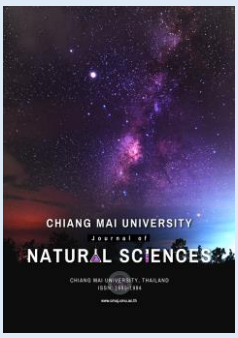

Editor:
Korakot Nganvongpanit,
Chiang Mai University, Thailand

Article history:
Received: February 4, 2021;
Revised: April 14, 2021;
Accepted: April 22, 2021;
Published online: May 11 , 2021

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Research article

Design of New Chlorochalcone Derivatives as Potential Breast Anticancer Compound Based on QSAR Analysis and Molecular Docking Study

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Abstract Quantitative structure-activity relationships (QSAR) proposes a model that relates the biological activities of drugs to their chemical structures, and the interaction between the drug and its target enzyme is revealed by molecular docking research. These studies were conducted on chalcone to produce a model that could design highly potent breast anticancer MCF7 cells. The compounds were optimized using ab initio using a basis set 6-31G, then their descriptors calculated using this method. Genetic Function Algorithm (GFA) was used to select descriptors and build the model. One of the six models generated was found to be the best with internal and external squared correlation coefficient (R^2) of 0.743 and 0.744, respectively, adjusted squared correlation coefficient (adjusted R^2) of 0.700, Standard estimate of error (SEE) of 0.198, F_{calc}/F_{table} of 6.423, and Predicted residual sum of squares (PRESS) of 1.177. The QSAR equation is pIC_{50} = 3.869 + (1.427 x qC1) + (4. 027 x qC10) + (0.856 x qC15) - (35.900 x ELUMO) + (0.208 x Log P). Hence, it can predict the breast anticancer activities of new chlorochalcones A-F. The compound with the best prediction was chlorochalcone A with pIC_{50} 2.65 and IC_{50} value of 2.26 µM. The chlorochalcones A-F were able to bind to the main amino acid residues, namely Arg120 and Tyr355, on the active site of the COX-2 enzyme. These results could serve as a model for designing novel chlorochalcone as inhibitors of COX-2 with higher breast anticancer activities.

Keywords: Chlorochalcone, COX-2, QSAR, MCF-7, Molecular docking

Funding: The authors are grateful for the financial support provided by The Ministry of Research, Technology, and Higher Education of The Republic of Indonesia.

Citation: Puspitasari, A.D., Pranowo, H.D., Astuti, E., and Wahyuningsih, T.D. 2021. Design of new chlorochalcone derivatives as potential breast anticancer compound based on QSAR analysis and molecular docking study. CMUJ. Nat. Sci. 20(3): e2021070