

## Individual Anteaox Phenols and Neurodegenerative Diseases

### Resveratrol

*“Noteworthy, even though Alzheimer’s Disease is the most common neurodegenerative disease, there are no effective therapies available. AD is considered multifactorial diseases due to the complexity of its aetiology and pathophysiology. Taking into account this consideration, new combined therapy treatments or multi-target approaches, which allow modifying several pathways that are involved in AD. As aforementioned, Resveratrol enhances the clearance of A $\beta$ , showing anti-amyloidogenic properties. Also reduces inflammation, improves synaptic plasticity and UPS functionality, induces autophagy, ameliorates mitochondrial dysfunction, modifies gut microbiota composition, and reduces neuronal cell death. Therefore, it prevents cognitive impairment and neurodegeneration in age-related diseases. Herein, we discussed the main pathways involved in the neuroprotective effects of RV as well as the potential therapeutic effect of RV on age-related cognitive decline and AD pathology.”* 117. Aging Research Reviews, 2021

### EGCG

*“The potential to treat neurodegenerative diseases (NDs) of the major bioactive compound of green tea, epigallocatechin-3-gallate (EGCG), is well documented. Numerous findings now suggest that EGCG targets protein misfolding and aggregation, a common cause and pathological mechanism in many NDs. Several studies have shown that EGCG interacts with misfolded proteins such as amyloid beta-peptide (A $\beta$ ), linked to Alzheimer’s disease (AD), and  $\alpha$ -synuclein, linked to Parkinson’s disease (PD). To date, NDs constitute a serious public health problem, causing a financial burden for health care systems worldwide. Although current treatments provide symptomatic relief, they do not stop or even slow the progression of these devastating disorders. Therefore, there is an urgent need to develop effective drugs for these incurable ailments. It is expected that targeting protein misfolding can serve as a therapeutic strategy for many NDs since protein misfolding is a common cause of neurodegeneration. In this context, EGCG may offer great potential opportunities in drug discovery for NDs.”* 118. Biomolecules, 2021

### Curcumin

*“Because of its pleotropic actions on the central nervous system, including preferential binding to amyloid proteins, Cur is being touted as a promising treatment for age-related brain diseases. Here, we focus on molecular targeting of Cur to reduce amyloid burden, rescue neuronal damage, and restore normal cognitive and sensory motor functions in different animal models of neurodegenerative diseases. We specifically highlight Cur as a potential treatment for Alzheimer’s, Parkinson’s, Huntington’s, and prion diseases.”* 119. International Journal of Molecular Sciences, 2018

### Kaempferol

*“Kaempferol has shown an important neuroprotective action in all addressed diseases (Alzheimer’s, Parkinson’s, Ischaemia Stroke, Epilepsy, Major Depressive Disorder, Anxiety Disorders, Neuropathic Pain and Glioblastoma), mainly promoting an anti-inflammatory and antioxidant effect. In addition, KPF promoted a protective effect on the brain, inhibiting proinflammatory cytotoxicity and the activity of important inflammatory pathways as NF-kB, p38MAPK, and AKT, resulting in an overall antiinflammatory action. In conclusion, we suggest that KPF and some glycosylated derivatives (KPF-3-O-rhamnoside, KPF-3-Oglucoside, KPF-7-O-rutinoside, and KPF-4’-methyl ether) have multipotential neuroprotective actions in the CNS diseases.”* 120. Frontiers in Pharmacology, 2021

## **Ferulic, Gallic, Caffeic, 3,4-dihydroxyphenylacetic, Protocatechuic, 3,4-dihydroxybenzoic, Benzoic Acids**

*“The ability of HCA derivatives to prevent amyloid transformation of some amyloidogenic proteins, and their presence not only in food products but also as natural metabolites in human blood and tissues, makes them promising for the prevention and treatment of neurodegenerative diseases of amyloid nature.”* 121. Biomolecules, 2020

## **Caffeic Acid Phenethyl Ester (CAPE)**

*“Taken together, we demonstrate the differentiation-inducing and therapeutic potential of CAPE for neurodegenerative diseases.”* 122. Frontiers in Aging Neuroscience, 2020

## **Ellagic Acid**

*“The primary pathological hallmarks of Alzheimer’s Disease are A $\beta$ ) aggregation and tau hyperphosphorylation.. Ellagic acid administration effectively decreased the level of pThr668APP and BACE1, which illustrated that ellagic acid administration reduced A $\beta$  production and improved cognitive impairment.”* 123. Current Pharmaceutical Design, 2021

*“The findings of the present study demonstrate that EA protects against MPTP-induced Parkinson’s Disease and the observed neuroprotective effects can be attributed to its potent antioxidant and anti-inflammatory properties.”* 124. Biomolecules, 2020

