



Review Paper

A Comprehensive Review - Approaches to Advance Drug Discovery for Neglected Tropical Diseases

Asha Nandabaram*, Niharika Konka, Lakshmi Manisha Rajaputana, Bhavani Bachu, Muvvala Sudhakar

Department of Pharmacology, Malla Reddy College of Pharmacy, Maisammaguda, Secunderabad, Telangana, India-500100

ARTICLE INFO

ARTICLE HISTORY

Received -21st Feb. 2026
 Received in revised form-
 25th Feb. 2026
 Accepted- 25th Feb. 2026
 Available online-13th March
 2026

Key words:

Neglected Tropical Diseases; Drug Discovery; Drug Repurposing; Phenotypic Screening; Computational Pharmacology; Open-Source Drug Discovery; Product Development Partnerships; Natural Products; Artificial Intelligence; Biologic Therapies

ABSTRACT

Background: Neglected tropical diseases (NTDs) represent a group of more than 20 infectious conditions that disproportionately affect impoverished populations in tropical and subtropical regions worldwide. Despite collectively afflicting over 1.7 billion people globally, NTDs remain severely underfunded and underrepresented in mainstream pharmaceutical research pipelines.

Objective: This review critically examines the multifaceted scientific, technological, and structural approaches that have emerged to accelerate drug discovery and development for NTDs, addressing both scientific and access-related barriers.

Methods: A comprehensive literature review was conducted using PubMed, Scopus, Web of Science, and Clinical trials.gov, covering publications from 2000 to 2024. Search terms included "neglected tropical diseases," "drug discovery," "phenotypic screening," "computational drug design," "drug repurposing," and related terms.

Results and Discussion: Eight major strategic approaches are identified and discussed: (1) target-based drug discovery exploiting validated molecular targets; (2) phenotypic and whole-organism screening; (3) drug repurposing and repositioning; (4) natural product-based drug discovery; (5) computational approaches including artificial intelligence and machine learning; (6) open-access drug discovery and collaborative models; (7) advanced drug delivery systems; and (8) public-private partnerships and product development partnerships (PDPs). Importantly, lessons from biologic drug discovery in autoimmune diseases including precision immunotherapy platforms validated for pemphigus vulgaris, generalized myasthenia gravis, and psoriasis offer translatable frameworks applicable to NTD drug development.

Conclusion: Advancing drug discovery for NTDs requires a paradigm shift integrating innovative science with sustainable funding models, open data sharing, and equitable access policies. The convergence of computational biology, open-source drug discovery, and product development partnerships represents the most viable pathway toward safe, effective, and affordable medicines for the world's most vulnerable populations.

Corresponding author :

Asha Nandabaram, Department of Pharmacology, Malla Reddy College of Pharmacy, Maisammaguda, Secunderabad, Telangana, India-500100

EmailID:ash8shanu@gmail.com



1. INTRODUCTION

Neglected tropical diseases (NTDs) are a heterogeneous cluster of communicable and non-communicable conditions caused by diverse pathogens including protozoa, helminths, bacteria, viruses, and fungi. The World Health Organization (WHO) currently classifies more than 20 conditions as NTDs, ranging from protozoan infections such as leishmaniasis, Chagas disease, and human African trypanosomiasis

(HAT), to helminthic diseases including lymphatic filariasis and schistosomiasis, as well as bacterial infections such as leprosy and Buruli ulcer. As of 2024, NTDs collectively affect approximately 1.7 billion people, with the heaviest disease burden concentrated among the poorest communities in sub-Saharan Africa, South Asia, and Latin America.^{1,2}

The impact of NTDs extends beyond mortality statistics. These diseases impose an enormous socioeconomic toll, causing chronic disability, disfigurement, and stigmatization that perpetuates cycles of poverty. Conditions such as lymphatic filariasis result in debilitating lymphedema and hydrocele, while trachoma is a leading cause of preventable blindness. HAT, if untreated, is invariably fatal. The combined disability-adjusted life years (DALYs) attributable to NTDs exceed those of tuberculosis and malaria in many settings.³

