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### The role of acetylcholinesterase in Alzheimer's disease: Enzymatic inhibition studies

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Alzheimer's disease (AD) is the most common form of dementia and causes a progressive and irreversible neurodegeneration. It is related with loss of cholinergic function, which affects memory, learning and behavior [1]. Neurophathologically, AD is characterized by the presence of beta-amyloid plaques (Aβ) and neurofibrillary tangles (NFT) [2] and consequent degeneration of the basal forebrain cholinergic neurons [3]. The loss of cholinergic neurons leads to the progressive reduction of acetylcholine (ACh) in the brain and resulting cognitive impairment in AD [3]. As such, the enzyme acetylcholinesterase (AChE) has been one of the prime targets in search for a treatment for AD, which uses reversible inhibitors of AChE, in order to increase levels of acetylcholine (ACh) in the brain [4].

In the present study a small library of quinolinone and indole derivatives was screened for their eeAChE inhibitory activity using the Ellman method. Rivastigmine was used as benchmark. The IC50 values ranged from 4 to 320 μM. These were promising results when compared to the benchmark; therefore our study will continue in order to determine the toxicity and metabolic stability of these potential inhibitors as well as screening them for other enzyme targets involved in AD.

References:

1. Price, D. Annual Reviews in Neuroscience, 1986. 9: p. 489-512.
2. Blennow, K., de Leon, M., Zetterberg, H. Lancet, 2006. 368: p. 387-403.
3. Garcia-Ayllon, M., Small, D., Avilla, J., Sáez-Valero, J. Frontiers in Molecular Neuroscience,2011. 4: p. 1-9.
4. Ingkaninan, K., Temkitthawon, P., Chuenchom, K., Yuyaem, T., Thongnoi, W. Journal of Ethnopharmacology, 2003(89): p. 261-264.

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