

N-Acetyl Cysteine and Catechin-Derived Polyphenols: A Path Toward Multi-Target Compounds Against Alzheimer's Disease

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JOURNAL OF ALZHEIMERS DISEASE

Volumen: 75

Número: 4

Páginas: 1219-1227

DOI: 10.3233/JAD-200067

Fecha de publicación: 2020

Tipo de documento: Article

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Abstract

Background: Alzheimer's disease (AD) is a multifactorial disease, that involves neuroinflammatory processes in which microglial cells respond to "damage signals". The latter includes oligomeric tau, iron, oxidative free radicals, and other molecules that promotes neuroinflammation in the brain, promoting neuronal death and cognitive impairment. Since AD is the first cause of dementia in the elderly, and its pharmacotherapy has limited efficacy, novel treatments are critical to improve the quality of life of AD patients. Multitarget therapy based on nutraceuticals has been proposed as a promising intervention based on evidence from clinical trials. Several studies have shown that epicatechin-derived polyphenols from tea improve cognitive performance; also, the polyphenol molecule N-acetylcysteine (NAC) promotes neuroprotection.

Objective: To develop an approach for a rational design of leading compounds against AD, based on specific semisynthetic epicatechin and catechin derivatives.

Methods: We evaluated tau aggregation in vitro and neuritogenesis by confocal microscopy in mouse neuroblastoma cells (N2a), after exposing cells to either epicatechin-pyrogallol (EPIC-PYR), catechin-pyrogallol (CAT-PYR), catechin-phloroglucinol (CAT-PhG), and NAC.

Results: We found that EPIC-PYR, CAT-PYR, and CAT-PhG inhibit human tau aggregation and significantly increase neuritogenesis in a dose-dependent manner. Interestingly, modification with a phloroglucinol group yielded the most potent molecule of those evaluated, suggesting that the phloroglucinol group may enhance neuroprotective activity of the catechin-derived compounds. Also, as observed with catechins, NAC promotes neuritogenesis and inhibits tau self-aggregation, possibly

through a different pathway.

Conclusion: EPIC-PYR, CAT-PYR, CAT-PhG, and NAC increased the number of neurites in Na2 cell line and inhibits tau-self aggregation in vitro.

Palabras clave

Palabras clave de autor: [Alzheimer's disease](#); [bioactive compounds](#); [molecular functions](#); [molecular networks](#); [natural compounds](#); [polyphenols](#); [prevalent neurological disorders](#); [tau oligomerization](#)

KeyWords Plus: [OXIDATIVE](#)

[STRESS](#); [ACETYLCYSTEINE](#); [BETA](#); [NEUROINFLAMMATION](#); [PROCYANIDINS](#); [INFLAMMATION](#); [IMPAIRMENT](#); [ACID](#); [NEUROIMMUNOMODULATION](#); [NEUROTOXICITY](#)

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Financiación

Entidad financiadora	Número de concesión
Innova, High Technology Project	CORFO 14IEAT-28658
International Center for Biomedicine (ICC)	
Ricardo B. Maccioni Foundation	
FONDEQUIP	EQM150025

[Ver texto de financiación](#)

Editorial

IOS PRESS, NIEUWE HEMWEG 6B, 1013 BG AMSTERDAM, NETHERLANDS

Información de la revista

- **Impact Factor:** [Journal Citation Reports](#)

Categorías / Clasificación

Áreas de investigación:Neurosciences & Neurology

Categorías de Web of Science:Neurosciences

Información del documento

Idioma:English

Número de acceso: WOS:000550022100014

ID de PubMed: 32390631

ISSN: 1387-2877

eISSN: 1875-8908