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SEARCH FOR ACETYLCHOLINESTERASE INHIBITORS FROM SRI LANKAN SPICES

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Acetylcholinesterase (AChE) is an enzyme present in cholinergic synapses of the nervous system and, it terminates the neurotransmission process by breaking down the neurotransmitter, acetylcholine. One of the approaches to treat Alzheimer's disease (AD) is to maintain the levels of acetylcholine through the inhibition of AChE. Inhibitors of AChE are used to treat many pathological conditions including AD, Parkinson's disease, myasthenia gravis, postural tachycardia syndrome etc. Galantamine, a plant derived natural product is among the cholinesterase inhibitors. Synthetic AChE inhibitors have side effects; hence there is a need to explore natural AChE inhibitors with high potency, low toxicity and minimal side effects. The aim of this study was to detect natural AChE inhibitors in spices used in Sri Lankan cuisine. Traditional Sri Lankan spices such as *Tamarindus indica* (tamarind), *Garcinia cambogia* (goraka), *Brassica repa* (mustard), *Coriandrum sativum* (coriander), *Trigonella foenum-graecum* (fenugreek), *Piper nigram* (pepper), *Foeniculum vulgare* (fennel), *Eugenia cryophyllis* (clove), *Myristica fragrans* (mace), *Cymbopogon citratus* (sera), *Zingiber officinale* (ginger) were sequentially extracted into hexane, dichloromethane, ethylacetate and methanol. The anticholinesterase inhibitory activities of the above extracts were tested *in vitro* according to Ellmen's method with slight modifications. Of the tested extracts, AChE was inhibited by crude extracts of *G. cambogia* and *M. fragrans* with following IC_{50} (concentration required for 50% inhibition of the activity) values. *Myristica fragrans* IC_{50}; hexane-29.03 mg ml^{-1},dichloromethane-21.37 mg ml^{-1}, ethylacetate- 18.29 mg ml^{-1} and methanol- 13.44 mg ml^{-1}.*Garcinia cambogia* showed significant AChE inhibition with IC_{50} of hexane- 8.53 mg ml^{-1} and dichloromethane- 11.89 mg ml^{-1}, which is comparable with the positive control donepezil hydrochloride (IC_{50} value 0.11 mg ml^{-1}). In addition, extracts of *P. nigrum* (ethyl acetate and methanol, 100% and 64% inhibitions respectively) and *B. rapa* (hexane, dichloromethane and ethyl acetate, 49%, 27% and 26% inhibitions respectively) showed AChE inhibitory activity at 100 ppm. This study revealed that *G. cambogia* and *M. fragrans* are potential sources of natural acetylcholinesterase inhibitors. Isolation of active constituents present in these sources is important to discover new therapeutics. Ongoing work focuses on isolating active constituents present in these crude extracts.

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