Prediction of drug-induced *QT prolongation* through integration of pharmacovigilance data, structural and physicochemical descriptors

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Cardiotoxicity refers to the potential of drugs, chemicals or other external factors to cause adverse effects of damage to the heart.[1] It is one of the main concerns during the development of new compounds for human use, as it may pose a serious risk to patients' health, potentially leading to fatal arrhythmias. Cardiotoxicity also represents an economic hurdle in the advanced stages of clinical trials, as there is evidence that it accounts for 10% of drug candidate withdrawals over the last four decades and is the third most common cause of adverse drug reactions.[2]

One of the principal cardiac complications related to drug use is QT prolongation, which refers to an extension of the ventricular action potential. When the QT interval is prolonged, it can lead to severe cardiac events, including fatal arrhythmias.[3] However, on occasion it can be only detected during post-market surveillance, making the pharmacovigilance data an extremely valuable source of knowledge to enhance drug security.

Computational methods are valuable to detect these risks prior to drug use, and to reduce time and costs in experimental research. Drug-induced cardiotoxicity, specifically QT prolongation, has been a research objective in previous cheminformatical studies.[4] However, there is still a lack of integration between pharmacovigilance data and QSAR studies, which is addressed in this project.

In this study, we propose a hybrid modeling framework that integrates molecular descriptors, structural fingerprints, and pharmacovigilance-derived signals to predict QT prolongation risk. A curated dataset of approved and withdrawn drugs is first assembled, for which physicochemical descriptors and molecular representations (e.g., circular fingerprints) are computed. Pharmacovigilance data will be extracted from the FDA Adverse Event Reporting System (FAERS),[5] and disproportionality metrics will be used to quantify QT-related signals at the drug level.

Bibliography:

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