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Tanshinone II-A inhibits invasion and metastasis of human hepatocellular carcinoma cells *in vitro* and *in vivo*

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ABSTRACT

Aims and background. Tanshinone II-A is an alcohol extract of the root of the traditional Chinese medicinal plant *Salvia miltiorrhiza Bunge*, whose effects and mechanism in tumor metastasis are still unclear. The aim of this study was to investigate the effects of tanshinone II-A on tumor invasion and metastasis in human hepatocellular carcinoma (HCC) and its possible mechanism of action.

Methods and study design. The HCC cell lines HepG2 and SMMC-7721 were treated with tanshinone II-A at different doses. Invasion and metastasis of tumor cells were examined by *in vitro* and *in vivo* assays. The molecular mechanisms of tanshinone II-A for inhibiting invasion and metastasis of HCC cells were investigated by Western blot and gelatin zymography.

Results. Treatment with tanshinone II-A had inhibitory effects on the migration and invasion of HCC cells. Increasing doses resulted in enhanced inhibitory effects. At 0.5 mg/L, the inhibitory effect was noticeable. At 1 mg/L, the inhibitory rate was 53.15%. The inhibitory effect became stronger with time; among 24, 48, 72 and 96 hours of treatment, the most significant effects were observed at 72 hours. Tanshinone II-A also significantly inhibited *in vivo* metastasis of HepG2 cells. Tanshinone II-A inhibited *in vitro* and *in vivo* invasion and metastasis of HCC cells by reducing the expression of the metalloproteinases MMP2 and MMP9 and by blocking NF-kappa B activation.

Conclusions. Tanshinone II-A effectively inhibited invasion and metastasis of HCC cells *in vitro* and *in vivo*, partly by inhibiting the activity of MMP2 and MMP9, and partly via the NF-kappa B signal transduction pathway.

Key words: metastasis, tanshinone II-A, metalloproteinase, liver cancer.

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