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# Approaches towards Drug Discovery Using Cheminformatics

**Archie Andrews***

Editorial office, ChemXpress, United Kingdom

***Corresponding author**: Archie Andrews, Editorial office, ChemXpress, United Kingdom, E-mail: chemxpress@tradescience.org

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## Abstract

**Neglected Tropical Illnesses (NTDs) are a category of infectious diseases that impact impoverished nations disproportionately. Because of their severity, NTDs have a negative influence on the Disability-Adjusted Life Year (DALY), a measure of a country's total illness burden. This measure calculates the number of years of healthy life lost owing to chronic disease and disability, as well as the number of years of life lost due to early death. As a result, NTDs alter the health of individuals as well as whole civilizations.**

***Keywords:** Drug discovery; Pharmacophore; Ligand-receptor; Cheminformatics; Medicines*

## Introduction

NTDs are estimated to impact over one billion people in 149 countries and cost developing economies billions of dollars each year, according to the World Health Organization (WHO). NTDs caused roughly 22 million DALYs worldwide in 2012. People with severe disorders frequently lose their ability to participate socially and economically, miss out on educational opportunities, and face high medical costs. As a result, NTDs are a major contributor to the poverty cycle in many countries [1]. Chemoinformatics has become an important element of the drug development process, helping to speed up the search for new compounds with desired physicochemical, pharmacological, toxicological, and pharmacokinetic characteristics.

A Dynamic Hybrid Pharmacophore Model (DHPM) was developed by some researchers to describe the combined interaction characteristics of various binding pockets. Mtb-DapB, a proven mycobacterial drug target, was utilized as the foundation for model systems to investigate the efficacy of DHPMs in screening novel, undiscovered compounds. The model systems were put through 200 ns molecular dynamics simulations, with the trajectories examined to find stable ligand-receptor interaction characteristics. Traditional Pharmacophore Models (CPM) was built from individual binding sites based on these interactions, whereas DHPMs were created from hybrid molecules occupying both binding sites [2-4]. CPMs and DHPMs screened a massive library of 1,563,764 publically accessible compounds. Tanimoto, Cosine, Dice, and Tversky similarity matrices were used to compare the screened hits produced from both types of models based on their Hashed binary molecular fingerprints and 4-point pharmacophore fingerprints. When compared to CPM-screened compounds, DHPM-screened molecules had much more structural diversity, binding strength, and drug-like characteristics, demonstrating DHPM's effectiveness in exploring novel chemical space for anti-TB drug development. The concept of DHPM can be used to explore uncharted chemical territory for a wide spectrum of mycobacterial or other disease targets [5].

Some studies suggested using integrated computational approaches to assess the druggability of the projected proteomes of *Leishmania braziliensis* and *Leishmania infantum*, the two species responsible for the various clinical presentations of leishmaniasis in Brazil. The structural, chemical, and functional contexts of the proteins in those proteomes were evaluated using techniques that combined data on molecular function, biological processes, subcellular localization, and drug binding sites, druggability, and gene expression. 31 and 37 proteins from *L. braziliensis* and *L. infantum*, respectively, have never been investigated as drug targets but have showed evidence of gene expression during the evolutionary period of pharmacological relevance [6]. In addition, when compared to the human proteome, several of the Leishmania targets revealed a 50% alignment similarity, making these proteins pharmacologically appealing since they have a lower risk of side effects. The technique employed in this work also allows for the assessment of prospective prospects for repurposing chemicals as anti-leishmaniasis medicines, inferring possible interactions between Leishmania proteins and over 1,000 compounds, only 15 of which have been evaluated as leishmaniasis treatments [7-9].

The use of artificial intelligence and machine learning for the discovery of medicines to cure tropical diseases has been ignored. Due to the increasing availability of large databases that can be used to train ML models, the ever-improving accuracy of these methods, and the lower entry barrier for researchers, and the widespread availability of public domain machine learning codes,

studies show that computational methods are starting to make significant inroads into the discovery of drugs for neglected tropical diseases. Modeling and prediction of biological processes, as well as the development of novel medicines for neglected tropical illnesses, using artificial intelligence, primarily the subset known as machine learning. The short- to medium-term development of machine learning approaches, as well as the application of other artificial intelligence methods for drug discovery, was also explored [10]. The present barriers to the application of ML techniques for neglected tropical disease medication discovery in the future, as well as the probable implications of synergistic new technical advancements, were also discussed.

## Conclusion

A multi-target model based on Quantitative Structure-Activity Relationships and a Multilayer Perceptron Neural Network (mt-QSAR-MLP) was developed by some researchers to virtually design and predict versatile inhibitors of proteins involved in the survival and/or infectivity of various pathogenic parasites. For the categorization of protein inhibitors, the mt-QSAR-MLP model showed good accuracy (>80%) in both training and test sets. The physicochemical and structural interpretations of the molecular descriptors in the mt-QSAR-MLP model were used to extract many fragments. As a result of these interpretations, four compounds were developed that were expected to be multi-target inhibitors against at least three of the five parasite proteins described here, with two of the molecules projected to block all five. In terms of the multi-target profile of the proposed compounds, docking calculations converged with the mt-QSAR-MLP model. The compounds that were created have drug-like characteristics.

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