

Potential Use of Xanthohumol in Carcinoid Cancer

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Background: Current treatment for carcinoid cancer, besides surgery, has proved inadequate. This results in a critical need to identify new anticarcinogenic agents in order to develop novel treatment options. Xanthohumol (XN), a natural compound from hop plants, is used in beer. XN has dose-dependent bioavailability and defined pharmacokinetics. The purpose of this study was to evaluate the effectiveness of XN on carcinoid cancer growth, with anticipation of developing this compound as a potential treatment for carcinoid cancer.

Methods: We treated human pancreatic BON, bronchopulmonary H727, and lung UMC-11 carcinoid cells, (representative of all carcinoids), with up to 15 $\mu\text{mol/L}$ of XN, and analyzed effect on cell growth by colony formation assay. Flow cytometry and western analysis were utilized to examine the mechanism of growth inhibition. BON carcinoid xenograft tumors were subjected to intraperitoneal injections of XN (3 mg/kg bwt), to determine the in vivo effect of this drug.

Results: XN treatment resulted in a reduction in the ability of carcinoid cells to form colonies, in a dose-dependent manner. Flow cytometry and western analysis confirmed the observed decrease in cell viability, and showed that the decrease was mediated through apoptosis. The carcinoid tumors in the mouse xenograft experiment showed a significant reduction in growth only in XN administered mice.

Conclusions: XN treatment reduced cell viability and colony forming ability, and increased cell death through apoptosis. In addition, administration of XN suppressed cancer cell growth in an in vivo xenograft mouse model. Orally administered XN showed high bioavailability and does not affect major organ functions, nor cause any adverse effects on female reproduction or offspring development in mice, supporting that XN may not be harmful to humans. This fact, combined with the potential anticarcinogenic activity found here, warrants further investigation in order to treat patients with carcinoid disease.