INTISARI

Epidermal Growth Factor Receptor (EGFR) merupakan anggota dari famili reseptor ErbB yang terhubung dengan reseptor tirosin kinase. EGFR memainkan peran penting dalam proliferasi dan *survival cell* pada beberapa jenis kanker, salah satunya adalah *triple negative breast cancer* (TNBC). Penelitian ini bertujuan untuk mengembangkan pengobatan dengan target inhibitor EGFR tirosin kinase secara *molecular docking* menggunakan senyawa derivat 1,5-difenil-3-stiril-2-pirazolin.

Desain senyawa dilakukan dengan memvariasikan substituen berdasarkan ketersediaan *starting material*, yakni variasi derivat vanillin yang tersedia secara komersial. Kode PDB ID : 1M17 digunakan untuk mewakili EGFR tirosin kinase dalam keadaan *wildtype* (tidak termutasi dan termodifikasi). Protokol *docking* yang digunakan pada penelitian ini (*Pocket atoms*, *Triangle Matcher*, *Induced Fit*, GBVI/WSA dG) dioptimasi menggunakan *re-docking* secara *cognate ligand* (Validasi pose) dan *re-scoring* menggunakan 50 *known ligand* yang telah diperoleh situs ChEMBL (Validasi *scoring function*).

Berdasarkan prediksi afinitas dan aktivitas senyawa uji, diperoleh senyawa 14 dengan variasi substituen gugus metoksi pada R2 dan R4 memiliki nilai skor *docking* (-8,0421 kkal/mol) mendekati dengan *native ligand* (-8,2018 kkal/mol). Namun, cincin 2-pirazolin pada senyawa 14 tidak memiliki interaksi dengan kunci asam amino residu, yakni Met^{323}. Sehingga diprediksi tidak memiliki aktivitas inhibisi melebihi *native ligand*.

Kata Kunci : EGFR, *molecular docking*, skor *docking*

ABSTRACT

Epidermal Growth Factor Receptor (EGFR) is a member of the ErbB receptor family that is linked to the receptor tyrosine kinase. EGFR plays an important role in cell proliferation and survival in several types of cancer, one of them is triple negative breast cancer (TNBC). This research was intended to develop a treatment by targeting EGFR tyrosine kinase inhibitor using derivative compound 1,5-diphenyl-3-styryl-2-pyrazoline with molecular docking method.

Compound design was carried out by varying the substituents based on the availability of starting material, namely the commercially available variations of vanillin derivatives. PDB ID code : 1M17 was used to represent EGFR tyrosine kinase in a wildtype state (unmutated and unmodified). The optimal docking protocol were pocket atoms, triangle matcher, induced fit, GBVI/WSA dG that optimized by re-docking as cognate ligand (pose validation) dan re-scoring 50 known ligands from ChEMBL website (scoring function validation).

Based on the predicted affinity and activity of the test ligands, Compound 14 with methoxy group substituents on R2 and R4 had a docking score (-8.0421 kcal/mol) close to the native ligand (-8.2018 kcal/mol). However, the 2-pyrazoline ring in compound 14 had no interaction with the key amino acid residue, namely Met^{323}. Compound 14 was predicted not have inhibitory activity than native ligand.

Keywords : EGFR, molecular docking, docking score