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IDENTIFICATION OF POTENTIAL *HER2* INHIBITORS FROM PHYTOCHEMICALS USING COMPUTER-AIDED DRUG DESIGN

A.A.H.E. Amarasinghe[1], L.R.L.S. Kumari[2] and W.R.P. Wijesinghe[2,3*]

[1]Department of Molecular Biology and Biotechnology, Faculty of Science, University of Peradeniya, Peradeniya, Sri Lanka.
[2]Department of Botany, Faculty of Science, University of Peradeniya, Peradeniya, Sri Lanka.
[3]Postgraduate Institute of Science, University of Peradeniya, Peradeniya, Sri Lanka.
**priyangaw@sci.pdn.ac.lk*

Computer-aided drug Design (CADD) combined with Machine Learning (ML) is a drug discovery technique that is more efficient than nonautomated traditional drug recognition methods. Small molecule Tyrosine Kinase Inhibitors (TKIs) act on Human Epidermal growth factor Receptor 2 (*HER2)* and suppress cell proliferation in breast cancer. Even though many synthetic drugs are available, few natural chemicals have been identified as TKIs for *HER2*. This analysis was carried out to recognize phytochemicals structurally analogous to available TKIs. Modified TechOpenCADD KNIME workflow combined Machine Learning (ML) with Quantitative Structure-Activity Relationship (QSAR). Version 4.7.0 of KNIME with Server Space, Cheminformatics, and RDKit extensions was utilized to examine the input data. A total of 422 phytochemicals were used together with 19 already existing TKIs and 20 drugs of some non-communicable diseases to feed in as Simplified Molecular Input Line Entry System (SMILES). "RDkit fingerprint node" was used to convert the dataset into FeatMorgan molecular fingerprints to make data readable for ML. Fundamental ML techniques Random Forest (RF), Support Vector Machine (SVM), and Artificial Neural Network (ANN) were employed to train the model with 98.26%, 97.18%, and 98.48% accuracy, respectively. Predicted data were tested for drug-likeness using Lipinski's Rule of Five to determine the eligibility as oral drugs. From RF and SVM, one phytochemical each and three phytochemicals from ANN were predicted to be structurally similar to TKIs. The results obtained overlapped in three ML algorithms and followed at least three or more of Lipinski's Rules, indicating the possibility of developing them as TKIs. In several previous studies, two of the three predicted phytochemicals have already been shown to be *HER2* inhibitors. The plant sources of predicted phytochemicals are commonly found in Sri Lanka. However, further studies should be done to ensure the effectiveness and validity of the results.

Keywords: *HER2*, KNIME, Machine Learning, Phytochemicals, Tyrosine Kinase Inhibitors