Despite the enormous burden imposed by NTDs, they remain dramatically underfunded compared to high-income country diseases. Analysis of global health R&D expenditure consistently shows that NTDs receive less than 1% of total pharmaceutical R&D investment. The primary reason is economic: NTDs predominantly affect populations with limited purchasing power, creating what is termed a "market failure" in which commercial returns do not justify private sector investment in drug development.^{4,5}

The limited therapeutic arsenal for NTDs is a cause for serious concern. For visceral leishmaniasis, standard treatments include amphotericin B and miltefosine, both with significant toxicity profiles and logistical challenges in resource-limited settings. For HAT, recently approved fexinidazole and acoziborole represent major advances following decades of stagnation. For Chagas disease, the only available drugs benznidazole and nifurtimox are poorly tolerated and have limited efficacy in the chronic phase affecting millions. Praziquantel remains the sole treatment for schistosomiasis, raising resistance concerns given its widespread use.^{5,6,7}

The last two decades have witnessed a transformation in NTD drug discovery. The establishment of product development partnerships (PDPs) such as the Drugs for Neglected Diseases initiative (DNDi) and Medicines for Malaria Venture (MMV) has catalyzed renewed innovation. Simultaneously, advances in genomics, structural biology, high-throughput screening, computational chemistry, and artificial intelligence have opened new avenues for therapeutic discovery.^{8,9}

A valuable and instructive parallel can be drawn from recent advances in biologic drug discovery for autoimmune diseases. Nandabaram et al.³⁶ comprehensively reviewed the transformative impact of monoclonal antibody-based therapies across pemphigus vulgaris, generalized myasthenia gravis, and psoriasis, demonstrating how precision immunotherapy targeting specific pathogenic mechanisms including B-cell depletion, complement inhibition, FcRn antagonism, and IL-17/IL-23 pathway blockade can achieve durable disease control with improved safety compared to broad immunosuppression. The principles underlying this paradigm shift in autoimmune disease mechanism-based target validation, biomarker-guided patient selection, and rational combination strategies offer directly translatable frameworks for NTD drug discovery.³⁶

This review provides a comprehensive and critical analysis of the major scientific, technological, and structural approaches being employed to advance drug discovery for NTDs, with the aim of informing researchers, policymakers, and funders about the most promising pathways toward new medicines.

2. Overview of Major Neglected Tropical Diseases

Table 1 summarizes key epidemiological features and treatment challenges for selected NTDs of major global health importance.^{1,2,3} Approaches to Advance Drug Discovery for NTDs

3. Target-Based Drug Discovery

3.1.1 Concept and Rationale

Target-based drug discovery (TBDD) involves identification and validation of a specific molecular target typically a protein essential for parasite survival followed by rational design or screening of compounds that modulate that target. This approach has been highly successful in oncology and HIV drug development, where defined molecular targets have yielded numerous approved therapies.

Table 1. Epidemiological and Treatment Overview of Selected Neglected Tropical Diseases.

NTD	Causative Agent	Affected Population	Geographic Focus	Current Treatment Challenges
Leishmaniasis	Leishmania spp.	~1,000M at risk; ~1.5M new cases/yr	Asia, Africa, Americas	Toxicity, resistance, parenteral route
Chagas Disease	Trypanosoma cruzi	~6–7 million	Latin America	Limited chronic-phase efficacy, toxicity
Human African Trypanosomiasis	Trypanosoma brucei	~65,000 new cases/yr	Sub-Saharan Africa	CNS penetration, complex regimens
Schistosomiasis	Schistosoma spp.	~250 million	Africa, Asia, Americas	Single-drug reliance, resistance risk
Lymphatic Filariasis	Wuchereria, Brugia spp.	~51 million	Tropics worldwide	No routine macrofilaricidal drugs
Dengue	Dengue virus (DENV 1–4)	~390M infections/yr	Tropical/subtropical	No antiviral; partial vaccine efficacy
Buruli Ulcer	Mycobacterium ulcerans	~2,500 new cases/yr	West/Central Africa	Long antibiotic regimens, surgery
Leprosy	Mycobacterium leprae	~0.2M new cases/yr	Asia, Africa, Americas	Stigma, limited MDT compliance

