Rosmarinic acid methyl ester induces apoptosis and inhibits migration in triple-negative breast cancer

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Breast cancer is the most common diagnosed cancer with the leading cause of cancer-related deaths in women worldwide. Almost 15% of all breast cancer is diagnosed as triple negative breast cancer (TNBC). Treatment of TNBC presents challenges due to limited targeted therapies, inefficacy of chemotherapy, and severe side effects. Thus, new strategies which overcome toxicity and drug resistance in TNBC are gaining attention. Rosmarinic acid (RA) is an abundant phenolic ester showing anti-inflammatory, anti-diabetes, anti-cancer and anti-metastatic effect. Epithelial–mesenchymal transition (EMT) is a key link to regulate tumor invasion and metastasis and studies show that RA can regulate this process. The current study investigates the anti-cancer effects of RA and its derivatives in cell line MDA-MB-231. Cytotoxicity of RA and its derivatives was observed in a dose and time dependent manner in TNBC cell line MDA-MB-231 and normal mammary epithelial cell line MCF-10A. However, the therapeutic index of rosmarinic acid methyl ester (RAME) was higher than other RA derivatives. Further growth inhibition studies revealed that RAME significantly inhibited clonogenic survival of MDA-MB-231 cell line. Cell cycle arrest at SubG0 phase shows improved anti-cancer characteristics and qPCR results showed significant increase in the apoptosis related gene expression level. RAME inhibited the cell migration and invasion ability by modulating EMT in MDA-MB-231 cell line. Furthermore, RAME regulated EMT through the downregulation of the mesenchymal markers, N-cadherin and upregulation of epithelial markers in MDA-MB-231 cell line. Taken together, our findings demonstrate the therapeutic potential of RAME in TNBC.

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