Chemopreventive Activity of *Ferulago angulate* against Breast Tumor in Rats and the Apoptotic Effect of Polycerasoidin in MCF7 Cells: A Bioassay-Guided Approach

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Abstract

*Ferulago angulata* leaf hexane extract (FALHE) was found to be a potent inducer of MCF7 cell apoptosis. The aims of the present study were to investigate the in vivo chemopreventive effect of FALHE in rats, to identify the contributing anticancer compound and its potential mechanism of action against MCF7 cells. Thirty rats harboring LA7-induced breast tumors were divided into five groups: tumor control, low-dose FALHE, high-dose FALHE, treatment control (tamoxifen) and normal control. Breast tissues were then subjected to histopathological and immunohistochemical analyses. A bioassay-guided investigation on FALHE was performed to identify the cytotoxic compound and its mechanism of action through flow cytometry, real-time qPCR and western blotting analyses. An in vivo study showed that FALHE suppressed the expression of the tumor markers PCNA and Ki67. The tumor size was reduced from 2031 ± 281 mm³ to 432 ± 201 mm³ after FALHE treatment. FALHE administration induced apoptosis in breast tumor cells, and this was confirmed by high expression levels of Bax, p53 and caspase 3. Cell cycle arrest was suggested by the expression of p21 and p27. The in vitro experimental results resulted in the isolation of polycerasoidin as a bioactive ingredient of FALHE with an IC₅₀ value of 3.16 ± 0.31 μg/ml against MCF7 cells. Polycerasoidin induced mitochondrial-dependent apoptosis in breast cancer cells via caspase activation and changes in the mRNA and protein expression of Bax and Bcl-2. In addition, flow cytometric analysis demonstrated that the treated MCF7 cells were arrested at the G₀ phase, and this was associated with the up-regulation of p21 and p27 at both the mRNA and protein levels. The results of the present study reinforce further investigations scrutinizing the promising potential of the *F. angulata* chemical constituents as breast cancer chemopreventive agents.