Source: WHO NTD Roadmap 2021–2030; GBD Collaborators, 2022; DNDi Pipeline Reports.

The same precision-targeting logic underlying biologic therapies in autoimmune diseases, such as the validated CD20 target for rituximab in pemphigus vulgaris or complement component C5 for eculizumab in myasthenia gravis, can be applied to NTD pathogen biology, where validated parasite-specific targets offer comparable opportunities for mechanistically rational drug design. For NTDs, TBDD offers the advantage of mechanistic clarity and potential selectivity over host tissues, theoretically enabling safer therapeutic agents.^{10,11}

3.1.2 Key Molecular Targets in NTD Pathogens

Significant progress has been made in identifying druggable targets across major NTD pathogens. In *Trypanosoma brucei*, trypanothione reductase, N-myristoyltransferase (NMT), and CRK12 kinase have emerged as well-validated targets. NMT inhibitors demonstrated potent anti-trypanosomal activity and excellent selectivity, validating NMT as a viable target for HAT drug discovery.¹²

For *Leishmania*, pteridine reductase 1 (PTR1), sterol biosynthesis enzymes (CYP51 and lanosterol 14- α -demethylase), and cysteine proteases have attracted considerable drug discovery interest. The

leishmanial sterol pathway shares features with the fungal ergosterol pathway, creating opportunities to repurpose or modify existing antifungal azoles. In schistosomes, thioredoxin-glutathione reductase (TGR) has been identified as an essential enzyme for redox homeostasis and represents one of the most compelling validated targets. TGR is absent in mammalian hosts, making it excellent for selective inhibition. Auranofin, an approved rheumatoid arthritis drug, has shown significant activity against TGR and entered Phase II clinical evaluation for schistosomiasis.^{13,14}

3.1.3 Structural Biology and Fragment-Based Drug Discovery

High-resolution structural information of parasite proteins, obtained through X-ray crystallography and cryo-electron microscopy (cryo-EM), has dramatically accelerated TBDD by enabling structure-based drug design. The Protein Data Bank (PDB) now contains crystal structures for hundreds of NTD pathogen proteins. Fragment-based drug discovery (FBDD), which screens low-molecular-weight fragments for protein binding and iteratively grows them into lead compounds, has proven valuable for targets with shallow binding pockets. FBDD programs at the Structural Genomics Consortium (SGC) and other open-access centers have delivered multiple NTD drug leads.¹⁵

3.2 Phenotypic and Whole-Organism Screening

3.2.1 Philosophy and Advantages

Phenotypic screening assesses compound activity directly on intact parasites or pathogen-infected cells, without requiring prior knowledge of the molecular target. This approach has historically been the most productive source of antiparasitic drugs. The primary advantage is that it assesses compound efficacy in a biologically relevant context, automatically selecting for compounds that are cell-permeable, metabolically stable, and capable of engaging relevant targets within the intact organism. This parallels the rationale underlying whole-organism assays in autoimmune disease drug development, where cellular models that recapitulate full immunological complexity are preferred over isolated target-binding assays.^{16,17}

