Berberine Suppresses the TPA-Induced MMP-1 and MMP-9 Expressions Through the Inhibition of PKC-α in Breast Cancer Cells.


Source

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Abstract

BACKGROUND:

Berberine (BBR) is one of the major alkaloids, and it has been reported to have a variety of pharmacologic effects, including inhibition of cell cycle progression. Here, we investigated the effect of BBR on the MMP-1 and MMP-9 expressions, which are predictors of metastasis and invasion in breast cancer cells.

METHODS:

MMP-1 and MMP-9 mRNA expressions were analyzed by real-time PCR. The levels of MMP-1 protein and PKC-α phosphorylation were detected by Western blotting. MMP-9 protein expression was detected by gelatin zymography. Cell cycle was analyzed by FACS analysis. PKC-α knock-down was examined by PKC-α siRNA transfection.

RESULTS:

The basal levels of both the MMP-1 and MMP-9 mRNA expressions were decreased by BBR treatment in a dose-dependent manner. In contrast, TPA, which is a tumor promoter, significantly increased the levels of the MMP-1 and MMP-9 mRNA and protein expressions in the MCF-7 breast cancer cells. We also observed that the TPA-induced MMP-1 and MMP-9 mRNA and protein expressions were prevented by BBR treatment. In addition, the TPA-induced MMP-1 and MMP-9 expressions were completely decreased by Go6983 and PKC-α siRNA, respectively. TPA-induced PKC-α phosphorylation was dose-dependently decreased by BBR treatment.

CONCLUSION:
The TPA-induced PKC-α phosphorylation is suppressed and then the MMP-1 and MMP-9 expressions are also inhibited by berberine. Therefore, we suggest that berberine may be used as a candidate drug for the inhibition of metastasis of human breast cancer.

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