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The role of the PAK-1 inhibitor, Frondoside A in the treatment of cancer

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Frondoside A is a triterpenoid glycoside isolated from the edible sea cucumber *Cucumaria frondosa*. Frondoside A is an inhibitor of p21 activated kinase 1 (PAK-1). This compound has been shown to be an effective anti-cancer agent in leukemias and several solid malignancies, including pancreatic, colonic, breast, prostate and lung cancers with induction of apoptosis, as evidenced by morphological changes, annexin V binding, up-regulation of the cyclin-dependent kinase inhibitor $p21^{waf1}$, up-regulation of proapototic proteins such as Bax, down-regulation of anti-apoptotic proteins such as Mcl-1 and Bcl2, activation of caspase 3, 6 and 9 activities and TUNEL assay. Frondoside A also inhibits invasion, metastases and angiogenesis in several models, potentiates the effects of other therapeutic agents, reduces multidrug resistance and shows anti-inflammatory and immunomodulatory effects with stimulation of innate immunity. Since PAK-1 activates multiple cellular pathways, including the ERK, p38 and Jnk mitogen-activated protein kinases (MAPK) and nuclear factor kappa B (NFκB), this explains the broad spectrum of anti-cancer and anti-inflammatory properties of frondoside A. Frondoside A, does not have toxic effects at therapeutic doses, as evidenced by lack of change in CBC, liver function tests, body weight, etc. It has an LD50 of 9.9 mg/kg in mice, which is 1000 times higher than the dose used therapeutically. Since its anticancer effects are not tissue specific Frondoside A may prove to be a valuable agent for the treatment for many malignant diseases.

Biography

Thomas E Adrian has his training at the Royal Postgraduate Medical School, Imperial College London, UK. He was the Director of the Gastrointestinal Surgical Research at Yale University. He was the Research Director in the Cancer Center at Creighton University and moved to Northwestern University School of Medicine in Chicago, where he was the Director of Gastrointestinal Cancer Research. In 2006, he became Professor and Chairman of the Department of Physiology in the College of Medicine and Health Sciences, UAE University. He has published more than 400 articles in peer-reviewed journals (>23,000 citations, H index 76) and 85 reviews and book chapters.

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