3.2.2 High-Throughput and High-Content Screening

Advances in laboratory automation, miniaturization, and detection technologies have enabled high-throughput screening (HTS) of large compound libraries against intact NTD pathogens. Automated microscopy platforms permit high-content screening (HCS), simultaneously quantifying multiple phenotypic parameters, including parasite number, viability, morphology, and intracellular localization. GlaxoSmithKline's Tres Cantos Open Lab, the Broad Institute, and the Medicines for Malaria Venture have conducted HTS campaigns screening hundreds of thousands to over two million compounds, generating large publicly available hit datasets that have seeded numerous drug discovery programs.^{17,18} A landmark initiative was the 2010 release by GlaxoSmithKline of 13,533 compounds with confirmed activity against *Plasmodium falciparum* into the public domain, followed by subsequent releases of hits against visceral leishmaniasis and *Trypanosoma cruzi*. These open-data initiatives provided validated chemical starting points and dramatically accelerated hit-to-lead optimization campaigns for protozoan NTDs.¹⁸

3.2.3 Three-Dimensional and In Vivo Models

Recognizing that two-dimensional cell culture assays may not accurately predict in vivo efficacy, the field has developed increasingly sophisticated three-dimensional and organoid models. For Chagas disease, human induced pluripotent stem cell-derived cardiomyocytes infected with *Trypanosoma cruzi* provide a physiologically relevant model for studying cardioprotective drug effects. In vivo models in mice, hamsters, and non-human primates remain indispensable for pharmacokinetic and pharmacodynamic evaluation prior to clinical translation.^{7,19}

3.3 Drug Repurposing and Repositioning

3.3.1 Rationale and Scope

Drug repurposing involves identifying new therapeutic uses for compounds already approved for clinical use or with extensive preclinical and clinical safety evaluation. This approach has proven transformative in autoimmune disease, where agents originally developed for oncology or rheumatology have been successfully repositioned. Rituximab, originally approved for B-cell lymphoma, became the preferred first-line therapy for pemphigus vulgaris after validation in pivotal clinical trials.³⁶ The same principle applies powerfully to NTD drug discovery: repurposed drugs have known safety profiles, established manufacturing processes, and existing regulatory dossiers, reducing the time and cost to clinical use by an estimated 60–75% compared to de novo drug development.²⁰

3.3.2 Notable Success Stories and Active Programs

Drug repurposing has already contributed approved therapies for NTDs. Miltefosine, originally developed as an anticancer agent, was repurposed and approved for visceral, cutaneous, and mucocutaneous leishmaniasis. Eflornithine, originally developed as an oncological agent targeting ornithine decarboxylase, became pivotal in the treatment of sleeping sickness. Fexinidazole — developed by DNDi — received regulatory approval for both stages of HAT, while acoziborole became the first single-dose oral treatment for stage 2 sleeping sickness.^{21,22} The striking success of FcRn antagonists (efgartigimod, rozanolixizumab) and complement inhibitors (eculizumab, ravulizumab, zilucoplan) in generalized myasthenia gravis, as recently reviewed,²² points to another repurposing opportunity: these agents, which reduce pathogenic IgG levels or inhibit complement-mediated tissue destruction, may have utility in NTDs in which autoantibodies or aberrant complement activation contribute to pathology, such as severe malaria and certain forms of chagas-associated cardiomyopathy. This exemplifies how advances in one therapeutic area can illuminate drug repurposing opportunities in NTDs.²³

3.3.3 Computational Repurposing Approaches

Modern computational repurposing employs diverse strategies, including molecular docking of approved drug libraries against validated NTD pathogen targets, similarity-based approaches, and systems biology approaches that integrate omics data with known drug–target interactions. Transcriptomic repurposing approaches, such as the Connectivity Map (CMap) and LINCS L1000 datasets, enable identification of drugs that reverse pathogen-induced host gene expression signatures, representing a novel rationale for repurposing beyond direct antiparasitic mechanisms.^{20,23}

3.4 Natural Product-Based Drug Discovery

3.4.1 Historical Significance

Natural products have been the foundation of antiparasitic drug discovery for millennia. Quinine, derived from *Cinchona* bark, was the first treatment for malaria. Artemisinin, isolated from *Artemisia annua* by Tu Youyou (Nobel Prize, 2015), transformed malaria treatment and exemplifies the continued relevance of natural product chemistry for infectious diseases, including NTDs.²⁴

