Abstract No: 235 ***AI in Biomedical Sciences***

PREDICTION OF POTENTIAL SULFONAMIDE-LIKE ANTIMICROBIAL PHYTOCHEMICALS USING KNIME AND MACHINE LEARNING-BASED APPROACH

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Sulfonamide drugs are the first synthesised, selectively toxic antibiotics. They mimic p-aminobenzoic acid (PABA) to hinder folate production, which is crucial for DNA replication and thereby inhibit bacterial growth. Sulfonamides have broad-spectrum activity and are vital in treating several bacterial infections, like urinary tract infections and respiratory infections. Though different antibiotics are currently available, sulfonamides are significant, especially for patients allergic to penicillin. This study aimed to discover novel sulfonamide-like compounds from phytochemicals using a quantitative structure-activity relationship (QSAR) approach, a productive and cost-effective technique that allows the determination of the structural and biological similarities between the chemical compounds. The QSAR approach was implemented on the KNIME platform, version 5.2.5, along with cheminformatics extensions. Structural data for 407 phytochemicals, 18 FDA-approved sulfonamide drugs, and 21 control drugs were obtained from the ChEMBL database in SMILES format. These data were processed in KNIME to generate MACCS molecular fingerprints using the RDKit nodes. Three types of Machine learning (ML) models, Random Forest (RF), Artificial Neural Network (ANN), and Support Vector Machine (SVM), were trained to detect sulfonamide-like molecules, and the models were able to achieve a high prediction accuracy of 99.30%, 99.55%, and 99.33%, respectively. Both RF and ANN predicted Kaempferol-3-O-P-D-glucoside, a phytochemical obtained from *Saraca indica*, as a potential sulfonamide drug, while the SVM model did not identify any phytochemicals. The bioavailability of the predicted compound was confirmed by a drug likeliness test using Lipinski's rule of five. In this study, Kaempferol-3-O-P-D-glucoside was identified as a promising compound for producing a novel sulfonamide antibiotic drug. However, further *in-vitro* and *in-vivo* experiments are required to confirm its potential to develop novel sulfonamides and utilise it for clinical purposes as an antibiotic. In addition, this study demonstrated the effectiveness of KNIME and ML models in computer-based drug discovery.

Financial assistance from the URC Multidisciplinary Research Grant 2024 (Grant No. 449) is acknowledged

Keywords: Antibiotic drug discovery, KNIME, Machine learning, QSAR, Sulfonamides