Carcinogenesis

# Anti-Cancer Effects Of Coptis Chinensis And Evodia Rutaecarpa In HepG2 Cells And In An Orthotopic Intrahepatic Xenograft Model

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Coptis chinensis (CC) and Evodia rutaecarpa (ER) are the components of a two-herb Chinese medicine formula, Zuo-Jin-Wan (ZJW). We investigated anti-cancer effects of ZJW, CC and ER, and their corresponding major alkaloidal components (berberine and evodiamine) in human hepatoma HepG2/NF-kB/Luc cells and in an intrahepatic xenograft mouse model. MTT assay revealed that treatment of HepG2/NF-kB/Luc cells with ZJW, CC, ER, berberine, and evodiamine significantly inhibited cell proliferation in a dose- and time-dependent manner. TC50 values after 48 hours treatment were 7.7, 4.3, 320, 5.9, and 0.3 μg/mL, respectively. Complementary DNA microarray analysis was performed on cells treated for 48 hours at TC50 doses. Hierarchical cluster analysis of genes differentially expressed after exposure to ZJW, CC, ER, berberine, and evodiamine revealed that CC and ZJW displayed a similar gene expression profile, suggesting that CC may be the main component responsible for the anti-cancer effects of ZJW. Network analysis of gene regulated by ZJW suggested that c-myc plays a critical role in its anti-cancer effects. A human hepatocellular carcinoma xenograft model was established in immunocompetent ICR mice by intrahepatic injection of HepG2/NF-kB/Luc cells. Three days after tumor cell implantation, in vivo bioluminescence imaging analysis revealed that cells had successfully been transplanted in mouse liver with acceptable variation. Seven daily treatments with ZJW (200 mg/kg, gavage) resulted in a significant decrease in accumulation of ascites fluid and in the ratio of xenograft tumor weight to liver weight, further confirmed by immunohistochemical staining of NF-kB in liver. In conclusion, ZJW significantly suppressed cancer cell growth in vitro and in HepG2/NF-kB/Luc-bearing mice. Moreover, c-myc seems to play a critical role in its anti-cancer effects.