DESAIN SENYAWA TURUNAN 4-*CHLOROPHENYLOXY* N-*ALKYL PHOSPHORAMIDATES* SEBAGAI AGEN ANTI KANKER SERVIKS MENGGUNAKAN MODEL QSAR

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INTISARI

Penelitian desain senyawa turunan turunan 4-*chlorophenyloxy* N-*alkyl phosphoramidates* sebagai agen anti kanker serviks menggunakan model *QSAR* telah dilakukan. Hal ini bertujuan untuk menentukan persamaan *QSAR* terbaik dari senyawa turunan 4-*chlorophenyloxy* N-*alkyl phosphoramidates* (3'-[4-*fluoroaryl*-(1,2,3-triazol-1-yl)]-3'-*deoxythymidine*) dan mendesain senyawa baru turunan 4-*chlorophenyloxy* N-*alkyl phosphoramidates* (3'-[4-*fluoroaryl*-(1,2,3-triazol-1-yl)]-3'-*deoxythymidine*) dengan aktivitas yang lebih baik dibandingkan senyawa turunan sebelumnya yang telah disintesis.

Penelitian dalam merancang senyawa obat anti kanker serviks dilakukan dengan menggunakan deskriptor elektronik dan deskriptor molekuler diperoleh dengan menggunakan perhitungan DFT/B3LYP/6-31G. Metode regresi linier digunakan untuk menyusun persamaan *QSAR* terbaik dan memprediksi tingkat aktivitas IC_{50}.

Model persamaan *QSAR* terbaik dalam merancang senyawa anti kanker serviks adalah log IC_{50} = -498,629 + (-69,645 × qCl) + (-1267,348 × qC_{12}) + (-25,627 × qC_{17}) + (-1209,52 × qO_4) + (0,541 × log P), dengan parameter statistik n = 21, r^2 = 0,867, SEE = 0,179, F_{hit}/F_{tab} = 6,758 Validasi eksternal persamaan *QSAR*, n = 5, r^2 = 0,7302, PRESS = 1,798. Desain senyawa usulan terbaik yaitu P-01 dengan acuan senyawa PHO-016 (R_1: 2-$COCH_3$-Ph dan R_2: CF_3CH_2): 3'-[4-(2-acetylphenyl)-(1,2,3-triazol-1-yl)]-3'-*deoxythymidine* 5'-O-[4-*chlorophenyl* N-(2,2,2-*trifluoroethyl*) *phosphate*] dengan nilai log IC_{50}: -10,69 dan nilai log P: 2,45. Dengan nilai aktivitas biologis yang lebih baik dan nilai log P yang tinggi diharapkan dapat sebagai senyawa usulan anti kanker serviks yang lebih baik dan lebih mudah menembus membran.

Kata Kunci: QSAR, DFT, anti kanker serviks

DESIGN 4-*CHLOROPHENYLOXY* N-*ALKYL PHOSPHORAMIDATES* DERIVATIVE COMPOUNDS AS ANTI-CERVICAL CANCER AGENTS USING THE *QSAR* MODEL

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ABSTRACT

Design of 4-*chlorophenyloxy* n-*alkyl phosphoramidates* derivative compounds as anti-cervical cancer agents using the *QSAR* model has been done. The purpose of this research were detemining the best *QSAR* equation from 4-*chlorophenyloxy* N-*alkyl phosphoramidates* (3'-[4-*fluoroaryl*-(1,2,3-triazol-1-yl)]-3'-*deoxythymidine*) derivative compound and design a new compound of 4-*chlorophenyloxy* N-*alkyl phosphoramidates* (3'-[4-*fluoroaryl*-(1,2,3-triazol-1-yl)]-3'-*deoxythymidine*) derivative who has better activity than derivative compounds that synthesized before.

Designing new anti-cervical cancer was done using electronic descriptor and molecular descriptor which is gotten using DFT/B3LYP/6-31G calculation. The linear regression method was used to arrange the best *QSAR* equation and predict the IC_{50}.

The best *QSAR* model to design the anti-cervical cancer compound is log IC_{50} = -498.629 + (-69.645 × qCl) + (-1267 .348 × qC_{12}) + (-25.627 × qC_{17}) + (-1209.52 × qO_4) + (0,541 × log P), with statistic parameter n = 21, r^2 = 0,867, SEE = 0,179, F_{hit}/F_{tab} = 6.758 external validation of *QSAR* equation, n = 5, r^2 = 0.7302, PRESS = 1.798. The best compound was P-01 with the compound reference was PHO-016 (R_1: 2-$COCH_3$-Ph dan R_2: CF_3CH_2): 3'-[4-(2-acetylphenyl)-(1,2,3-triazol-1-yl)]-3'-*deoxythymidine* 5'-O-[4-*chlorophenyl* N-(2,2,2-*trifluoroethyl*) *phosphate*] who has IC_{50}: -10.69 and log P: 2.45. This result can be the best suggestion for anti-cervical cancer candidate who has better biology activity and can enter the membrane cell.

Keywords: QSAR, DFT, anti-cervical cancer