RESEARCH ARTICLE

Cycloart-24-ene-26-ol-3-one, a New Cycloartane Isolated from Leaves of Aglaia exima Triggers Tumour Necrosis Factor-Receptor 1-Mediated Caspase-Dependent Apoptosis in Colon Cancer Cell Line

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Abstract

Plants in the Meliaceae family are known to possess interesting biological activities, such as antimalarial, antihypertensive and antitumour activities. Previously, our group reported the plant-derived compound cycloart-24-ene-26-ol-3-one isolated from the hexane extracts of Aglaia exima leaves, which shows cytotoxicity towards various cancer cell lines, in particular, colon cancer cell lines. In this report, we further demonstrate that cycloart-24-ene-26-ol-3-one, from here forth known as cycloartane, reduces the viability of the colon cancer cell lines HT-29 and CaCO-2 in a dose- and time-dependent manner. Further elucidation of the compound’s mechanism showed that it binds to tumour necrosis factor-receptor 1 (TNF-R1) leading to the initiation of caspase-8 and, through the activation of Bid, in the activation of caspase-9. This activity causes a reduction in mitochondrial membrane potential (MMP) and the release of cytochrome-C. The activation of caspase-8 and -9 both act to commit the cancer cells to apoptosis through downstream caspase-3/7 activation, PARP cleavage and the lack of NFkB translocation into the nucleus. A molecular docking study showed that the cycloartane binds to the receptor through a hydrophobic interaction with cysteine-96 and hydrogen bonds with lysine-75 and -132. The results show that further development of the cycloartane as an anti-cancer drug is worthwhile.