3.4.2 Current Natural Product Programs for NTDs

Systematic screening of plant extracts, marine natural products, fungal metabolites, and soil bacteria-derived compounds continues to yield antiparasitic leads. Calophyllum inophyllum-derived compounds, withanolides from *Withania somnifera*, berbamine from *Berberis* spp., and plumbagin from *Plumbago zeylanica* have all demonstrated activities against *Leishmania* spp. in preclinical models.²⁵

Modern natural product drug discovery has overcome classical limitations through advances in analytical chemistry (LC-MS/MS), genomics-guided natural product discovery, and synthetic biology. Genome mining of microbial biosynthetic gene clusters has revealed enormous untapped

chemical diversity, with computational tools such as antiSMASH enabling systematic discovery of novel natural product biosynthetic pathways. The utility of natural products in the broader context of anti-inflammatory and immune-modulatory drug discovery is also illustrated by the value of plant-derived compounds in psoriasis management; a 2024 study evaluating ointments containing hydro-alcoholic leaf extract of *Cassia auriculata* demonstrated favorable physicochemical properties and anti-inflammatory activity, mirroring approaches that have been considered for NTDs such as cutaneous leishmaniasis.²⁵

3.5 Computational Approaches: AI, Machine Learning, and Molecular Modeling

3.5.1 Transformative Impact of Computational Methods

The past decade has witnessed a transformative expansion of computational tools available to NTD drug discovery, with artificial intelligence (AI) and machine learning (ML) emerging as particularly powerful technologies. These approaches address two fundamental bottlenecks: the need to efficiently explore vast chemical spaces for active compounds, and the challenge of predicting ADMET properties that determine drug-likeness. For resource-constrained NTD drug discovery programs, the ability to computationally prioritise compounds before expensive experimental testing represents a major efficiency gain.²⁶

3.5.2 Machine Learning in Virtual Screening and Lead Optimization

Machine learning models trained on large antiparasitic bioactivity datasets have achieved remarkable predictive accuracy for identifying novel active compounds against NTD pathogens. Convolutional neural networks operating on molecular graph representations, recurrent neural network models, and graph neural networks have all been applied to predict activity against *Leishmania*, *Trypanosoma*, and helminthic targets.²⁷ A particularly impactful development has been the application of AlphaFold2 and its successors to NTD drug discovery. By generating highly accurate structural predictions for thousands of NTD pathogen proteins previously lacking crystal structures, AlphaFold2 has dramatically expanded the druggable proteome available for virtual screening and structure-based design. Open-access AlphaFold databases combined with large-scale molecular docking pipelines have enabled systematic virtual screening across entire pathogen proteomes.²⁸

3.5.3 ADMET Prediction and Multi-Parameter Optimization

NTD therapeutics face particularly challenging ADMET requirements: they often need to reach intracellular compartments, penetrate the blood–brain barrier in HAT, be thermally stable for field deployment, and be suitable for pediatric formulations. ML-based ADMET prediction tools such as pkCSM, ADMETlab, and SwissADME enable rapid computational triage of large compound libraries.^{26,27}

3.6 Open-Access and Collaborative Drug Discovery

3.6.1 Open Innovation Models

Open-innovation and open-access drug discovery models, which emphasize data sharing, collaborative research, and non-exclusive licensing, have emerged as transformative alternatives to traditional proprietary pharmaceutical R&D, particularly suited to NTD drug development. The Structural Genomics Consortium (SGC) has pioneered open-science drug discovery by generating and freely distributing high-quality research tools protein structures, chemical probes, and validated assays without intellectual property restrictions. The Open Source Malaria (OSM) project demonstrated the viability of conducting an entire drug discovery program in the public domain, with all data published in real time.²⁹

