Abstract

Although scientific evidences are lacking, *Antrodia cinnamomea* is widely prescribed in Taiwan as an adjuvant to cancer chemotherapy including hepatocellular carcinoma (HCC).We therefore hypothesize that ethanol extract of fruiting bodies of *Antrodia cinnamomea* (EEAC) is able to modulate migration and invasion to human HCC including HepG2 and Hep3B. Our results demonstrate that non-toxic EEAC exhibit an inhibitory effect on cell migration and invasion of HCC. Gelatin zymography assays confirmed that non-toxic EEAC repressed the activities of matrix metalloproteinase (MMP)-2, MMP-9, and MMP-14. Western blotting data illustrated that non-toxic EEAC decreased the expression of MMP-2, MMP-9, and MMP-14; while the expression of the endogenous inhibitors of these proteins, *i.e.*, tissue inhibitors of MMP (TIMP-1 and TIMP-2) increased. Additional, non-toxic EEAC inhibited the phosphorylation of ERK1/2, p38, and JNK1/2. Non-toxic EEAC inhibited the phosphorylation of FAK and Akt. Besides, treatment of zhankuic acid A, and cordycepin, active ingredients from EEAC decreased the expression of MMP-2, and MMP-9 through a MAPK, FAK and AKT signaling pathway. Our *in vivo* study, EEAC-treated animals demonstrate less tumor volume and immunohistochemical MMP-2, MMP-9 and MMP-14 expressions. Clinically, these results may propose further insight into the molecular mechanisms of EEAC as an adjuvant to human HCC cells.

Keywords: *Antrodia cinnamomea*; hepatocellular carcinoma; Metastasis; Invasion; Matrix metalloproteinase