



Evaluation of sesquiterpene coumarins from *Ferula assa-foetida* on VEGF, MMP9, MMP2 and study of binding modes using computational methods

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Background and objectives: *Ferula assafoetida* of Apiaceae family bears sesquiterpene coumarins from phenolic class. Studies have shown that phenolic compounds at physiological concentration can inhibit two groups of gelatinase matrix metalloproteinases. So, the ability of compounds of this plant to inhibit the enzymes mentioned above seems to be useful. **Methods:** Acetone extract of plant was prepared and sesquiterpene coumarins were purified using column chromatography and HPLC preparative analyses and their structures were elucidated. After culturing the cell to proper confluence, the cells were isolated and the supernatant was removed. The pure substances were applied on cell lines U87MG and WEHI. In the computational part, the structure has been docked in the active site of metalloproteinase, and significant interactions were determined. Subsequently, ligand-protein complexes were subjected to molecular dynamics simulation in water and thermodynamic properties were calculated. **Results:** In the phytochemistry field galbanic acid, mogoltadone, kellerin, polyanthin and polyanthinin were extracted from *F. assafoetida*. Biological investigation demonstrated significant changes in the amount and activity of matrix metalloproteinase and vascular endothelial growth factor. Ligand binding to the active site of the protein was studied in computational causing conformational changes in the active site of the protein. **Conclusion:** Investigation revealed that the coumarins have inhibitory effects on the content and activity of MMP 2.9 and showed anti-angiogenic effect. So, they can be potentially effective in the treatment of cancer. Interactive and competitive binding between MMP-9 and galbanic acid were studied with FT-IR, UV-Vis and fluorescence methods and MMP-9 structure was changed in these interactions.

Keywords: galbanic acid, kellerin, matrix metalloproteinases, mogoltadone, polyanthin