

# Polyphenols- novel therapeutic Agents to Treat Amyloid Associated Disorders in Humans

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**Abstract**—Humans consume a vast number of foods, drugs and plant-based products. Polyphenols are natural plant secondary metabolites which exhibit remarkable multipotent ability to control and modulate reactive oxygen species, metal toxicity, inflammation, apoptosis, signal transduction, ion channels and neurotransmitters. Dietary intake of polyphenols is known to attenuate oxidative stress and reduce the risk for amyloid associated disorders such as Alzheimer's disease (AD), Parkinson's disease (PD), and other neurodegenerative or non-neuropathic systemic/localized amyloidosis are characterized by the appearance of protein aggregates or plaques in tissues of affected individuals. Several studies have reported that certain polyphenols inhibit the elongation phase of fibril assembly or assembly of large oligomers and do not interfere with early nucleation events. This observation was in agreement with the reports that polyphenols do not interact with amyloidogenic monomers and the inhibitor binding is conformation dependent and not sequence dependent. The molecular modelling data also suggests that polyphenols have the ability to adopt a specific three-dimensional pharmacophore conformation that might be essential for binding to  $\beta$ -amyloid and preventing it from forming typical amyloid fibrils. Polyphenolic dietary antioxidants, particularly resveratrol, epigallocatechin-3-gallate, quercetin, and other fruit polyphenols are potent neuroprotectants that activate antioxidant pathways –Nrf2/HO1, MAP Kinase and down regulate NFK  $\beta$ , MMPs, HIF-1, STAT pathways. Polyphenols also modulate immune responses by inhibiting biomarkers namely CCL17, CCL22, CCR2, IFN- $\gamma$ , MIP1  $\beta$ , IL (1 $\beta$ , 6, 17A, 22) and TNF- $\alpha$ . The activation of novel spectrum of these molecular targets forms the underlying mechanism of neuroprotection by polyphenols. The lack of toxic effect and availability from natural sources makes polyphenols as clinically relevant therapeutic agents for the treatment of amyloid related disorders in humans.

**Keywords:** Polyphenols, Protein aggregates, pharmacophore, Amyloid associated disorders, Neuroprotectants