enhanced synaptic transmission in hippocampal slices through LPA receptor signaling pathways. We showed that gintonin is the active component of ginseng extract and attenuates AD-related neuropathies via activation of non-amyloidogenic pathways; gintonin significantly improved Aβ-induced cognitive dysfunctions in mice. In addition, long-term oral administration of gintonin attenuated amyloid plaque deposition in the hippocampus as well as short- and long-term memory impairment in a transgenic AD mouse model.

Fig. 1. Effects of gintonin (GT) on [Ca2+]i transients in neural progenitor cells (NPCs) and its signal transduction.

Results and Discussion

- **Materials and Methods**
  - **Animals**
    - Male ICR or C57BL/6 mice (4- or 8-weeks-old)
  - **Drug Treatment**
    - Donepezil (DPZ; 1 mg/kg, i.p.) was used as a reference drug.
  - **Measurement of intracellular Ca2+ levels**
    - Neural progenitor cells
  - **Measurement of Acetylcholinesterase (AChE) Activity**
    - Choline acetyltransferase assay kit
  - **Immunocytochemistry**
  - **Passive avoidance Test**
  - **Morris Water Maze Test**
  - **Induction of LTP in acute slices in the absence or presence of gintonin**

We found that gintonin stimulates acetylcholine release, has a protective effect on the cholinergic system, and attenuates acute Aβ-induced and long-term cholinergic dysfunction in the transgenic AD animal model. Gintonin-mediated activation of LPA receptors could be coupled to anti-AD effects via dual actions of the non-amyloidogenic pathway and modulation of the cholinergic system in the brain according to the described pathways.