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MEETING ABSTRACTS

4-AMINOQUINIOLINES AS REVERSIBLE INHIBITORS OF HUMAN CHOLINESTERASE ACTIVITY

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We synthesised eight derivatives of 4-aminoquinolines differing in the substituents attached to the C(4)-amino group and C(7) carbon of 4-aminoquinoline, and tested their potency to inhibit human AChE and BChE. All of the compounds reversibly inhibited both enzymes with dissociation inhibition (K_i) constants from 0.50 to 50 μM exhibiting selectivity. In other words, for all compounds, AChE exhibited higher affinity than BChE. The most potent inhibitors of AChE were compounds with an octyl chain or adamantane, regardless of the group in position C(7). The shortening of the chain length caused the AChE inhibition decrease by 5-20 times. Docking studies made it clear that the high AChE affinity resulted from simultaneous interactions of the quinoline group with aromatic residues of both the catalytic active site and the peripheral site. In conclusion, the inhibition potency and selectivity classify several novel compounds as leads for further modification and optimization towards the development of new inhibitors of AChE and potential drugs for treatment of neurodegenerative diseases.

Keywords: acetylcholinesterase; butyrylcholinesterase; treatment; 4-aminoquinoline; Alzheimer's disease

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