Elucidation of the effect o fplumbagin on the metastatic potential of B16F10 murine melanoma cells via MAPK signaling pathway

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Abstract

Aims of the work: Melanoma is the most dangerous form of skin cancer and it is characterized by an uncontrolled growth of the melanin producing cells the melanocytes. The incidence of metastatic melanoma keeps increasing over the past years, but the current therapy is limited by the high ability of melanoma to metastasize rapidly. Plumbagin is a naphtoquinone (5-hydroxy-2-methyl-1,4-naphthoquinone) isolated from the roots of medicinal plant Plumbago zeylanica L and widely present in Lawsonia inermis L. In this study we investigated the effect of plumbagin on the inhibition of the metastasis of B16F10 murine melanoma cells through the modulation of MAPK pathway often muted in melanoma.
Methods: MTT assay was performed to study the cytotoxicity of plumbagin on B16F10 cells. The effect of plumbagin on the invasion, migration, and adhesion of the cells was investigated as well. Global gene expression analysis was carried out to study the molecular mechanism of plumbagin, and the protein expression of cell adhesion molecules and matrix metalloproteinases (MMP's) was also checked upon plumbagin treatment.

Results: Results showed that plumbagin decreased the proliferation of melanoma cells at dose and time-dependent manner. Moreover, the migration, adhesion, and invasion of B16F10 was inhibited upon treatment. Global gene expression analysis revealed that plumbagin down-regulated MAPK and MMP's-related genes, and upregulated genes involved in apoptosis and

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response to reactive oxygen species (ROS).
Conclusion: Plumbagin can be a powerful candidate in the treatment of metastasis melanoma. It decreased the metastasis process of B16F10 by downregulating the MAPK pathway, and the induction of ROS leading to cell apoptosis. We expect that the results from this study would contribute to the understanding of plumbagin mechanism of action, and to establish plumbagin as a drug against metastatic cancer.

Keywords: Plumbagin, metastasis, MAPK pathway, invasion, migration, adhesion