

Synthesis and Evaluations of Lipo-phenolic Derivatives as Anti-carbonyl Stressors in Retina Pathologies

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Carbonyl and oxidative stress play a substantial role in various neurodegenerative diseases such as Alzheimer's Disease, Parkinsonism or Age-related Macular Degeneration (AMD). In retinal pathologies, both mechanisms are involved in the transformation of all-*trans*-retinal (AtR, reactive aldehyde) to bis-retinoid A2E. Since accumulation of *trans*-retinal and A2E contribute to photoreceptor apoptosis, we designed and synthesized a resorcinol derivatives (phloroglucinol and resveratrol) featuring enhanced anti-carbonyl stress properties. Structural modifications include alkylation to increase nucleophilic and carbonyl trap properties. To improve their bioavailability and to induce a vectorization process to retinal tissue, more lipophilic derivatives have been considered. Regarding the high level of polyunsaturated fatty acids (PUFAs) present in the membrane of photoreceptors, the phenolic moiety was linked to polyunsaturated lipid moieties such as docosahexaenoic acid (DHA, C22:6 n-3), or *sn*2-Lyso-PC-DHA, eicosapentaenoic acid (EPA, C20:5 n-3), alpha linolenic acid (ALA, C18:3, n-3) and linoleic acid (LA, C18:2, n-6). Biological evaluations in ARPE-19 cell lines pointed out the benefit of isopropyl and PUFA substituents for cell survival in the presence of a carbonyl stressor.