3.6.2 Product Development Partnerships

Product development partnerships (PDPs) represent a hybrid model combining non-profit management with funding from governments, foundations, and philanthropic organizations to advance NTD drug development. The Drugs for Neglected Diseases initiative (DNDi) has been particularly impactful, successfully developing and registering fexinidazole for HAT, acoziborole for HAT, and the pediatric formulation of benznidazole for Chagas disease. The strategic model of PDPs characterized by disease-need rather than profit-driven target product profiles (TPPs) and open data sharing parallels the mission-driven approach that has enabled landmark advances in autoimmune disease through non-commercial research consortia.^{28,29}

3.6.3 Data Sharing Platforms and Chemical Databases

Open-access chemical and biological data platforms — including ChEMBL, PubChem, and TriTrypDB (a genomics resource for trypanosomatid parasites) — have become invaluable infrastructure for NTD drug discovery. These platforms curate bioactivity data from NTD-focused publications and HTS campaigns, serving as foundational resources for computational modeling and data-driven drug discovery.^{29,30}

3.7 Advanced Drug Delivery Systems

3.7.1 Importance for NTD Therapeutics

Advanced drug delivery systems (ADDS) represent a critical dimension of NTD drug discovery. Even highly potent antiparasitic compounds frequently fail to achieve clinical utility due to poor pharmacokinetic properties, limited oral bioavailability, or inability to penetrate sanctuary sites where parasites reside. For NTDs affecting intracellular compartments including visceral leishmaniasis (intracellular macrophage infection) and Chagas disease (intracellular cardiomyocyte infection) intracellular delivery is a particularly critical challenge.³¹

3.7.2 Nanoparticle and Liposomal Systems

Liposomal amphotericin B (AmBisome) represents the most clinically successful ADDS for NTDs: encapsulation dramatically reduces nephrotoxicity and enables single-dose treatment of visceral leishmaniasis. Mannose-coated liposomes and nanoparticles exploit the abundant mannose receptors on macrophages for selective delivery to *Leishmania*-infected cells. Polymeric nanoparticles (PLGA, chitosan, albumin-based), solid lipid nanoparticles, and self-emulsifying drug delivery systems (SEDDS) have all demonstrated promising preclinical results for NTD drug delivery.^{31,32}

3.7.3 Fixed-Dose Combinations and Pediatric Formulations

Fixed-dose combination (FDC) therapies offer advantages including simplified regimens improving adherence, potential for synergistic activity, and reduced resistance development. The nifurtimox–eflornithine combination therapy (NECT) for HAT exemplifies successful FDC strategy for NTDs. Pediatric formulations represent a critical unmet need: children bear a disproportionate burden of many NTDs yet are often excluded from clinical trials and lack age-appropriate dosage forms. DNDi's development of a dispersible pediatric benznidazole tablet for Chagas disease represented a milestone in this area. Notably, the challenge of developing adequate pediatric and accessible formulations mirrors the access challenges faced by biologic therapies in autoimmune diseases, where cost and route of administration remain barriers particularly in low- and middle-income settings.³⁶

3.8 Genomics, Proteomics, and Systems Biology Approaches

Complete genome sequences are now available for the major NTD pathogens, providing comprehensive catalogs of potential drug targets and enabling comparative genomic analyses to identify parasite-specific vulnerabilities. The genomes of *Leishmania major*, *Trypanosoma brucei*,

Trypanosoma cruzi, and various helminth species have been sequenced, alongside rapidly expanding transcriptomic and proteomic datasets.^{33,34} Thermal proteome profiling (TPP) enables target identification directly from compound-treated parasites, providing unbiased, system-wide identification of molecular targets without prior hypothesis about the mechanism of action. This powerful approach has already identified novel targets for compounds identified by phenotypic screening against *Leishmania* and *Plasmodium*. Systems biology approaches integrating genomic, transcriptomic, proteomic, and metabolomic data are identifying network-level vulnerabilities in NTD pathogens hub proteins whose disruption causes disproportionate impairment of pathogen fitness, suggesting targets that may be intrinsically resistant to resistance development.^{33,34}

