

Effects of prantschimgin and grandivitin from *Ferulago macrocarpa* on VEGF, MMP9, MMP2 and research of binding modes using computational methods

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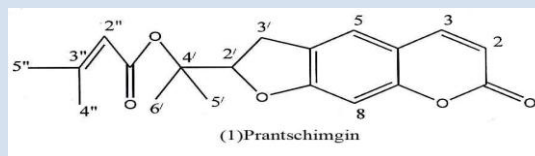
Abstract: *Ferulago macrocarpa* contains prantschimgin and grandivitin from phenolic class. Studies have shown that phenolic compounds at physiological concentrations could inhibit two groups of gelatinase matrix metalloproteinases (MMP2, MMP9). Due to the high diversity of coumarin in the plant, the possibility ability of the compounds to inhibit plant enzymes seem to be mentioned.

introduction: *Ferulago macrocarpa* of Apiaceae, native to the highlands of the West of Iran (Zagros Mountains) includes Prantschimgin and Grandivitin from phenolic class. researches have shown that phenolic compounds at physiological concentrations could prevent two groups of gelatinase matrix metalloproteinases (MMP2, MMP9). Because of the high variety of coumarin in the plant, the potency of the compounds to inhibit plant enzymes seem to be referred.

Methods and Results: Acetone extract of the plant was provided and then winterized. Thereafter, Prantschimgin and Grandivitin were purified using normal phase column chromatography and preparative HPLC, and their structures were verified. After culturing the cells, at confluence step, Supernatants were collected at 24 and 48h soup (broth supernatant containing medium containing 2% albumin, and glutamine and antibiotics and enzymes secreted by the different concentrations of active ingredients) and non-proliferation medium containing 2% albumin was amplified. The pure substances were applied on cell lines U87MG and Wehi for evaluation of VEGF, MMP-2 and 9 activities. In the computational processing, the structures have been docked in the active site of metalloproteinases9, and important interactions were detennined. then, ligand-protein complexes were subjected to molecular dynamics simulation in water, and thermodynamic attributes were calculated. (MMP9 code= 1L6J, MMP2 code= 1CK7).

prantschimgin and grandivitin were purified from *F. macrocarpa* fruits. Regarding cytotoxicity results IC50 of Prantschimgin and Grandivitin in Wehi cell line were 521.63, 232.66, and in U87MG cell line were 575.58, 322.0 lpg/ml, respectively. Biological experiment indicated significant changes in the amount and activity of matrix metalloproteinase and vascular endothelial growth factor.

Conclusion: Two coumarins, prantschimgin and grandivitin with the potential inhibitory effects on the activity of MMP2,9 and anti-angiogenesis were purified from *F. macrocarpa* fruits. The application can be expected to have therapeutic efficacy in cancer cell lines U87MG and Wehi.



Keywords: *F. macrocarpa*, Prantschimgin, Grandivitin, Matrix Metalloproteinase, Ovarian cancer