ABSTRACT

Breast cancer is the most common cancer and is the second leading cause of cancer-related deaths among women worldwide. Despite of many available therapies against breast cancer such as chemotherapy, radiotherapy, surgery, the disease is incurable and the treatments have many side effects. Many studies have proven that immune system plays a significant role in shaping and molding the tumor microenvironment. Immune system can eradicate cancerous cells by the process of immunoediting nevertheless the tumors have evolved the ability to evade from immune surveillance predominantly by overexpressing the immune checkpoint molecules especially CTLA-4, PD-1 and PD-L1 on their surfaces. *Senegalia modesta* plant extract (P.E.) was evaluated for its immunomodulatory activity in breast cancer. *In silico* and *in vitro* analyses were conducted to explore the immunomodulating role of S. modesta extract. Thymol, a monoterpene, was identified by HPLC and the breast cancer cells were treated with different concentrations of thymol and plant extract. Expression analysis was checked through qPCR. For computational studies, molecular docking was implemented in the AutoDock vina and the interactions between CTLA-4, PD-1, PD-L1 and thymol were evaluated. The docking complexes of CTLA-4, PD-1 and PD-L1 with thymol exhibited binding free energy of 4.3 kcal/mol, 5.2 kcal/mol and 4.4 kcal/mol respectively. The expression of CTLA-4 was downregulated while that of PD-1 and PD-L1 was upregulated. The results indicated that *S. modesta* extract has a remarkable role in modulating the tumor microenvironment and could be hailed as an immunomodulatory agent.