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Development of polyfunctional flavonoids based compounds for Alzheimer's disease

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Polyfunctional compounds comprise a novel class of therapeutic agents for the treatment of multi-factorial diseases like Alzheimer's disease (AD). Following this approach, a new series of flavonoids were designed, synthesized and biologically evaluated against acetylcholinesterase (AChE), advanced glycation end products formation (AGEs) with additional free radical scavenging activity. The *in vitro* studies showed that the majority of synthesized derivatives inhibited acetylcholinesterase (AChE) with IC₅₀ values in the nanomolar range. Among them, inhibitors FLV-16 and FLV-32, strongly inhibited AChE, and were more potent than the reference compound donepezil. Moreover, the molecular docking study displayed that most potent compounds simultaneously bind to catalytic active site (CAS) and peripheral anionic site (PAS) of AChE. Besides, these compounds also exhibited greater ability to inhibit advanced glycation end products formation with additional radical scavenging property. Thus, flavonoids might be the promising lead compound as potential poly-functional anti-Alzheimer's agents.

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