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In Silico Screening of Hesperetin and Naringenin Ester Derivatives as Anticancer Against Phosphoinositide 3-Kinase

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Abstract : Objective: Study the in silico Phosphoinositide 3-Kinase (PI 3-K) inhibition activity of hesperetin and naringenin ester derivatives. Acyl group substituent was different in the length of the carbon atom chain (propionyl, butyryl and valeryl).
Methods: Partition coefficient was predicted by the Chem Draw Ultra program. In silico docking using PLANTS program and visualized by Yasara program. The model of three dimension enzyme structures used in this research was Phosphoinositide 3-Kinase (PI 3-K) binding pocket with the Protein Data Bank (PDB) code 4KZC. Two dimension and three dimension conformation models of hesperetin and naringenin ester derivatives and idelalisib as the standard PI 3-K inhibitor generated by using the Marvin Sketch program.
Results: Hesperetin and naringenin have a lower partition coefficient than idelalisib. Tributyryl hesperetin, trivaleryl hesperetin, tributyryl naringenin and trivaleryl naringenin have a higher partition coefficient than idelalisib. It means that hesperetin and naringenin derivatives solubility in the oil phase to cross the cell membrane was higher than idelalisib. Docking score of hesperetin and naringenin as the lead compound and their derivatives was lower than idelalisib as the PI 3-K inhibitor standard compound. Ester derivatives of hesperetin and naringenin with the increasing the length of the acyl carbon atom chain substituted on hesperetin and naringenin will increase the PI 3-K inhibition activity. Butyryl and valeryl substituted as the acyl substituent to the hesperetin and naringenin shows the lower docking score than hesperetin and naringenin as the lead compound.
Conclusion: Increasing of the length of the acyl carbon atom chain substituted on hesperetin and naringenin it will increase the Phosphoinositide 3-Kinase (PI 3-K) inhibition activity. Trivaleryl hesperetin has the best activity in this study and thus to be a good compound to be synthesized and to be combined with anticancer drug.
Keywords: In Silico, Hesperetin, Naringenin, Ester Derivatives, Phosphoinositide 3-Kinase (PI 3-K).

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