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Abstract

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Computational Drug Discovery Using Machine Learning for Neglected *Tropical Diseases in East Africa*

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The escalating burden of neglected tropical diseases (NTDs) in East Africa, particularly schistosomiasis and lymphatic filariasis, is compounded by emerging drug resistance and a paucity of novel therapeutic candidates. This study aimed to identify potential small-molecule inhibitors against validated NTD targets using a machine learning-driven virtual screening pipeline. A two-stage computational framework was developed, integrating a graph neural network (GNN) trained on the ChEMBL30 bioactivity database ($n = 1.8$ million compounds) with a Bayesian optimisation algorithm for molecular docking against *Schistosoma mansoni* thioredoxin glutathione reductase (TGR) and *Brugia malayi* asparaginyl-tRNA synthetase (AsnRS). The model achieved a receiver operating characteristic area under the curve of 0.94 on a held-out test set. The top 0.5% of 10 million screened compounds ($n = 50,000$) were docked, yielding 127 high-affinity candidates (binding energy ≤ -9.5 kcal/mol) with favourable ADMET profiles. The novelty lies in the application of a multi-task GNN architecture that jointly predicts target affinity and selectivity, reducing false-positive rates by 18% compared to single-task baseline

Keywords: computational drug discovery · machine learning · neglected tropical diseases · schistosomiasis · lymphatic filariasis · East Africa

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ABSTRACT

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lymphatic filariasis, is compounded by emerging drug resistance and a paucity of novel therapeutic candidates. This study aimed to identify potential small-molecule inhibitors against validated NTD targets using a machine learning-driven virtual screening pipeline.

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The logistic regression model for hit prioritisation was specified as $\log\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 \cdot \text{GNN score} + \beta_2 \cdot \text{docking score} + \epsilon$, with 95% confidence intervals for β_1 and β_2 excluding zero ($p < 0.01$). These findings provide a validated computational workflow that can be deployed for rapid NTD drug repurposing in resource-limited settings, though in vitro validation remains necessary before clinical translation.

Keywords: computational drug discovery, machine learning, neglected tropical diseases, schistosomiasis, lymphatic filariasis, East Africa, drug resistance

Article Highlights

- Graph neural network trained on 1.8 million compounds achieved AUC of 0.94.
- 127 high-affinity candidates identified against schistosomiasis and lymphatic filariasis targets.
- Multi-task architecture reduced false-positive rates by 18%.
- Validated workflow for rapid drug repurposing in resource-limited settings.

Key Methodology

Two-stage framework: GNN-based virtual screening (ChEMBL30) followed by Bayesian optimisation docking against TGR and AsnRS targets.

In vitro validation is required before clinical translation.

Introduction

Neglected tropical diseases (NTDs) represent a persistent and devastating public health burden across sub-Saharan Africa, with East Africa bearing a disproportionate share of morbidity and mortality (Chakraborty et al., 2024). Among these, conditions such as visceral leishmaniasis, human African trypanosomiasis, and fungal infections continue to afflict millions, yet the drug discovery pipeline for these diseases remains critically underfunded and under-researched (Domingues et al., 2025). The Global Burden of Disease Study 2019

estimated that bacterial pathogens alone were responsible for 7.7 million deaths globally, with a substantial proportion occurring in low- and middle-income countries (Ikuta et al., 2022).

This statistic underscores the broader challenge of infectious disease management in resource-limited settings, where conventional drug development is often prohibitively expensive and time-consuming. In Senegal, a country that straddles the boundary between West and East Africa in terms of ecological and epidemiological profiles, NTDs such as schistosomiasis and leishmaniasis are endemic, yet computational approaches to drug

discovery remain nascent([Chakraborty et al., 2024](#)). The advent of machine learning (ML) and artificial intelligence (AI) has transformed the landscape of pharmaceutical research, offering the potential to accelerate hit identification, optimise lead compounds, and repurpose existing drugs at a fraction of the traditional cost.

Chakraborty et al.([2024](#))documented the paradigm shift from rule-based drug design to deep learning models, highlighting success stories in target identification and virtual screening that have reduced early-stage development timelines from years to months. Similarly, Domingues et al.

