THE USE OF AI AND ADVANCED COMPUTER SYSTEMS TO DEVELOP DRUGS AGAINST NEW EMERGING THREATS

Implementing Ai-driven Approaches For Development Of The Target-specific Compounds With High Affinity As An Effective Countermeasure Against Chemical Threats

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Warfare chemicals present a severe threat with their potential to inflict mass casualties, reduce the effectiveness of warfighters and affect the long-term health of veterans. Countermeasures involve advanced systems that swiftly and accurately identify these chemicals, quantify their effects, and provide medical countermeasures (MCMs) solutions to mitigate or reverse poisoning effects. Artificial intelligence (AI) accelerates MCM development by rapidly screening and modeling potential therapeutics, predicting their efficacy against specific toxins, and optimizing their molecular structures to increase potency and broaden coverage against chemically similar compounds. VeriSIM Life's innovative AI-driven BIOiSIM® platform supports drug-like molecule information management and delivers detailed insights into efficacy, safety, and target exposure of potential MCMs against chemical threat agents including distribution across critical body compartments such as the brain.

In this study, we employed the BIOiSIM™ platform to identify potential MCMs against toxic chemicals with a competitive mechanism of action. We utilized a comprehensive array of classification and regression models to analyze interactions between these chemicals and specific target proteins that trigger toxicity. For each target, we generated a diverse array of descriptors covering physicochemical properties, molecular fingerprints, 2D and 3D structural properties, stereochemistry, and quantum mechanical charges. An extensive set of virtual compounds with high affinity for these targets was created and evaluated for affinity and selectivity. The predicted affinity, selectivity, and intrinsic potency of these compounds suggest their suitability as antidote compounds. We further evaluated through our platform the synthesizability of these virtual molecules in order to guide their developmental potential.

A list of molecular structures was identified, demonstrating affinity to the selected targets that significantly exceeds that of potential toxic chemicals. Most of the predicted compounds formed covalent bonds with acetylcholinesterase, a common target of many toxic chemicals, and with the adenosine A1 receptor. These compounds exhibited high affinity and selectivity towards the aforementioned targets. The complexation and reaction energies of those compounds engaging with acetylcholine centers were also greater than those of toxic chemicals. Validation of the machine learning models used to predict interactions between compounds and targets indicated an accuracy range of 0.761 to 0.951, reflecting accurate predictions of drug-receptor interactions.

The application of the BIOiSIM® platform has demonstrated significant promise in addressing the urgent need for effective antidotes against warfare chemicals. By leveraging a comprehensive suite of AI-driven models, our study has not only predicted but also validated the efficacy of novel compounds with high specificity to critical protein targets involved in toxicity mechanisms. These findings underscore the potential of AI in revolutionizing the field of chemical defense, enhancing our preparedness against chemical threats by enabling rapid development and deployment of targeted antidotes. The accuracy of our predictive models, validated through rigorous testing, offers a robust framework for future advancements in antidote research and development, ensuring a proactive stance against the evolving landscape of chemical warfare.