

## Design, synthesis and biological evaluation of polyfunctional flavonoids: Anti-Alzheimer's agents

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**A**lzheimer's disease (AD), a complex neurodegenerative brain disorder, a most common cause of dementia among elderly people. To date, the AD is being managed by maintaining the levels of acetylcholine by inhibiting acetylcholinesterase (AChE). Polyfunctional compounds comprise a novel class of therapeutic agents for the treatment of multi-factorial disease like AD. Following this approach integrated with polyfunctional nature of flavonoids, a novel flavonoid based compounds were designed, synthesized and biologically evaluated against AChE, advanced glycation end products (AGEs) formation with additional free radical scavenging activity. The *in vitro* studies showed that the majority of synthesized derivatives inhibited AChE with  $IC_{50}$  values in the nanomolar range along with good AGEs

inhibitory and radical scavenging activity. Among them, 7m, strongly inhibited AChE and was found to be more potent than the reference compound donepezil. Its potent inhibitory activity has been justified by docking analysis that revealed its dual binding simultaneously to catalytic active site (CAS) and peripheral anionic site (PAS) of AChE. Besides, this compound also exhibited greater ability to inhibit advanced glycation end products formation with additional radical scavenging property. It (7m) also ameliorated scopolamine-induced memory deficit in mice employing Morris water maze test, at the dose of 2, 5 and 10 mg/kg. Thus, flavonoids might be the promising lead compound as potential poly-functional anti-Alzheimer's agents.

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