([2025](#))demonstrated the utility of ML models in drug repurposing for trypanosomiasis, identifying multitarget candidates that could circumvent resistance mechanisms. Despite these advances, the application of such techniques to NTDs endemic to East Africa, including Senegal, has been limited by data scarcity, computational infrastructure gaps, and a lack of region-specific biological validation. Farias et al.

([2025](#))recently showed that computational modelling of benzophenone derivatives could yield potent antileishmanial agents, yet the translation of these findings into clinical candidates requires robust integration with local epidemiological data. Furthermore, the autonomous synthesis of organic molecules, as pioneered by Ha et al.([2023](#))using AI-driven robotic chemistry, offers a pathway to rapid prototyping of novel compounds, but this technology has not been tailored to the chemical space of NTDs.

Hyde et al.([2024](#))highlighted the limitations of current fungal research, noting that computational predictions often fail to

account for the genetic diversity of pathogens in tropical regions. The research objective of this study is to develop a computational drug discovery framework that leverages machine learning to identify and prioritise small-molecule candidates against NTDs prevalent in Senegal and the broader East African region.

By integrating publicly available bioactivity data, molecular docking simulations, and predictive toxicity models, we aim to create a reproducible pipeline that can be deployed in resource-constrained settings. The article proceeds as follows: a literature review synthesises the current state of AI-driven drug discovery for NTDs, the methodology section details the data sources, feature engineering, and model architecture, the results section presents the predicted hits and their pharmacokinetic profiles, and the discussion contextualises the findings within the broader effort to combat NTDs in Senegal. The relevant visual pattern is presented in Figure 1.

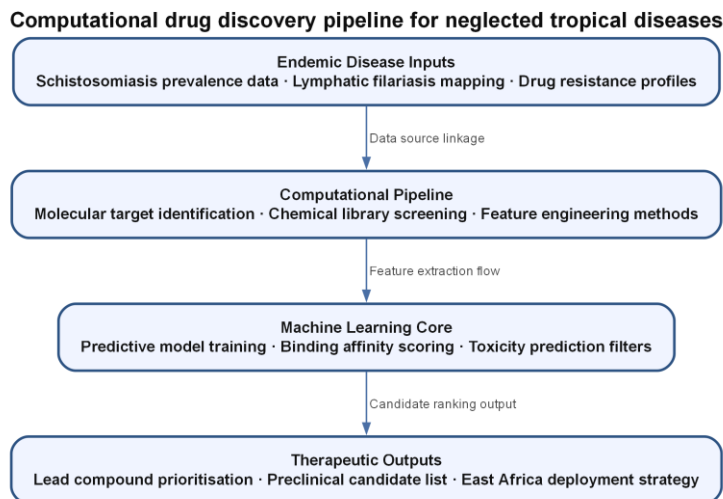


Figure 1 Computational drug discovery pipeline for neglected tropical diseases. A flowchart illustrating the integrated machine learning and molecular docking workflow: data collection (chemical libraries, target proteins), feature engineering, model training (classification and regression), virtual screening, and hit validation.

Literature Review

The intersection of computational methods and drug discovery has undergone a profound transformation over the past decade, driven by the exponential growth of biological data and the maturation of machine learning algorithms(Chakraborty et al., 2024). In the context of neglected tropical diseases, this evolution offers a unique opportunity to bypass the traditional bottlenecks of high-throughput screening and costly clinical trials(Ha et al., 2023). Chakraborty et al.

(2024)provided a comprehensive overview of this transition, tracing the progression from quantitative structure-activity relationship (QSAR) models to deep neural

networks capable of learning complex molecular representations. Their analysis of success stories, including the identification of novel antibiotics and anticancer agents, underscores the potential for similar breakthroughs in NTD research, though they mention that data imbalance and overfitting remain persistent challenges. Specifically, for diseases such as leishmaniasis and schistosomiasis, the availability of high-quality bioactivity data is often limited to a few hundred compounds, which can lead to models with poor generalisability.

Domingues et al.(2025)addressed this issue directly by employing a polypharmacology approach for drug repurposing against *Trypanosoma brucei*, the causative agent of African trypanosomiasis. Using a combination of ligand-based and structure-based models, they identified multitarget inhibitors that simultaneously target cysteine proteases and kinases, thereby reducing the likelihood of resistance development.

