

Insights into the discovery of novel neuroprotective agents: A comparative study between sulfanylcinnamic acid derivatives and related phenolic analogues

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Exogenous antioxidants may be beneficial therapeutic tools to tackle the oxidative damage in neurodegenerative diseases by regulation of the redox state that is critical for cell viability and organ function. Inspired by natural plant polyphenols, a series of cinnamic acid-based thiophenolic and phenolic compounds were synthesized and their antioxidant and neuroprotective properties were studied. In general, our results showed that the replacement of the hydroxyl group (OH) by a sulfhydryl group (SH) increased the radical scavenging activity and enhanced the reaction rate with 1,1-diphenyl-2-picrylhydrazyl radical (DPPH[•]) and galvinoxyl radical (GO[•]). These results correlated well with the lower oxidation potential (E_p) values of thiophenols. However, a lower peroxy radical (ROO[•]) scavenging activity was observed for thiophenols in oxygen radical absorbance capacity (ORAC-FL) assay. Furthermore, the introduction of 5-methoxy and 5-phenyl groups in the aromatic ring of 4-thioferulic acid (TFA) **2** and ferulic acid (FA) **1** did not significantly improve their antioxidant activity, despite the slight decrease of E_p observed for compounds **5**, **6**, and **9**. Concerning cinnamic acid amides, the antioxidant profile was similar to the parent compounds. None of the compounds under study presented significant cytotoxic effects in human differentiated neuroblastoma cells. Thiophenolic amide **3** stands out as the most promising thiophenol-based antioxidant, showing

cellular neuroprotective effects against oxidative stress inducers (hydrogen peroxide and iron). ©

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4-thioferulic acid derivatives

Antioxidant activity

Cinnamic acid

Cytotoxicity

Ferulic acid derivatives

Neuroprotection

antioxidant

cinnamic acid

cinnamic acid derivative

neuroprotective agent

phenol derivative

scavenger

thiol derivative

thiophenol

chemical phenomena

chemical structure

chemistry

drug development

human

oxidation reduction reaction

structure activity relation

tumor cell line

Antioxidants

Cell Line, Tumor

Chemical Phenomena

Cinnamates

Drug Discovery

Free Radical Scavengers

Humans

Molecular Structure

Neuroprotective Agents

Oxidation-Reduction

Phenols

Structure-Activity Relationship

Sulfhydryl Compounds