

Inhibitory Effect of Pimelotides E on PMA-Induced Tumor Cell Invasion through Blocking NF- κ B - Dependent MMP-9 Expression

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Objectives

Several studies to detect new anticancer drugs have demonstrated that natural compounds with chemo-preventive potential inhibit the invasiveness of several types of cancer by suppressing MMP-9 expression. Very recently we have isolated an active single compound, Pimelotides E (1,2-Dihydro-5-hydroxy-9'R-methyl-6r,7r-epoxy-12-acetoxy-9,13,14-ortho-1r-decenoate-resiniferonol-10'-oic acid, PE) from traditional Chinese formulation (HTR), showing a strong inhibition of MMP-9 activity, from the ethyl acetate fraction of HTR. The present study was undertaken to investigate the molecular mechanisms involved in inhibitory effects of Pimelotides E on MMP-9 activity. Because the expression of MMP-9 has been implicated in invasion and metastasis of cancer cells, we also examined for its molecular mechanism on PMA-induced cell invasion and migration.

Materials and Methods

- Isolation of new compound from the traditional Chinese formulation
- MTT assay
- Gelatin zymography
- Transient transfection and luciferase promoter assay
- Reverse transcriptase-polymerase chain reaction (RT-PCR)
- Western blot analysis
- Invasion and wound healing assay

Results and Discussion

In the present study, Pimelotides E (PE) was examined for its potentials on PMA-induced MMP-9 expression in MCF-7 cells with detailed molecular mechanisms. Pimelotides E significantly suppresses PMA-induced MMP-9 secretion

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through inhibition of its transcriptional activity. Here we provide evidence showing that Pimelotides E inhibits PMA-induced MMP-9 secretion and protein expression through inhibition of the NF- κ B dependent transcriptional activity of MMP-9 gene via ERK and JNK signaling pathways. Matrigel invasion assay and wound healing assay showed that the inhibitions of cell invasion and migration by Pimelotides E is correlated well with inhibition of MMP-9 expression. These results indicate that Pimelotides E can be use as the potential anti-metastatic and anti-invasive agents. Futhermore, this beneficial effect of Pimelotides E may expand future clinical researches on the regulation of tumor invasion and metastasis in vivo.

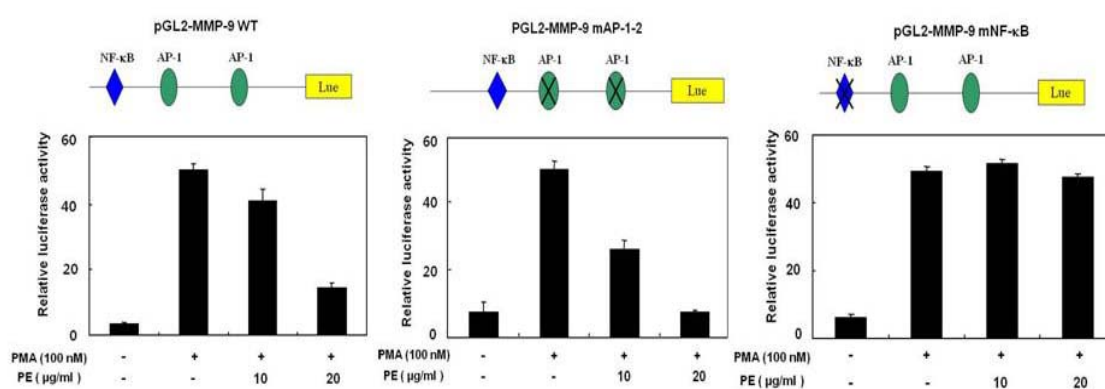


Fig. 1. Effects of Pimelotides E (PE) on the PMA-induced MMP-9 promoter activity in MCF-7 cells.

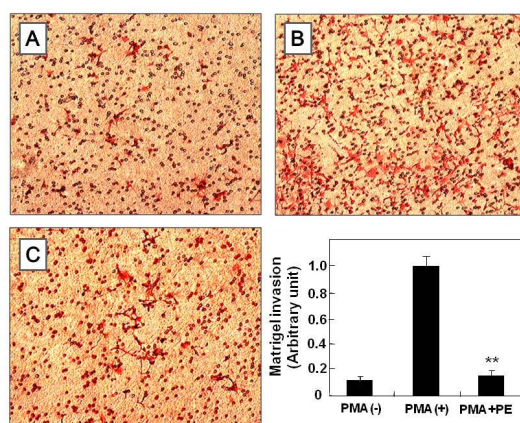


Fig. 2. Effects of Pimelotides E (PE) on the PMA-induced invasion in MCF-7 cells.