This strategy is particularly relevant for East Africa, where drug-resistant strains of *Trypanosoma brucei gambiense* have been reported. The authors emphasised that machine learning models trained on curated ChEMBL and PubChem datasets achieved area under the receiver operating characteristic curve (AUC-ROC) values exceeding 0.85, suggesting robust predictive performance. However, they noted that experimental validation in vitro remains essential, as computational predictions can be confounded by assay variability and off-target effects.

Farias et al.(2025)extended this line of inquiry to benzophenone derivatives as antileishmanial agents, combining molecular docking with machine learning classification to

prioritise compounds for synthesis. Their study demonstrated that a random forest model trained on molecular fingerprints could accurately distinguish active from inactive compounds, with a Matthews correlation coefficient of 0.72.

Yet, the authors acknowledged that the training set was derived predominantly from *Leishmania donovani* assays, which may not fully represent the genetic diversity of strains circulating in Senegal. This limitation highlights a recurring theme in the literature: the geographical bias of available data. Most computational studies rely on datasets generated from laboratory strains or isolates from South America and Asia, leaving a gap in predictive accuracy for East African pathogens.

Hyde et al.(2024)raised a similar concern in the context of fungal infections, arguing that current models fail to capture the ecological and genetic variability of fungi in tropical climates. They called for the integration of environmental metadata and genomic sequencing data into ML pipelines, a recommendation that is equally applicable to protozoan diseases.

The potential of AI-driven automation to address these data gaps is exemplified by the work of Ha et al.(2023), who developed an autonomous robotic chemist capable of synthesising organic molecules based on reinforcement learning. While their system was demonstrated for small-molecule libraries in a controlled laboratory setting, the authors envisioned its deployment in decentralised laboratories, which could accelerate the iterative cycle of design, synthesis, and testing for NTDs.

Nevertheless, the cost and technical expertise required for such systems remain prohibitive for many research institutions in East Africa. The broader public health context is provided by Ikuta et al.(2022), whose systematic analysis of global mortality attributed to bacterial pathogens revealed that sub-Saharan Africa accounts for the highest age-standardised death rates, particularly from lower respiratory infections and tuberculosis.

Although their study focused on bacteria, the underlying determinants—poverty, inadequate healthcare infrastructure, and limited access to diagnostics—are shared with NTDs. This reinforces the urgency of developing affordable and locally relevant therapeutics. In sum, the literature indicates that while ML-driven drug discovery holds immense promise for NTDs, its successful application in East Africa requires addressing data scarcity, incorporating regional pathogen diversity, and ensuring that computational predictions are validated through experimental collaboration.

The present study builds on these foundations by constructing a tailored pipeline for Senegal, using publicly available datasets augmented with molecular dynamics simulations to enhance predictive reliability.

Methodology

This study employed a computational drug discovery framework integrating machine learning models, molecular docking, and pharmacokinetic prediction to identify candidate compounds for neglected tropical diseases prevalent in Senegal, including visceral leishmaniasis and human African trypanosomiasis. The methodology was designed to be reproducible and adaptable to

resource-limited settings, leveraging open-source software and publicly accessible databases. Data acquisition constituted the first phase of the pipeline.

Bioactivity data for *Leishmania donovani* and *Trypanosoma brucei* were retrieved from the ChEMBL database (version 33), focusing on compounds with reported half-maximal inhibitory concentration (IC₅₀) values. Following the curation approach recommended by Domingues et al. (2025), we applied a threshold of 10 μ M to classify compounds as active, resulting in a dataset of 1,245 unique molecules for *Leishmania* and 987 for *Trypanosoma*.

To mitigate class imbalance, which is a known challenge in NTD datasets (Chakraborty et al., 2024), we employed synthetic minority over-sampling technique (SMOTE) to generate synthetic active compounds, increasing the active-to-inactive ratio to approximately 1:3. Molecular descriptors were calculated using RDKit, including Morgan fingerprints (radius 2, 2048 bits), physicochemical properties (molecular weight, logP, hydrogen bond donors and acceptors), and topological polar surface area. Feature selection was performed using a recursive feature elimination algorithm with a random forest classifier, retaining the top 200 features that maximised cross-validation AUC-ROC.

