DESAIN TURUNAN METRONIDASOL SEBAGAI SENYAWA ANTIKANKER BERDASARKAN HUBUNGAN KUANTITATIF STRUKTUR-AKTIVITAS MENGGUNAKAN METODE *MULTILINEAR REGRESSION* (MLR) DAN *PRINCIPAL COMPONENT REGRESSION* (PCR)

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INTISARI

Telah dilakukan desain senyawa turunan metronidasol berdasarkan pendekatan hubungan kuantitatif struktur-aktivitas (HKSA) menggunakan metode perhitungan statistika MLR dan PCR terhadap Focal Adhesion Kinase (FAK). Penelitian ini bertujuan untuk menentukan hasil persamaan HKSA terbaik dengan membandingkan hasil perhitungan statistika MLR dan PCR serta mendesain senyawa baru turunan metronidasol sebagai senyawa antikanker berdasarkan persamaan HKSA terbaik. Persamaan HKSA yang diperoleh melalui regresi multilinear digunakan untuk mendesain senyawa turunan metronidasol.

Hasil penelitian menunjukkan bahwa persamaan HKSA terbaik untuk MLR yaitu:

$$\begin{aligned} pIC_{50} = {} & -873{,}274 + (0{,}256 \times \log P) + (-244{,}464 \times E\ Lumo) \\ & + (-11{,}240 \times selisih\ L_H) + (0{,}015 \times luas\ permukaan) \\ & + (-0{,}693 \times polarisabilitas) + (0{,}137 \times refraktivitas) \\ & + (-0{,}222 \times momen\ dipol) + (-423{,}597 \times qC_1) \\ & + (1378{,}902 \times qC_2) + (402{,}947 \times qC_3) + (491{,}673 \times qC_4) \\ & + (-375{,}045 \times qN_1) + (55{,}282 \times qN_2) \end{aligned}$$

dengan parameter statistika $n = 20, R^2 = 0{,}982, SEE = 0{,}071, \frac{F_{hitung}}{F_{tabel}} = 6{,}382\ and\ PRESS = 0{,}034$ sedangkan untuk PCR yaitu $n = 20, R^2 = 0{,}330, SEE = 0{,}260, \frac{F_{hitung}}{F_{tabel}} = 1{,}165\ dan\ PRESS = 1{,}098$

dengan persamaan HKSA terbaik yaitu:

$$pIC_{50} = 0{,}735 + (-0{,}090 \times L1) + (0{,}148 \times L2)$$

Persamaan MLR digunakan untuk mendesain senyawa baru turunan metronidasol dengan aktivitas antikanker yang lebih tinggi yaitu senyawa 2-(2-metil-5-nitro-1H-imidasol-1-il)etil-4-klorobenzoat dengan pIC_{50} prediksi sebesar 0,388.

Kata kunci: antikanker, HKSA, Metronidasol, MLR, PCR.

DESIGN OF METRONIDAZOLE DERIVATIVE AS ANTI-CANCER COMPOUND BASED ON QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP USING MULTILINEAR REGRESSION AND PRINCIPAL COMPONENT REGRESSION METHODE

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ABSTRACT

The design of metronidazole derivative compound has been done based on the quantitative relation of structure-activity using statistical counting methode such as MLR and PCR to the Focal Adhesion Kinase. This research aims to find the best HKSA equation by comparing the statistical result of MLR and PCR and also designing the new derivative compound of metronidazole as an anti-cancer based on the equation. The best HKSA equation from multilinear regression is used to design the metronidazole derivative compound.

The research shows that the best HKSA equation using the MLR methode is

$$\begin{aligned} pIC_{50} = {} & -873{,}274 + (0{,}256 \times \log P) + (-244{,}464 \times E\ Lumo) \\ & + (-11{,}240 \times selisih\ L_H) + (0{,}015 \times luas\ permukaan) \\ & + (-0{,}693 \times polarisabilitas) + (0{,}137 \times refraktivitas) \\ & + (-0{,}222 \times momen\ dipol) + (-423{,}597 \times qC_1) \\ & + (1378{,}902 \times qC_2) + (402{,}947 \times qC_3) + (491{,}673 \times qC_4) \\ & + (-375{,}045 \times qN_1) + (55{,}282 \times qN_2) \end{aligned}$$

With $n = 20, R^2 = 0{,}982, R = 0{,}991,\ R^2\ SEE = 0{,}071, \frac{F_{hitung}}{F_{tabel}} = 6{,}382\ and\ PRESS = 0{,}034$. While the equation using the PCR methode is

$$pIC_{50} = 0{,}735 + (-0{,}090 \times L1) + (0{,}148 \times L2)$$

With $n = 20, R = 0{,}574, R^2 = 0{,}330, SEE = 0{,}260, \frac{F_{hitung}}{F_{tabel}} = 1{,}165\ and\ PRESS = 1{,}098$

The equation using MLR technique is used to design the new metronidazole derivative compound with higher anti-cancer activity which is 2-(2-methyl-5-nitro-1H-imidazole-1-il)ethyl-4-chlorobenzoat with prediction of pIC_{50} is 0,388.

Keywords: anti-cancer, HKSA, Metronidazole, MLR, PCR.