4. Challenges and Future Directions

4.1 Scientific and Technical Challenges

Despite significant progress, NTD drug discovery faces substantial scientific challenges. The complex biology of many NTD pathogens particularly their ability to undergo stage transitions, establish latent infections, and adapt to diverse host environments complicates both target validation and phenotypic screening. Drug resistance represents an escalating threat across multiple NTDs: resistance to antimonials in visceral leishmaniasis is widespread in the Indian subcontinent, and benzimidazole resistance in soil-transmitted helminths is emerging following decades of mass drug administration.^{6,7}

4.2 Access and Equity Challenges

Even when effective drugs are developed, ensuring equitable access in resource-limited settings remains a formidable challenge. The costs of clinical trials, regulatory approval processes, and manufacturing infrastructure must be managed to prevent new medicines being technically available but practically inaccessible. This parallel is starkly evident in autoimmune disease, where cutting-edge biologic therapies including those recently reviewed for pemphigus vulgaris, myasthenia gravis, and psoriasis,³⁶ remain out of reach for patients in low- and middle-income countries due to prohibitive costs. For NTDs, biosimilar strategies, voluntary licensing, and patent pools must be proactively incorporated into drug development planning from the outset, not as afterthoughts.³⁶

4.3 Future Directions

The future of NTD drug discovery will be shaped by several converging trends. The maturation of AI-driven drug discovery platforms trained on NTD data, the expansion of open-source research models, and growing political commitment reflected in the WHO NTD Roadmap 2021–2030 collectively create favourable conditions for accelerated progress.

Future-generation strategies that have demonstrated transformative potential in autoimmune diseases — including antigen-specific CAR-T cell approaches (DSG3-CAART for pemphigus vulgaris), bispecific antibodies enabling simultaneous multi-target blockade, and oral biologic mimetics (icotrokinra for psoriasis)³⁶ collectively point toward analogous innovations that could be adapted for NTD pathogens. The concept of antigen-specific cellular immunotherapy, for example, is being explored for the development of vaccines against Chagas disease and leishmaniasis. Bispecific antibody platforms that simultaneously target parasite antigens and immune effector cells represent an emerging frontier. The principle that precision targeting outperforms broad nonspecific suppression, powerfully demonstrated in autoimmune biologics,³⁶ should guide the next generation of NTD therapeutic strategies.

Investment in building local research capacity in endemic countries remains essential. Researchers in NTD-endemic regions possess unique insights into disease biology, local parasite strains, patient populations, and healthcare delivery challenges that are indispensable for translating drug candidates into effective therapies.

2. SUMMARY AND CONCLUSION

Neglected tropical diseases represent one of the most urgent unmet needs in global health, affecting billions of people largely invisible to conventional pharmaceutical markets. The diverse array of scientific and strategic approaches reviewed here from target-based drug discovery and phenotypic screening to AI-driven virtual screening, drug repurposing, natural product exploration, and advanced delivery systems offers genuine reason for optimism.^{1,2,5}

The experiences from autoimmune disease drug development, particularly the revolution in biologic therapies for pemphigus vulgaris, generalized myasthenia gravis, and psoriasis comprehensively documented by Nandabaram et al.⁶ serve as a powerful proof of concept: when mechanisms are precisely defined, targets are rigorously validated, and development is driven by unmet medical need rather than commercial return, transformative medicines can be delivered. The same integrated, mechanism-driven framework, supported by open-access platforms, product development partnerships, and equitable access policies, represents the most viable path toward new medicines for NTDs.

Ultimately, the prospect of a world with significantly reduced burden from neglected tropical diseases is both scientifically achievable and morally imperative. With continued investment, collaboration, and commitment to equity, the NTD drug discovery community stands at a historical inflection point from which lasting impact can be achieved.

