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Enzyme inhibitors from an endophytic fungus associated with *Myristica fragrans*

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Myristica fragrans (Nutmeg) of the family Myristicaceae is a popular spice used worldwide and known to be rich in bioactive compounds and natural enzyme inhibitors. Endophytic fungi are searched for their potential to produce bioactive metabolites due to their symbiotic association with plants. This study was conducted to isolate and investigate the enzyme inhibitory activities of secondary metabolites of an endophytic fungus associated with *M. fragrans.* An endophytic fungus was isolated from triple sterilized fresh leaves of *M. fragrans* collected from Central Province, Sri Lanka. Pure culture of an emerged fungus was inoculated to Potato Dextrose Broth and kept for 21 days with shaking at room temperature. The broth was filtered and extracted to EtOAc and mycelium was separately extracted to EtOAc followed by MeOH. EtOAc extract was separated using chromatographic techniques (Silica gel column, Sephadex LH-20, HPLC, PTLC) to furnish four pure compounds and their structures were elucidated using NMR spectra and reported data. The endophytic fungus obtained was tentatively identified as *Phyllosticta* sp. by amplification of ITS regions of the fungal rDNA gene. Further identification using other gene regions is in progress. The isolated compounds were aurasperone F (**1**), foncesin B (**2**), rubrofusarin B (**3**) and 4-methoxy-6-(2-methyl-1-oxopropyl)-2H-pyran-2-one (**4**). Compounds were screened for enzyme inhibitory activities against α-glucosidase, acetylcholinesterase and lipase enzymes. Compounds **1**, **2**, and **3** showed high α-glucosidase inhibitory activity with IC_{50} values of 16.13 mg l^{-1}, 15.66 mg l^{-1} and 15.29 mg l^{-1} respectively. Positive control Acarbose showed IC_{50} of 107.76 mg l^{-1}. Compound **3** resulted in high acetylcholinesterase inhibitory activity (IC_{50} 70.29 mg l^{-1}) whereas **2** showed mild activity for acetylcholinesterase inhibition with IC_{50} 310.82 mg l^{-1}. Compound **1** showed very low acetylcholinesterase activity. Positive control Donepezil showed IC_{50} of 0.03 mg l^{-1}. Compound **2** had moderate lipase inhibitory activity with IC_{50} 131.53 mg l^{-1}. Positive control Orlistat showed IC_{50} of 3.125 mg l^{-1}. Results suggest the potential of this endophytic fungus as a source of natural enzyme inhibitors.

Keywords: *α-glucosidase, acetylcholinesterase, Myristica fragrans, secondary metabolites*

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