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New furoquinoline alkaloids from the leaves of *Evodia lepta* as potential cholinesterase inhibitors and their molecular docking studies

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A lzheimer's disease (AD) is the most common cause of neurodegenerative disorder and dementia in elderly people. The cholinergic hypothesis proposes that AD is caused by reduced synthesis of the neurotransmitter acetylcholine (ACh) in the brain. In addition, a substrate non-specific butyrylcholinesterase (BChE) is also found to play a significant role in the hydrolysis of ACh. Moreover, there are several reports that have revealed that the reduction of AChE activity can be compensated for BChE activity. Thus, all of the above reasons have stimulated a great interest in screening natural cholinesterase (ChE) inhibitors as lead compounds for the intended treatment of AD as they should have significant inhibition activities towards both AChE and BChE.

Previous reports have shown that some furoquinoline alkaloids and other constituents of the plants from Rutaceae family have ChEs activities revealed to the treatment of AD. Therefore, the successive extraction and isolation of bioactive ChE inhibiting compounds from the plants of this family were interesting, as they can themselves be active and used directly as a drug. *Evodia lepta* (Spreng.) Merr. (Rutaceae) is a traditional medicinal plant used for the treatment of arthritis, fever, chickenpox, epidemic influenza, meningitis, infectious hepatitis, antipruritic, depurative and febrifuge diseases. Several furoquinoline alkaloids, flavonoids and chromones have been also reported from this plant in previous studies.

Three new furoquinoline alkaloids (1-3) along with six known furoquinoline compounds (4-9) were isolated from the leaves of *Evodia lepta* based on bioassay-guided fractionation and chromatographic techniques. All isolates were evaluated for their in vitro cholinesterase (ChEs) inhibitory activities, in which compounds 7 and 5 exhibited the highest activity toward AChE and BChE, respectively. Lineweaver-Burk plots indicated that 5 and 7 were mixed mode inhibitors of both ChE enzymes. Finally, the molecular docking studies on the binding sites of AChE and BChE were performed in order to afford a molecular insight into the mode of action of these active compounds in a good agreement with their anti-ChE results. Therefore, this information can help in designing a new inhibitor in the class of furoquinoline alkaloids in against Alzheimer's disease.

Biography

Jirapast Sichaem has completed his PhD at the age of 26 years from Chulalongkorn University. He is doing postdoctoral studies in the field of anticholinesterase compounds from Thai medicinal plants at Natural Products Research Unit, Department of Chemistry, Faculty of Science, Chulalongkorn University. He has published more than 22 papers in scientific journals.

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