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Effects of Zerumbone on Cytotoxicity and Inhibition of Colony Formation in Bile Duct Carcinoma

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Zerumbone derived from *Zingiber zerumbet* Smith, was reported to have a variety of pharmacological effects, including antioxidants, antiviral, anti-inflammatory, hepatoprotection, antiplatelet aggregation, and antibacterial. Recently, the increasing attention was paid to the anticancer actions of zerumbone. It was reported that zerumbone exhibited a strong ability to treat liver cancer, lung carcinogenesis, and leukemia through increasing the apoptosis and inhibiting the invasion. But, whether zerumbone played the inhibitory roles in bile duct carcinoma remains fully unknown. The present study was undergone aiming to evaluate whether zerumbone could inhibit the growth of bile duct carcinoma (HuH-28 cells). Zerumbone were tested in vitro for cytotoxicity and colony formation inhibition and MAPK family (ERK, p38, JNK) inactivation in HuH28 cells after co-treatment with TPA. Extracellular signal-regulated kinase (ERK), p38, and Jun N-terminal Kinases (JNKs) are members of the Mitogen-Activated Protein Kinase (MAPK) pathway. These kinases are activated via phosphorylation in response to growth factors, cellular and environmental stress, and cytokines. These kinases play roles in a variety of biological processes, including cell division, survival, differentiation, and metabolism. We found that zerumbone showed evident cytotoxicity against the human bile duct carcinoma cell line (HuH28 cells) in a dose-dependent manner. Moreover, this study showed that inhibition of p38 MAPK phosphorylation was important for zerumbone to interfere TPA-induced colony formation in HuH28 cells. Results suggested that pharmacological inhibition of the p38 MAPK pathway might inhibit tumor cell growth. This article provides data to support a mechanism regarding an important role of inhibition of p38 mitogen-activated protein kinase (MAPK) signal pathway in zerumbone's antitumor effect.