Abstract form

Title: Polyphenolic compounds protect against synuclein-induced membrane permeabilization in a liposomal model

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Abstract

Parkinson’s disease is the second most common progressive neurodegenerative disorder and is characterised by the self-assembly of the alpha-synuclein (α-syn) protein into well-ordered oligomeric assemblies, which eventually form amyloid fibrils and deposit intracellularly as Lewy bodies. It has been proposed that α-syn oligomers are highly toxic, possibly by interacting with and damaging cellular membranes. We therefore studied whether a select group of polyphenolic compounds, natural substances that are ubiquitously found in fruits and vegetables, can prevent permeabilization of small unilamellar liposomes by aggregated α-syn. Out of seventeen polyphenols that were tested, five potently inhibited permeabilization of liposomes to < 20% of the maximal α-syn effect. These polyphenols include baicalein, morin, nordihydroguaiaretic acid, black tea extract, and tannic acid. In comparison, Zn2+ ions, which have been reported to block membrane pores formed by α-syn, prevented permeabilization to only 40%. Furthermore, 6 μg/ml of black tea extract had a similar inhibitory effect to that of 100 μg/ml of anti-oligomer (A11) antibody. We conclude that polyphenols efficiently destabilize α-syn oligomers, thereby preventing them from inserting into lipid membranes. Aromatic and hydroxyl elements allow the polyphenolic compounds to bind strongly to the α-syn assemblies. A better understanding of the ability of polyphenols to prevent alpha-synuclein induced membrane destabilization may provide key insights into the role of dietary supplementation in delaying the onset/severity of Parkinson’s disease.