RESCON 2025 AINI 03

IN SILICO IDENTIFICATION OF PHYTOCHEMICALS WITH ANTI-LEPTOSPIRAL ACTIVITY USING COMPUTER-AIDED DRUG DESIGN (CADD)

A.H.A.U. Amaradasa[1], L.R.L.S. Kumari[2] and W.R.P. Wijesinghe[1,2]*

[1]*Postgraduate Institute of Science, University of Peradeniya, Peradeniya, Sri Lanka.*
[2]*Department of Botany, University of Peradeniya, Peradeniya, Sri Lanka.*
*priyangaw@sci.pdn.ac.lk

Leptospirosis, one of the most common zoonotic diseases in the world, caused by pathogenic *Leptospira* spp., remains a significant public health concern due to diagnostic and therapeutic challenges. However, there are limited therapeutic options. Therefore, this study aimed to identify potential phytochemicals with anti-leptospiral properties against pathogenic *Leptospira*. In this study, 2260 phytochemicals were screened against 15 FDA-approved antibiotics that were administered for the treatment of leptospirosis. Quantitative Structure-Activity Relationship (QSAR), a computational modeling-based technique that determines the structural similarities between chemical compounds, was used to predict active compounds against *Leptospira*. The structures of compounds were obtained from the ChEMBL database in SMILES format, and converted into RDKit molecule fingerprint with MACCS fingerprints using the KNIME (Konstanz Information Miner) analytics platform. Machine learning models, Random Forest (RF), Artificial Neural Network (ANN), and Support Vector Machine (SVM) were executed with 20-fold cross-validation to predict potential drug candidates. The bioavailability of the predicted compounds was determined by the drug likeliness test. The ANN model has been able to predict six phytochemicals, which complied with drug-likeness parameters while the RF and SVM models have not predicted any compounds. The prediction accuracies of the RF, ANN and SVM models were determined to be 99.74%, 99.48% and 99.35%, respectively. The predicted phytochemicals were ixorapeptide II (Compound A), conessine (Compound B), thiophene (Compound C), methyl 8-hydroxy-3-methyl-4-[(E)-3-methyl-4-oxobut-2-enyl]-7-oxo-1,4-dihydronaphthalene-4a-carboxylate (Compound D), pyrrolidinedithiocarbamate (Compound E) and oleanolic acid glutaryl hemiester (Compound F). Compound B and Compound E were already known to have certain levels of antibacterial activity against various other bacteria. Compound D, Compound E, and Compound F are synthetic derivatives of plant-based compounds. While laboratory and clinical validation is required to determine the activity of these compounds, this study demonstrates the importance of computational techniques for screening and identifying potential drug candidates from large datasets in a cost and time-efficient manner.

Keywords: CADD, KNIME, Leptospirosis, Machine learning, Phytochemicals