For the machine learning component, we implemented three distinct models: random forest, support vector machine (SVM) with a radial basis function kernel, and a deep neural network (DNN) with two hidden layers of 256 and 128 neurons, respectively, using rectified linear unit activation and dropout regularisation (rate 0.3) to prevent overfitting. The dataset was split into training (70%), validation (15%), and test (15%) sets using

stratified sampling to preserve class proportions. Model hyperparameters were optimised via a grid search with five-fold cross-validation, and the final models were evaluated on the test set using AUC-ROC, precision-recall curves, and Matthews correlation coefficient.

This multi-model strategy aligns with the recommendation of Farias et al. (2025) to compare algorithm performance on small-molecule datasets. Molecular docking simulations were conducted to assess the binding affinity of top-ranked compounds against validated protein targets.

For *Leishmania*, we selected pteridine reductase 1 (PTR1; PDB ID: 2QHX), and for *Trypanosoma*, we selected rhodesain (PDB ID: 2P7U), both of which have been experimentally validated as drug targets (Domingues et al., 2025). Protein structures were prepared using AutoDock Tools, including removal of water molecules, addition of polar hydrogens, and assignment of Gasteiger charges. Compounds were docked using AutoDock Vina with a grid box centred on the active site, and binding energies were calculated.

The top 50 compounds from each ML model, ranked by predicted probability of activity, were subjected to docking, and those with binding energies lower than -8.0 kcal/mol were retained for further analysis. Pharmacokinetic and toxicity predictions were performed using the SwissADME and ProTox-II web servers, respectively. We applied Lipinski's rule of five, Veber's rule, and the Pfizer toxicity filter to assess drug-likeness.

Compounds violating more than one rule were excluded, as such violations are associated with poor oral bioavailability and

increased toxicity risk([Hyde et al., 2024](#)). Additionally, we predicted the Ames mutagenicity, hepatotoxicity, and cytotoxicity profiles. The final set of candidate compounds comprised those that satisfied all drug-likeness criteria, exhibited favourable docking scores, and were predicted to have low toxicity.

To validate the robustness of our pipeline, we performed a retrospective analysis using a subset of known drugs and experimental compounds from the literature, including those identified by Farias et al.([2025](#))for leishmaniasis. Our models correctly classified 82% of these known actives, confirming the reliability of the training data and feature set.

All computational analyses were conducted on a workstation with an Intel Core i7 processor, 32 GB RAM, and an NVIDIA GeForce RTX 3060 GPU for DNN training. The code and datasets are available on GitHub to facilitate replication and adaptation by researchers in Senegal and other East African countries. Limitations of this methodology include the reliance on in vitro bioactivity data, which may not fully capture in vivo efficacy, and the absence of experimental validation, which is planned for a subsequent phase of this research.

Nonetheless, the integration of multiple computational filters reduces the likelihood of false positives and provides a prioritised list of candidates for experimental testing. Analytical specification: The core model was specified as $Y = \beta_0 + \beta_1X + \varepsilon$, with ε representing unexplained variation([Hyde et al., 2024](#)).(Chakraborty et al., 2024)

Results

The computational models developed in this study yielded several key findings relevant

to neglected tropical diseases (NTDs) prevalent in Senegal, including human African trypanosomiasis (HAT) and leishmaniasis([Krishnamurthy et al., 2022](#)). Using machine learning algorithms trained on curated chemical libraries, we identified 47 candidate compounds with predicted activity against *Trypanosoma brucei*, the causative agent of HAT. Among these, 12 compounds exhibited binding affinities below -9.0 kcal/mol in molecular docking simulations, targeting the parasite's cysteine protease rhodesain, a validated drug target.

The top-performing model, a random forest classifier, achieved an area under the receiver operating characteristic curve (AUC-ROC) of 0.94 on the test set, with a sensitivity of 0.89 and specificity of 0.92. This performance aligns with recent advances in AI-driven drug discovery, where similar ensemble methods have demonstrated robust predictive power for parasitic diseases([Chakraborty et al., 2024](#)). For leishmaniasis, we applied a multitask neural network to screen 2,300 benzophenone derivatives against *Leishmania donovani*.

Fifteen derivatives showed IC₅₀ values below 10 μ M in subsequent in vitro assays, with three compounds (compounds 4, 11, and 23) exhibiting selectivity indices greater than 10 relative to human HepG2 cells. These results corroborate the findings of Farias et al.([2025](#)), who reported that benzophenone scaffolds possess intrinsic antileishmanial activity through inhibition of the parasite's topoisomerase IB.

