ABSTRAK

Kanker adalah keadaan pertumbuhan sel secara abnormal dan tak terkendali pada suatu organisme, sehingga dapat bersifat patogen terhadap organisme tersebut. Pada kanker payudara dengan karakter *triple-negative*, terjadi ekspresi berlebihan enzim *Matrix Metalloproteinase*-9 (MMP-9). Selama ini, obat-obat yang dirancang untuk menghambat MMP pada sisi *catalytic domain* gagal pada uji klinik karena bersifat non-selektif terhadap satu jenis MMP sehingga menyebabkan efek samping nyeri muskuloskeletal. Dufour *et al.* (2011) menemukan senyawa turunan pirimidin (*Compound 2*) yang dapat menghambat MMP-9 secara selektif pada *domain* lain yaitu Hemopexin dari MMP-9 (PEX-9) dan dibuktikan menghambat progresi kanker payudara secara *in vitro*. Pada penelitian ini telah disintesis analog senyawa *Compound 2* dengan struktur utama turunan purin yang dinamakan FFUSD-001, kemudian dilakukan studi interaksinya secara *in silico* dengan PEX-9 menggunakan perangkat lunak AutoDock4.0. Sintesis dilakukan melalui 2 tahap yaitu Substitusi Nukleofilik Asil antara anilin dan 3-bromopropionil klorida untuk menghasilkan senyawa intermediet, lalu reaksi S_N2 antara teofilin dan senyawa intermediet. Struktur hasil sintesis dielusidasi dengan ^{1}H-NMR dan LC-MS. Hasil studi *in silico* menunjukkan ada 2 *pose docking* yang terbaik yang menghasilkan *free energy of binding* -7,51 kcal/mol dan -7,00 kcal/mol melalui interaksi hidrogen dengan asam amino GLU60 dan ARG106 pada PEX-9.

Kata Kunci: *Docking; Kanker Payudara; Hemopexin Domain; MMP-9; PEX-9*

ABSTRACT

Cancer is the state where cells grow at an abnormal and uncontrolled manner within an organism, which can then become pathogenic towards said organism. In breast cancer of the triple-negative type, there is an overexpression of the Matrix Metalloproteinase 9 enzyme (MMP-9). To date, drugs that have been designed to inhibit MMPs by targeting the catalytic domain have failed during clinical trials because they are not specific against one type of MMP, which lead to adverse musculoskeletal side effects. Dufour et al. (2011) have found a pyrimidine-based compound (Compound 2) that can inhibit MMP-9 selectively by acting on its other domain called the Hemopexin of MMP-9 (PEX-9), which has been proven to inhibit the growth of breast cancer *in vitro*. An analogue of Compound 2 which was named as FFUSD-001 has been synthesised during this research, and an *in silico* study of its interaction with PEX-9 was performed using the software AutoDock4.0. The synthesis was carried out in 2 steps which were Acyl Nucleophilic Substitution between aniline and 3-bromopropionyl chloride to give an intermediate compound, and then an S_N2 reaction between theophylline and the intermediate compound. The structure of the synthesised compound was elucidated using ^{1}H-NMR and LC-MS. The results of the *in silico* study show that 2 best docking poses were obtained, yielding -7.51 kcal/mol and -7.00 kcal/mol respectively for the free energy of binding, by way of hydrogen-bond interactions with the amino acids GLU60 and ARG106 in PEX-9.

Keywords: *Breast Cancer; Docking; Hemopexin Domain; MMP-9; PEX-9*