HKSA SECARA *IN SILICO* SENYAWA INDUK 1-BENZIL-3-BENZOILUREA DAN TERSUBSTITUSI SEBAGAI CALON OBAT ANTIKANKER PAYUDARA

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ABSTRAK

Telah dilakukan penelitian terhadap delapan belas senyawa 1-benzil-3-benzoilurea tersubstitusi (4-CH_3Cl; 3-CH_3Cl; 2-CH_3Cl; 4-$N(CH_3)_2$; 2-F, 4-CF_3; 3-F, 4-CF_3; 3-CF_3; 2-F, 3-CF_3; 2-CF_3; 4-F, 2-CF_3; 5-F, 2-CF_3; 4-SCH_3; 2-OCF_3; 3-OCF_3; 4-OCF_3; 4-$COCF_3$; 4-SCF_3; 4-CH_3Br) secara *in silico* sebagai calon obat antikanker payudara. Penelitian ini merupakan studi hubungan kuantitatif perubahan struktur (sifat fisikokimia: lipofilik, elektronik, dan sterik) terhadap prediksi bioavailabilitas (F), aktivitas (*rerank score*), dan toksisitas (LD_{50}). Struktur dua dan tiga dimensi dibuat menggunakan program *ChemBioDraw Ultra* dan *ChemBio3D Ultra*. Program *ACD I-Lab* digunakan untuk mencari sifat fisikokimia serta nilai F dan LD_{50}. Program *docking* yang digunakan adalah *Molegro Virtual Docker* dengan reseptor c-Abl kinase kode 3HEG. Hasil analisis regresi delapan belas senyawa 1-benzil-3-benzoilurea tersubstitusi menggunakan IBM® SPSS® *Statistic* 20 menunjukkan adanya hubungan linier dan non linier antara sifat fisikokimia (lipofilik, elektronik, dan sterik) dengan bioavailabilitas ($F = -0.007\ M_w + 0.001\ Etot + 0.257\ \pi + 2.048$), aktivitas (*Rerank score* = $1.182\ ClogP^2 - 12.999\ ClogP - 65.305$), dan toksisitas ($LD_{50}$ (*mouse*) oral = $-264.255\ CMR + 4.174\ Etot - 39.721\ ClogP + 3629.432$; LD_{50} (*rat*) oral = $350.146\ CMR + 3.228\ \sigma - 1060.622\ \pi + 152.961$) secara *in silico* sebagai calon obat antikanker payudara. Hasil *docking* untuk HKSA menunjukkan 1-benzil-3- (3-trifluorometoksi)benzoilurea memiliki nilai *rerank score* terbaik (-102,1963 kkal/mol), lebih baik daripada hidroksiurea (-38,1604 kkal/mol) dan senyawa induk 1-benzil-3-benzoilurea (-91,3796 kkal/mol).

Kata Kunci: HKSA, 1-benzil-3-benzoilurea tersubstitusi, *in silico*, antikanker payudara

ABSTRACT

A research has been conducted to eighteen compound 1-benzyl-3-benzoylurea substituted (4-CH_3Cl; 3-CH_3Cl; 2-CH_3Cl; 4-$N(CH_3)_2$; 2-F, 4-CF_3; 3-F, 4-CF_3; 3-CF_3; 2-F, 3-CF_3; 2-CF_3; 4-F, 2-CF_3; 5-F, 2-CF_3; 4-SCH_3; 2-OCF_3; 3-OCF_3; 4-OCF_3; 4-$COCF_3$; 4-SCF_3; 4-CH_3Br) using in silico method as a potential drug for breast cancer. This is quantitative relationship study between structure changes (physicochemical properties: lipophilic, electronic and steric) and the prediction of bioavailability (F), activity (rerank score), and toxicity (LD_{50}). Two and three-

dimensional structure created using ChemBioDraw Ultra and ChemBio3D Ultra. *ACD I-Lab* program used to find the physicochemical properties as well as the value of F and LD_{50}. Docking program used is Molegro Virtual Docker with c-Abl kinase receptor code 3HEG. Regression analysis of eighteen compound 1-benzyl-3-benzoilurea and substituted using IBM® SPSS® Statistics 20 showed a linear and non linear relationship between physicochemical properties (lipophilic, electronic and steric) and the bioavailability ($F = -0.007\ M_w + 0.001\ Etot + 0.257\ \pi + 2.048$), activity (*Rerank score* = $1.182\ ClogP^2 - 12.999\ ClogP - 65.305$), and toxicity ($LD_{50}$ (*mouse*) oral = $-264.255\ CMR + 4.174\ E\,tot - 39.721\ ClogP + 3629.432$; LD_{50} (*rat*) oral = $350.146\ CMR + 3.228\ \sigma - 1060.622\ \pi + 152.961$) using in silico method as a potential drug for breast cancer. Docking results for QSAR showed that 1-benzyl-3- (3-trifluoromethoxy) benzoylurea had the best rerank score (-102,1963 kcal/mol), better than hydroxyurea (-38,1604 kcal/mol) and lead compound 1-benzyl-3-benzoylurea (-91,3796 kcal/mol).
Keywords: QSAR, 1-benzyl-3-benzoylurea substitued, *in silico*, drug for breast cancer