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Development of novel antiestrogenic estrone analogs targeting breast cancer

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Breast cancer is one of the highly diagnosed diseases among women and has a high incidence of mortality. The major problems associated with drugs treatment in breast cancer are drug resistance and side effects. Studies have found that estrogen, progesterone, and human epidermal growth factor 2 (HER2/neu) receptors on the surface of the breast cancer cells play a vital role in the growth of human breast cancer. Estrogens are considered to be the major causative factors of human breast cancer and most cases of breast cancer (60%-80%) composed of the luminal/estrogen-α positive (ERα +) tumors. Therefore, development of anti-estrogenic compounds is one of the major strategies in the treatment of breast cancer. Rational drug design was used for selecting higher affinity ligands to estrogen receptor/molecular target in breast cancer. A virtual library of more than 400 compounds of estrone analogs was developed and docked to estrogen receptors (alpha and beta) by using OpenEye® software applications OMEGA and FRET. Docking study showed that many compounds had higher affinity to the molecular target compared to tamoxifen (the drug of first choice for endocrine therapy of postmenopausal breast cancer). Nineteen novel estrone analogs were synthesized and selected for biological evaluation. Cytotoxicity, estrogenic and anti-estrogenic activities were examined using estrogen-responsive human breast cancer cell lines MCF-7. Results indicated that LCK-4 (novel estrone analog) exhibited 2-fold increase in anti-estrogenic activity compared to 4-hyroxytamoxifen in the concentrations ranging from (0.8-20 μM).

Biography

Abdulrhman Alsayari received his B.A. in Pharmacy from King Saud University, Riyadh, Saudi Arabia in 2006. He is currently pursuing his Ph.D. degree in Natural Product Chemistry at South Dakota State University, in the laboratories of Professor Fathi Halaweish. His research focuses on Drug discovery from natural products aimed towards novel analogs as anticancer and antiviral.

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