

New class of acetylcholinesterase inhibitors from the stem bark of *Knema laurina* and their structural insights

ABSTRACT

Bioassay-guided extraction of the stem bark of *Knema laurina* showed the acetylcholinesterase (AChE) inhibitory activity of DCM and hexane fractions. Further repeated column chromatography of hexane and DCM fractions resulted in the isolation and purification of five alkenyl phenol and salicylic acid derivatives. New compounds, (+)-2-hydroxy-6-(10'-hydroxypentadec-8'(E)-enyl)benzoic acid (1) and 3-pentadec-10'(Z)-enylphenol (2), along with known 3-heptadec-10'(Z)-enylphenol (3), 2-hydroxy-6-(pentadec-10'(Z)-enyl)benzoic acid (4), and 2-hydroxy 6-(10'(Z)-heptadecenyl)benzoic acid (5) were isolated from the stem bark of this plant. Compounds (1-5) were tested for their acetylcholinesterase inhibitory activity. The structures of these compounds were elucidated by the 1D and 2D NMR spectroscopy, mass spectrometry and chemical derivatizations. Compound 5 showed strong acetylcholinesterase inhibitory activity with IC₅₀ of 0.573 ± 0.0260 M. Docking studies of compound 5 indicated that the phenolic compound with an elongated side chain could possibly penetrate deep into the active site of the enzyme and arrange itself through π - π interaction, H-bonding, and hydrophobic contacts with some critical residues along the complex geometry of the active gorge.

Keyword: *Knema laurina*; Myristicaceae; Acetylcholinesterase inhibition; Alkyl resorcinol; Molecular docking