

Genistein and Gintonin as Emerging Nutraceuticals in Treatment of Alzheimer's Disease

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Introduction

Over 35 million people are reported to suffer from Alzheimer's Disease (AD) and other related dementia diseases globally. This morbidity is expected to increase to 65 million by 2030 and exponentially to 115 million 2050 [1]. Causes of AD have not been established, but some factors responsible for the disease have been identified which include ageing [1].

Several drugs and techniques aided by scientist for the treatment of neurodegenerative disorders have been developed but none have shown a promising pharmacological activity after clinical trials within the last 3 decades for AD. The most active documented drug for its treatment is memantine which was launched 25 years ago, after this, about 4000 compounds tested gave low activity in treatment [2].

Studies have shown that dietary supplements are better approach to reduce the risks of AD. The link between diet and human disease has become area of interest among AD and Dementia researchers. Nutraceuticals are identified as foods or a part of foods like dietary supplements that produces a medical or health benefit in the prevention and treatment of a particular ailment [3].

Future treatments of AD will basically target the neurofibrillary tangles which composed of the *p*-tau (a microtubule-associated protein that promotes stabilization and assembling of microtubules, essential for normal configuration of neuronal extensions, axonal transport and polarization of cells) and also the senile plaques. However, an issue remains on whether halting neurology, decline similarly as how soon treatment should be initiated. Variety immunotherapy drugs which are undergoing clinical trials have been suspended due to the reported side effect of microhaemorrhages in the brain. For example, Bapineuzumab and intravenous immunoglobulin (IVAg) have been reported to have shown reduction in plasma A₄₂ levels [4,5]. Genistein and Gintonin are two nutraceuticals that have been reported to have neurodegenerative activities [6,7].

Genistein

This is also known as 4,5,7-trihydroxyisoflavone, an isoflavone obtained from Soybean (soy) that contains phytoestrogen. Uddin and Tanvir, 2019 reported that Genistein protect cells by increasing the α -secretase and attenuation of the β -secretase, via upregulation of the protein kinase C signalling pathway in rat hippocampal neuronal cells. Recent studies showed that most of the isoflavones from soybean are considered agonists of estrogen receptors and liable for the observed memory improving effects of soybean supplementation, because the isoflavones appear to enhance cognitive function [8]. Several studies indicated that isoflavones improve visual spatial memory and learning mentality in rats. Additionally, isoflavones found in soybean especially genistein could influence the brain cholinergic system and reduces age-related neuronal loss and cognition in male rats [9]. However, random control trials study on soybean supplements showed no immediate activity on the ladies who used soybean supplement for global cognition but a slight activity in their visual memory after a thirty months post administration, whereas spatial working memory improved in men within twelve weeks compared to the placebo group. Also, a study in postmenopausal women who received soy protein for twelve months had no benefit in cognitive performance [9,10].

Gintonin

This is a lysophosphatidic acid receptor agonist isolated from *Panax ginseng*. Gintonin has been found to activate a non-amyloidogenic pathway resulting in the formation of a soluble neuroprotective amyloid precursor variant. Studies have shown that gintonin treatment reduced the production, attenuated the toxicity, and reversed cognitive defects of β -amyloid in AD transgenic mice. The administration of fermented ginseng to scopolamine-treated (2-weeks) and transgenic mice (4-months) AD models resulted in significant reduction of soluble β -amyloid level and recovery of memory functions. At last, ginseng protein administration to galactose/ AlCl_3 -induced AD mice reduced the levels of soluble β -amyloid and tau-protein. In addition, increased the expression and activation of PI3K/Akt pathway in the hippocampus. Hence Gintonin also possess the ability to improve cognitive functions. Other constituents of Ginseng which have significant effects on memory and cognitive performances include the Ginsenosides Rb1 glycosides which have been reported to increase the uptake of choline in cerebral cholinergic nerve endings [11,12].

Conclusion

Therefore, the mechanisms of both Genistein and Gintonin should be evaluated and their safety and efficacy studied to conclusively add them among the drugs to be used in the management of neurodegenerative conditions.

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