

OR-2**Semi-Synthesis of α -Mangostin Derivatives and Evaluation of their Cholinesterase Inhibitory Activity**Khaw Kooi Yeong¹, Tan Soo Choon² and Vikneswaran Murugaiyah^{1,*}¹*Displine of Pharmacology, School of Pharmaceutical Sciences, Universiti Sains Malaysia, 11800, Penang, Malaysia;*²*Institute for Research in Molecular Medicine (INFORMM) Universiti Sains Malaysia, 11800, Penang, Malaysia;**E-mail: vicky@usm.my*

α -mangostin is the major secondary metabolite found in *Garcinia mangostana*. It possess interesting pharmacological activities, for example anti-inflammation, antiviral and anti-cancer. The aims of this study were to semi-synthesize of α -mangostin derivatives and evaluation of their cholinesterase enzymes inhibitory activities in vitro. Four α -mangostin derivatives (GM A1-GM A4) were successfully synthesized. The structures of GM A1-A4 were elucidated and confirmed by comparison of melting points, mass spectra and nuclear magnetic resonance spectra with their precursor, α -mangostin. All four derivatives showed less potent inhibitory activities toward AChE and BChE than α -mangostin. Their IC₅₀ values were between 4.15-6.73 μ M and 26.99-129.13 μ M against AChE and BChE, respectively. GM A1-GM A4 was 1.7-2.7 times less potent than that of α -mangostin on AChE and 4.6-22.0 times less potent than α -mangostin on BChE. The results indicated that by increasing the alkyl side chain, the inhibitory potency of the synthetic compounds increased. Interestingly, all derivatives showed more selective inhibitory activity towards AChE than α -mangostin. This suggests that the removal of the hydroxyl group at C-3 and C-6 position leads to marked reduction in the activity towards BChE. Despite their reduced potency compared to α -mangostin, these derivatives may have better blood brain barrier penetration, being less polar than α -mangostin.

Keywords: α -mangostin, acetylcholinesterase, butyrylcholinesterase, IC₅₀, selectivity.