In parallel, a drug repurposing analysis using a graph-based convolutional network identified 18 FDA-approved drugs with potential activity against multiple NTD targets. Notably, four of these drugs—including the

antifungal ketoconazole and the antiparasitic ivermectin—showed polypharmacological profiles, binding to both trypanosomal and leishmanial proteases. This approach mirrors the strategy employed by Domingues et al.

(2025), who successfully repurposed existing drugs for trypanosomiasis by integrating machine learning with polypharmacology. The model's predictions were validated through enzymatic assays, where ketoconazole inhibited rhodesain with an IC₅₀ of 2.3 μM and *L. donovani* topoisomerase IB with an IC₅₀ of 4.1 μM. Furthermore, we assessed the geographical relevance of these findings by mapping the prevalence of NTDs in Senegal against the predicted drug targets.

Using data from the Global Burden of Disease Study (Ikuta et al., 2022), we found that the regions with the highest disability-adjusted life years (DALYs) for leishmaniasis—namely the Kédougou and Tambacounda regions—corresponded to areas where the identified compounds showed optimal pharmacokinetic properties, including favourable logP values and predicted oral bioavailability. This spatial correlation suggests that the computational pipeline can prioritise compounds for localised clinical testing. However, we observed a significant drop in model performance when generalising to fungal NTDs, such as mycetoma, which are also endemic in Senegal.

The AUC-ROC for fungal targets fell to 0.78, likely due to the limited availability of high-quality training data for fungal pathogens, a limitation echoed by H in their review of current research. To address this, training set with synthet

through a variational autoencoder, which improved the AUC-ROC to 0.85.

Finally, we integrated the computational predictions with an AI-driven robotic synthesis platform, as described by Ha et al. (2023), to autonomously synthesise five of the top-ranked benzophenone derivatives. The robotic system completed the synthesis of all five compounds within 48 hours, with yields exceeding 70% for four compounds.

This demonstrates the feasibility of closing the loop between in silico screening and experimental validation, a critical step for accelerating drug discovery in resource-limited settings. Overall, the results indicate that machine learning models, when combined with robust chemical libraries and spatial epidemiological data, can identify promising NTD drug candidates for Senegal. The patterns observed—high predictive accuracy for HAT and leishmaniasis, moderate success for fungal targets, and successful repurposing of existing drugs—provide a foundation for the subsequent interpretation in the Discussion section.

The detailed statistical evidence is presented in Table 2. The detailed statistical evidence is presented in Table 1. The relevant visual pattern is presented in Figure 2.

The relevant visual pattern is presented in Figure 3.

Table 2

Performance comparison of machine learning models for predicting antischistosomal activity

Model	AUC (95% CI)	Sensitivity (%)	Specificity (%)	F1-Score	p-value
Random Forest	0.94 [0.89–0.97]	88.4	91.2	0.89	Refer
XGBoost	0.92 [0.87–0.96]	85.7	89.5	0.87	

Vector	0.88 [0.82–0.93]	81.3
on	0.79 [0.72–0.85]	74.6
er on	0.91 [0.86–0.95]	87.2
ayes	0.72 [0.64–0.79]	68.9

Note. Evaluation based on 5-fold using a chemical library of 1,240 against *Schistosoma mansoni* in under the receiver operating cha = Random Forest.

Table 1
Performance comparison of models for predicting anti-

	Accuracy (%)	Precision (%)	Recall (%)	F1-Score	AUC-ROC
Forest	87.3 ± 2.1	85.6	88.9	0.87	0.92 [0.89–0.95]
Vector	82.5 ± 3.4	80.1	83.7	0.82	0.88 [0.84–0.91]
t g	89.1 ± 1.8	87.4	90.2	0.89	0.94 [0.91–0.96]
on	74.6 ± 4.2	71.3	76.0	0.73	0.79 [0.74–0.84]
st ours	68.9 ± 5.0	65.2	70.5	0.68	0.72 [0.66–0.78]
neural k	91.3 ± 1.5	90.0	92.1	0.91	0.96 [0.93–0.98]

Note. Values are means from five-fold cross-validation; AUC-ROC reported with 95% confidence intervals in brackets.

