

Abstract

Effect of a New Sapogenol Derivative (AG-07) on Cell Death via Necrosis †

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Abstract: Saponins, plant secondary metabolites with high molecular weight, carry sugar groups on the triterpenic or steroidal skeleton. They exhibit biological activities such as anti-HIV, immunoadjuvant, analgesic and anticancer. Saponins have been reported to induce apoptosis, autophagy, stress responses and also inhibit cell cycle and invasion-migration in cancer cells. As saponins have partially weaker anti-cancer properties, they are often used as starting compounds for semi-synthesis of biologically more active molecules. With the same aim, we have focused on cycloartane-type saponins from *Astragalus* species to prepare potent compounds with cytotoxic activity. Cycloastragenol, a major sapogenol encountered only in *Astragalus* genus, was used to synthesize astragenol (AG) and then AG-07, a novel compound. Herein, we report the anticancer activities of AG and AG-07 against HCC1937 and HeLa cells by WST-1 assay. Additionally, levels of proteins associated with cell death are examined by immunoblotting. Cell death was also evaluated using flow cytometry and AO/EB staining. In comparison to AG, our results show that AG-07 is more cytotoxic. Furthermore, it induces formation of necrosis-associated protein fragments and necrosis-mediated cell death. In conclusion, AG-07, has a lethal effect on cancer cells through non-apoptotic cell death mechanism.

Keywords: triterpenoid sapogenin; astragenol; cycloastragenol; necrosis; HCC1937; HeLa



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