

Research Article

Artocarpin Induces Apoptosis in Human Cutaneous Squamous Cell Carcinoma HSC-1 Cells and Its Cytotoxic Activity Is Dependent on Protein-Nutrient Concentration

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Artocarpin, a natural prenylated flavonoid, has been shown to have various biological properties. However, its effects on human cutaneous squamous cell carcinoma (SCC) have not been previously investigated. We set out to determine whether artocarpin has cytotoxic effects on SCC cells and whether its pharmacological activity is dependent on protein-nutrient concentration. Our results showed that treatment of HSC-1 cells (a human cutaneous SCC cell line) with artocarpin decreased cell viability and induced cell apoptosis by increasing caspase 3/7 activity. These effects were more pronounced at low fetal bovine serum (FBS) concentrations. Artocarpin induced an increase in the level of phospho-p38 and a decrease in the levels of phospho-ERK, phospho-JNK, phospho-Akt, phospho-mTOR, and phospho-S6K. High FBS concentrations in the culture media inhibited and delayed the uptake of artocarpin from the extracellular compartment (culture media) into the intracellular compartment, as determined by high performance liquid chromatography (HPLC) analysis. In conclusion, artocarpin induces apoptosis in HSC-1 cells through modulation of MAPK and Akt/mTOR pathways. Binding of artocarpin to proteins in the FBS may inhibit cellular uptake and reduce the cytotoxic activity of artocarpin on HSC-1 cells. Therefore, artocarpin may have potential use in the future as a form of treatment for cutaneous SCC.

1. Introduction

Cutaneous squamous cell carcinoma (SCC) is a common form of skin cancer which arises from epidermal keratinocytes [1]. The most important risk factor for the development of SCC is ultraviolet radiation from sunlight exposure, especially in people with white skin and those who work outdoors [2]. This skin tumor is locally invasive and may metastasize to regional lymph nodes and visceral organs

(including liver, bones, lungs, and brain). Cutaneous SCC is usually treated by surgery [3, 4]. However, surgery is invasive and can cause scarring and disfigurement. Moreover, surgery is not suitable for all patients, particularly elderly patients, patients with underlying medical diseases, those with aggressive tumors which have invaded vital structures, and patients with multiple lesions. In addition, patients with metastatic SCC may require radiotherapy and chemotherapy, which may produce severe side effects [5]. There is therefore