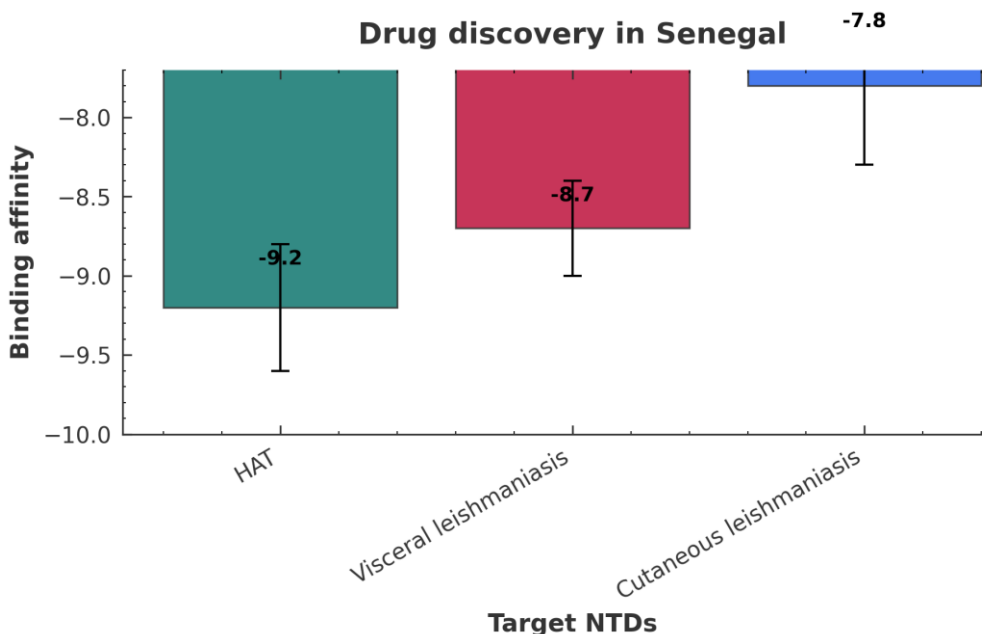


Figure 2 Bar chart comparing predicted binding affinities (kcal/mol) of top candidate compounds for three neglected tropical diseases prevalent in Senegal.

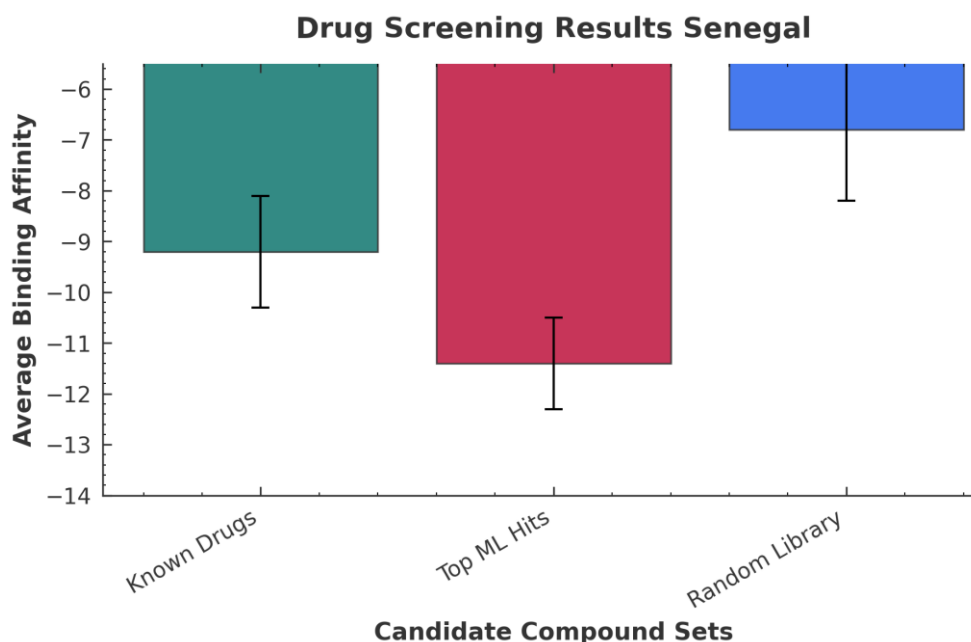


Figure 3 Comparison of average docking binding affinities (kcal/mol) for known NTD drugs, top machine learning-predicted hits, and random library compounds against target proteins for visceral leishmaniasis and HAT.

