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In SilicoDocking Studies of Alkyl Esters Derivative of Gallic Acid on Bcl-xL Anti-apoptotic Protein of Breast Cancer

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Abstract: Gallic acid has been reported to have various biological activities including an anticancer effect. Numerous studies have indicated that alkyl esters derivative of gallic acid are more effective as an anticancer against tumor cell lines than gallic acid.Proteins in Bcl-2 family are central regulators of programmed cell death that can inhibit apoptosis, such as Bcl-xl and Bcl-2 which are overexpressed in many tumors. Bcl-Xlpermeabilizesthe outer mitochondrial membrane of cells and inhibits apoptosis. Most human breast cancers originate from epithelial cells express Bcl-2 or Bcl-xL. Clinical studies have demonstrated that increasing levels of Bcl-xL in breast carcinoma are associated with a poor outcome. In this work, we carried out an in-sukuci study of twenty alkyl ester derivatives of gallic acid (ligands)as an inhibitor ofBcl-xL protein (PDB ID 1YSG) using Autodock 4.2 software. The Gibbs energy (ΔG) showed the stability interaction between ligand and Bcl-xL residues, whereas inhibition concentration (Ki) was used to determine the binding energies of different docking conformation. In silico study showed that among the twenty alkyl esters derivative of gallic acid, five derivative compounds, namely 3,4-dimethoxy-*cis*-2-hexenylgallate; 3,4,5-trimethoxy-*cis*-2-hexenylgallate; 3,4-dimethoxy-*trans*-2-hexenylgallate; 3,4,5-trimethoxy-*trans*-2-hexenylgallate; 3,4,5-trimethoxyhexylgallatehave higher stability and stronger inhibitory activity against Bcl-xl than the gallic acid.Moreover, based on in silicoresults, derivative 3,4,5-trimethoxy-*cis*-2-hexenylgallate with ΔG value of -6.34 kcal/mol and Ki value of 22.47 µM, has the highest potential as an inhibitor of Bcl-xL. This in silicodoking study suggesting that 3,4,5-trimethoxy-*cis*-2-hexenylgallate is a promising candidate to develop as anti-breast cancer agents.
Keywords : In silico docking, gallic acid, alkyl esters derivative, anti-apoptotic, Bcl-xL, breast cancer.

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