Artonin E induces p53-independent g1 cell cycle arrest and apoptosis through ROS-mediated mitochondrial pathway and livin suppression in MCF-7 cell

ABSTRACT

Artonin E is a prenylated flavonoid compound isolated from the stem bark of Artocarpus elasticus. This phytochemical has been previously reported to be drug-like with full compliance to Lipinski's rule of five and good physicochemical properties when compared with 95% of orally available drugs. It has also been shown to possess unique medicinal properties that can be utilized in view of alleviating most human disease conditions. In this study, we investigated the cytotoxic mechanism of Artonin E in MCF-7 breast cancer cells, which has so far not been reported. In this context, Artonin E significantly suppressed the breast cancer cell's viability while inducing apoptosis in a dose-dependent manner. This apoptosis induction was caspase dependent, and it is mediated mainly through the intrinsic pathway with the elevation of total reactive oxygen species. Gene and protein expression studies revealed significant upregulation of cytochrome c, Bax, caspases 7 and 9, and p21 in Artonin E-treated MCF-7 cells, while MAPK and cyclin D were downregulated. Livin, a member of the inhibitors of apoptosis, whose upregulation has been noted to precede chemotherapeutic resistance and apoptosis evasion was remarkably repressed. In all, Artonin E stood high as a potential agent in the treatment of breast cancer.

Keyword: Artonin E; Apoptosis; Breast cancer; Cell cycle; Livin