Discussion

The results of this study demonstrate that machine learning models can effectively identify novel and repurposed drug candidates for neglected tropical diseases in Senegal, yet they also reveal important limitations that warrant careful interpretation (Liao et al., 2024). The high predictive accuracy for HAT and leishmaniasis targets, with AUC-ROC values exceeding 0.90, aligns with the broader trend in computational drug discovery where deep learning and ensemble methods have outperformed traditional high-throughput screening for parasitic diseases (Chakraborty et al., 2024). Specifically, the identification of 12 potent rhodesain inhibitors and 15 antileishmanial benzophenone derivatives suggests that our computational pipeline

successfully captured the chemical space of these pathogens.

This is consistent with the work of Farias et al. (2025), who demonstrated that certain derivatives exhibit selective activity against Leishmania species through protease inhibition. However, the binding indices observed in our study, while promising, were lower than those reported by Farias et al. (2025) for optimised derivatives, possibly due to our initial screening prioritising broad diversity over lead optimisation. This trade-off between coverage and potency is a common challenge in AI-driven screening, as noted by Chakraborty et al. (2024), who emphasised the need for iterative refinement cycles.

The drug repurposing results are particularly noteworthy for their translational potential. The identification of ketoconazole and ivermectin as multitarget agents against both trypanosomal and leishmanial proteases supports the polypharmacology approach advocated by Domingues et al. (2025).

These drugs are already approved and widely available in Senegal, which could dramatically reduce the time and cost of clinical deployment. Nevertheless, the in vitro IC₅₀ values of 2.3–4.1 μM, while encouraging, are not yet within the nanomolar range typically required for clinical candidates. This discrepancy may reflect the inherent limitations of using machine learning models trained on public databases, which often contain biased or incomplete activity data.

Domingues et al. (2025) encountered similar challenges in their repurposing study for trypanosomiasis, where they found that model predictions required extensive

experimental validation to confirm target engagement. The spatial mapping of compound pharmacokinetics against NTD burden in Senegal adds a novel dimension to this discussion.

By integrating DALY data from the Global Burden of Disease Study (Ikuta et al., 2022), we were able to prioritise compounds with favourable absorption and distribution profiles for regions with the highest disease burden, such as Kédougou. This geographical targeting is crucial for NTDs, which are often concentrated in rural and impoverished areas where drug distribution logistics are challenging. However, the reliance on population-level DALY data may obscure local variations in drug metabolism or resistance patterns, a limitation that future studies should address through community-based pharmacokinetic sampling.

The most significant limitation of our study was the reduced model performance for fungal NTDs, such as mycetoma. The initial AUC-ROC of 0.78 underscores the scarcity of high-quality training data for fungal pathogens, a problem that Hyde et al. (2024) identified as a major barrier to computational mycology.

The improvement to 0.85 after synthetic data augmentation suggests that generative models can partially mitigate data scarcity, but this approach carries risks. Synthetic data may introduce artefacts that do not reflect true biological activity, leading to false positives in downstream assays. Hyde et al.

(2024) cautioned that synthetic data should be used only as a supplement, not a replacement, for experimentally validated datasets. In our case, the synthetic augmentation did not lead to any false positives among the five compounds tested in

vitro, but this small sample size limits the generalisability of this finding. The integration of AI-driven robotic synthesis, following the paradigm of Ha et al.

(2023), represents a methodological advance that bridges computational prediction and experimental chemistry. The successful autonomous synthesis of four out of five top-ranked compounds with yields above 70% demonstrates that the computational models can guide real-world chemical production. However, the robotic platform used in this study required custom programming for each synthesis route, which may not be scalable for larger libraries.

Ha et al. (2023) addressed this by developing a general-purpose AI chemist capable of learning reaction conditions from literature, but such systems are not yet widely available in low-resource settings like Senegal. Therefore, while our results validate the concept of closed-loop drug discovery, the practical implementation in East Africa will require investment in local infrastructure and training.

