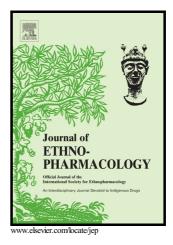
Author's Accepted Manuscript

Bufalin inhibits pancreatic cancer by inducing cell cycle arrest via the c-Myc/NF- κ B pathway

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ACCEPTED MANUSCRIPT

Bufalin inhibits pancreatic cancer by inducing cell cycle arrest via

the c-Myc/NF-κB pathway

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ABSTRACT

Ethnopharmacological relevance: Bufalin, a cardiotonic steroid isolated from toad venom (bufo gargarizans Cantor or B. melanotictus Schneider), has widely demonstrated antitumor effects and exhibits potential antitumor activity in various human cancer cells lines.

Aims of the study: The main characteristic of cancers including pancreatic cancer is the ability of uncontrolled proliferation. The aim of this study is to clarify the underlying mechanism by which bufalin inhibits pancreatic cancer cell proliferation.

Materials and methods: The effect of bufalin on the suppression of tumor growth in vivo was studied in a bioluminescent mouse model generated using the pancreatic cancer cell line BxPC3-luc2 and the cytotoxicity was evaluated in BcPc3 and Sw1990 cells with MTT. Flow cytometry and western blotting analyses were utilized to detect the effect of bufalin on the cell cycle and to detect the cell cycle-related proteins, respectively. Then, a luciferase reporter assay was applied to screen the activity of potent transcription factors following bufalin exposure and their expression was detected by western blotting.

Results: Bufalin suppressed tumor growth in a bioluminescence mouse model generated using BxPC3-luc2 cells and inhibited cell proliferation in vitro through inducing cell cycle arrest at S phase. Bufalin treatment inhibited cyclin D1 and cyclin E1 expression and therefore increased expression of p27, a regulatory molecular that controls cell cycle transition from S to G2 phase. Furthermore, luciferase reporter screening studies revealed that bufalin inhibited the expression and activity of the transcription factors c-Myc and NF- κ B, which might cause cell cycle arrest at S phase and the inhibition of cell proliferation.

¹ These authors contributed equally to this paper.

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