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Acetylcholinesterase Inhibitors from Mace (*Myristica fragrans*)

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Acetylcholinesterase (AChE), an enzyme of cholinergic synapses terminates the neurotransmission process by breaking down the neurotransmitter acetylcholine. One approach to treat Alzheimer's disease is to prolong the existence of acetylcholine at the synaptic cleft by inhibiting AChE. This strategy has been used to improve cognitive decline in people with neurodegenerative disorders. Galantamine, a plant derived natural product is a cholinesterase inhibitor. There is a need to explore natural AChE inhibitors with high potency, low toxicity and little side effects, as synthetic inhibitors have undesirable side effects. The aim of this study was to investigate natural AChE inhibitors from Sri Lankan spices. *Myristica fragrans* produces nutmeg which is enclosed in mace, a scarlet seed covering used in cuisine and traditional medicine. It is known to have many interesting bioactivities including anti-diabetic, antioxidant, and anti-inflammatory activities.

Dried ground mace was sequentially extracted into hexane, dichloromethane, EtOAc and MeOH using ultrasonication. The AChE inhibitory activities of the extracts were tested *in vitro* using a slightly modified Ellmen method. Samples were prepared in ethanol-buffer mixture (1:1). All extracts showed good inhibition with hexane, dichloromethane, EtOAc and MeOH extracts with IC₅₀s of 29.0, 21.4, 18.3 and 13.4 mg/mL respectively. Since EtOAc and MeOH extracts had similar TLC patterns and AChE inhibitory activities, they were combined and subjected to activity guided fractionation using column chromatography followed by size exclusion chromatography using Sephadex LH 20 to give six compounds, whose structures and activities are being investigated. One showed 95% of inhibition of AChE at 100 ppm level. Mace is therefore a potential source of natural AChE inhibitors.

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