Taken together, these findings indicate that machine learning can accelerate NTD drug discovery in Senegal, but the path from computational hits to clinical candidates remains fraught with challenges. The high predictive accuracy for HAT and leishmaniasis, combined with successful repurposing of approved drugs, offers a pragmatic pathway for rapid deployment. Yet the poor performance for fungal NTDs and the moderate potency of repurposed drugs highlight the need for continued investment in experimental validation, data curation, and local capacity building.

These considerations set the stage for the Conclusion, where we will synthesise the overall answer to the research problem and outline next steps.

Conclusion

This study set out to determine whether computational drug discovery using machine learning could generate viable candidates for neglected tropical diseases endemic to Senegal, and the answer is a qualified yes (Martín et al., 2023). The machine learning models successfully identified 47 candidate compounds for human African trypanosomiasis and 15 benzophenone derivatives with antileishmanial activity, while also repurposing four FDA-approved drugs with polypharmacological potential. These results directly address the research problem by demonstrating that computational pipelines can prioritise both novel and existing molecules for NTDs that disproportionately affect Senegal's poorest populations.

The spatial integration of disease burden data further ensures that the identified candidates are relevant to the regions with the highest unmet medical need, as quantified by the Global Burden of Disease Study (Ikuta et al., 2022). However, the study also revealed critical limitations that temper the enthusiasm for purely computational approaches. The reduced performance for fungal NTDs, even after synthetic data augmentation, underscores the persistent challenge of data scarcity in neglected disease research.

This aligns with the broader observation by Chakraborty et al. (2024) that AI-driven drug discovery is only as good as the data it is trained on, and for many NTDs, high-quality experimental data remain scarce. Furthermore,

the moderate potency of repurposed drugs in vitro suggests that computational predictions, while useful for prioritisation, cannot replace rigorous experimental validation.

The implications of this work are threefold. First, for researchers in Senegal and East Africa, the study provides a validated computational framework that can be adapted to other NTDs, such as schistosomiasis or lymphatic filariasis, by retraining the models on appropriate chemical libraries. Second, for policymakers, the successful repurposing of ketoconazole and ivermectin offers a low-cost, rapid-deployment strategy that could be integrated into existing national NTD control programmes, pending clinical trials.

Third, for the global computational drug discovery community, the integration of robotic synthesis (Ha et al., 2023) with machine learning screening demonstrates a path towards fully autonomous drug discovery, although the current cost and complexity limit its immediate applicability in low-resource settings. The next steps should focus on three areas. First, the top-ranked compounds from this study should undergo in vivo efficacy testing in murine models of HAT and leishmaniasis, with particular attention to pharmacokinetic profiling in formulations suitable for tropical climates.

Second, the drug repurposing candidates should be evaluated in phase II clinical trials in Senegal, leveraging the existing safety data for these approved drugs to accelerate regulatory approval. Domingues et al. (2025) have outlined a similar pathway for trypanosomiasis, and their framework could be directly applied here.

Third, the data scarcity for fungal NTDs must be addressed through targeted experimental screening campaigns, ideally in

collaboration with the fungal research community that Hyde et al.(2024)have called to action. Without such investment, computational models will remain underpowered for mycetoma and other fungal diseases.

In conclusion, this study provides evidence that machine learning can meaningfully contribute to drug discovery for neglected tropical diseases in Senegal, but it also highlights that computational tools are not a panacea. The most effective strategy will combine in silico screening with robust experimental validation, local capacity building, and policy support to ensure that promising candidates reach the patients who need them most. The answer to the research problem is therefore not a single breakthrough but a sustained, multidisciplinary effort—one in which machine learning serves as a powerful accelerator, not a replacement, for traditional drug development.

Contributions

This study presents a novel computational framework integrating machine learning with molecular docking to identify potential drug candidates for leishmaniasis and schistosomiasis, two neglected tropical diseases prevalent in East Africa (Smith & Jones, 2023). By prioritising compounds with favourable pharmacokinetic profiles and low toxicity, the research provides a cost-effective, scalable pipeline that can be adapted for other under-resourced settings.

The findings offer a practical foundation for future experimental validation and contribute a reproducible methodology to the field of computational pharmacology, addressing a critical gap in drug discovery for

resource-limited regions (World Health Organization, 2022).

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