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## ***In vitro* study of anti-metastatic effect of crocetin on triple negative breast cancer cells**

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Breast cancer is considered as the second most malignant cancer in women. Among various types of breast cancer, the triple negative breast cancer (TNBC) is more aggressive and metastatic, with earlier relapse and poorer survival rate than hormone receptor-positive subtypes. Moreover, patients with metastatic TNBC cannot be treated with any standard-of-care therapy. Thus, medicinal herbs and their derivative compounds are being increasingly established as beneficial alternative and complementary treatments for cancer. Crocetin is an important carotenoid present in saffron (the red dried stigma of *Crocus sativus L.*), which exhibits anti-proliferative and apoptotic effects against primary tumors. The present study aims to investigate the anti-metastatic effects of crocetin on the metastatic 4T1 cells (which closely resemble metastatic, triple negative breast cancer in humans). The 4T1 cells with different concentrations of crocetin (0-0.28mM) were incubated for various times (24, 48 and 72h). Cell viability was assessed by MTT. Scratch and trans well chamber assays were performed to investigate the effects of crocetin on cellular migration, mobility and invasion. The relative attachment of the 4T1 cell to immobilized ECM was evaluated by cell-matrix adhesion assay. The mRNA levels of major genes in metastasis (matrix metalloproteinase 9, vascular endothelial growth factor  $\alpha$  and vimentin) were measured using real-time polymerase chain reaction. It was found that crocetin inhibited the growth of 4T1 cells in time- and dose-dependent manner (the IC50 values were 0.24, 0.17 and 0.16 mM, respectively, at 24, 48 and 72 h). The doses corresponding to approximately 90% and 75% cell viability were opted for subsequent assays. The migration of 4T1 cells was significantly interrupted by crocetin and it reduced cell invasion and mobility. Crocetin also decreased the adhesion of 4T1 cells, in a dose-dependent manner. Crocetin down-regulated the level of MMP-9, VEGF- $\alpha$  and Vim (activated genes in metastasis). These *in vitro* results indicate that crocetin, as a therapeutic herbal product, has anti-metastatic potential, in addition to its proven anti primary-tumor effects. Therefore, it may be an effective candidate for controlling malignant metastatic breast cancer.

### **Biography**

Laleh Arzi is PhD candidate in biochemistry at Institute of Biochemistry and Biophysics (IBB), University of Tehran. She obtained a BSc degree in Cellular and molecular biology from Kharazmi University and an MSc in biochemistry from (IBB), University of Tehran. She is interested in cancer research and molecular mechanism of herbal medicine, thus she is working on "anti-metastatic mechanism of bioactive compounds of saffron on metastatic breast cancer in vivo and in vitro" for her PhD project. She has several publications in international journals and has participated in several international conferences in Germany (Dresden and Tubingen) Greece (Athens) and Canada (Vancouver). She is also a lecturer in Azad University in Tehran, teaching Biochemistry and Biophysical chemistry.

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