## **Quercetin**

*In Alzheimer’s Quercetin “Improves working memory and reduces the production of A $\beta$ , Reduces the markers of oxidative stress, LPO and activates the ERK pathway.”*

*In Huntington’s Quercetin “Reduce motor deficits, improve mitochondrial function, and attenuate some markers of oxidative stress.”*

125. Biomedicines, 2021

## **Gallic Acid**

*“During the past years, it has been reported that gallic acid is effective against nervous system’s disorders including Alzheimer’s disease, Parkinson’s disease, ischemia and reperfusion, depression and anxiety. These indicate that gallic acid can be considered as a valuable agent for nutraceutical interventions. In this study, several clinical studies suggested that gallic acid can improve human health by preventing or delaying the onset of neurological diseases. The present study indicated the neuroprotective features of gallic acid including the pre-clinical evidence for its effects in AD and PD and other diseases related to the nervous system.”*

126. INTERNATIONAL JOURNAL OF FOOD PROPERTIES, 2020

## **Cinnamic Acid**

*“We delineate that cinnamic acid activates the nuclear hormone receptor PPAR $\alpha$  to transcriptionally upregulate TFEB and stimulate lysosomal biogenesis. Moreover, using in-silico and biochemical approaches we established that cinnamic acid serves as a potent ligand for peroxisome proliferator-activated receptor  $\alpha$  (PPAR $\alpha$ )... Therefore, stimulation of lysosomal biogenesis by cinnamic acid may have therapeutic implications for treatment of Alzheimer’s disease and other lysosomal disorders originating from accumulation of toxic protein aggregates.”* 127. Neurobiology of Disease, 2019

## **Protocatechuic Acid**

*“Experimental studies strongly support the role of protocatechuic acid in the prevention of neurodegenerative processes, including Alzheimer’s and Parkinson’s diseases, due to its favourable influence on processes underlying cognitive and behavioural impairment, namely accumulation of the  $\beta$ -amyloid plaques in brain tissues, hyperphosphorylation of tau protein in neurons, excessive formation of reactive oxygen species and neuroinflammation. There is a growing evidence that protocatechuic acid may become in the future efficacious and safe substance that protects against neurodegenerative disorders.”* 128. Nutritional Neuroscience, 2017

## **Formononetin**

*“We found that FMN significantly improved learning and memory ability by suppressing A $\beta$  production from APP processing, RAGE-dependent inflammatory signaling and promoted LRP1-dependent cerebral A $\beta$  clearance pathway. Moreover, FMN treatment alleviated ultrastructural changes in hippocampal vascular endothelial cells. In conclusion, we believe that FMN may be an efficacious and promising treatment for Alzheimer’s Disease.”*

129. Bioscience, Biotechnology, and Biochemistry, 2018

## **Catechin**

*“These findings suggest that GTCs (Green Tea Catechins) have the potential to be used in the prevention and treatment of neurodegenerative diseases and could be useful for the development of new drugs.”* 130. Molecules, 2018

## **Ferulic Acid**

*“The aim of the present review is to illustrate the potential of FA as a therapeutic agent against neurodegeneration, in particular against damage caused by Alzheimer’s Disease. FA has given positive results in the inhibition of neurotoxic A $\beta$ -aggregation in vitro and in vivo in animal models. Furthermore, FA is able to interfere with the biological pathways involved in apoptotic programmed cell death induced by oxidative stress and inflammation due to A $\beta$  aggregation.”*

131. Nutrients, 2015

## **Caffeic Acid**

*“Taken together, the findings of the present study demonstrated that caffeic acid attenuated the development of Alzheimer’s Disease (AD), by increasing cognitive function, attenuating cerebral damage, and inhibiting the AD-induced increase in AChE activity and nitrite generation in a model of AD. Furthermore, caffeic acid induced the inhibition of oxidative stress, inflammation and apoptosis through the p53 and p38 MAPK signaling pathways. These findings suggest that the effects of caffeic acid in the treatment of AD occur through the p53 and p38 MAPK signaling pathways.”*

132. INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE, 2016

## **3, 4-Dihydroxyphenylacetic Acid (DOPAC)**

*“ $\alpha$ -Synuclein ( $\alpha$ -Syn), a 140-residue presynaptic protein of unknown function, is one of the major components of Lewy bodies and Lewy neurites, proteinaceous fibrillar inclusions found in brains of patients with Parkinson’s disease (PD) and several other neurodegenerative diseases... We are showing here that the interaction of DOPAC with  $\alpha$ -Syn decreases the binding affinity of  $\alpha$ Syn to lipids, suggesting that DOPAC might lead to the gain-of-toxicity of  $\alpha$ -Syn aggregates and loss-of-function of  $\alpha$ Syn, both of which could be related to progression of PD.”*

133. The Open Proteomics Journal, 2010