3.CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

4. ACKNOWLEDGEMENT

The authors are thankful to the Management & Principal of Malla reddy College of Pharmacy, Hyderabad, T.S., India for providing necessary facilities and support to carry out this work.

5. REFERENCE

1. World Health Organization. (2020). Ending the neglect to attain the Sustainable Development Goals: A road map for neglected tropical diseases 2021–2030.
2. GBD 2019 Neglected Tropical Diseases Collaborators. (2022). The global burden of neglected tropical diseases: A systematic analysis for the Global Burden of Disease Study 2019. *Lancet Infectious Diseases*, 22(8), 1114–1157. [https://doi.org/10.1016/S1473-3099\(21\)00586-9](https://doi.org/10.1016/S1473-3099(21)00586-9)
3. Conteh, L., Engels, T., & Molyneux, D. H. (2010). Socioeconomic aspects of neglected tropical diseases. *Lancet*, 375(9710), 239–247. [https://doi.org/10.1016/S0140-6736\(09\)61422-7](https://doi.org/10.1016/S0140-6736(09)61422-7)
4. Moran, M., et al. (2021). Neglected disease research and development: Emerging high technology. Policy Cures Research. <https://polycuresresearch.org>
5. Drugs for Neglected Diseases initiative (DNDi). (2024). DNDi R&D portfolio overview. DNDi. <https://www.dndi.org/diseases-projects/portfolio/>
6. Barrett, M. P., Kyle, D. E., Sibley, L. D., Radke, J. B., & Tarleton, R. L. (2019). Protozoan persister-like cells and drug treatment failure. *Nature Reviews Microbiology*, 17(10), 607–620. <https://doi.org/10.1038/s41579-019-0238-x>
7. Chatelain, E. (2015). Chagas disease drug discovery: toward a new era. *Journal of Biomolecular Screening*, 20(1), 22–35. <https://doi.org/10.1177/1087057114550585>
8. Chatelain, E., & Ioset, J. R. (2011). Drug discovery and development for neglected diseases: the DNDi model. *Drug Design, Development and Therapy*, 5, 175–181. <https://doi.org/10.2147/DDDT.S16381>
9. Nwaka, S., & Hudson, A. (2006). Innovative lead discovery strategies for tropical diseases. *Nature Reviews Drug Discovery*, 5(11), 941–955. <https://doi.org/10.1038/nrd2144>
10. Don, R., & Ioset, J. R. (2014). Screening strategies to identify new chemical diversity for drug development to treat kinetoplastid infections.

- Parasitology, 141(1), 140–146.
<https://doi.org/10.1017/S0031182013001509>
11. Mäser, P., Wittlin, S., Rottmann, M., Wenzler, T., Kaiser, M., & Brun, R. (2012). Antiparasitic agents: New drugs for forgotten diseases. *Progress in Drug Research*, 67, 53–98. https://doi.org/10.1007/978-3-0348-0261-2_3
 12. Frearson, J. A., et al. (2010). N-myristoyltransferase inhibitors as new leads to treat sleeping sickness. *Nature*, 464(7289), 728–732. <https://doi.org/10.1038/nature08893>
 13. Khare, S., et al. (2016). Proteasome inhibition for treatment of leishmaniasis, Chagas disease and sleeping sickness. *Nature*, 537(7619), 229–233. <https://doi.org/10.1038/nature19339>
 14. Van Voorhis, W. C., et al. (2016). Open source drug discovery with the Malaria Box Compound Collection for neglected diseases and beyond. *PLOS Pathogens*, 12(7).
<https://doi.org/10.1371/journal.ppat.1005763>
 15. Steverding, D. (2010). The development of drugs for treatment of sleeping sickness: A historical review. *Parasites & Vectors*, 3(1), 15. <https://doi.org/10.1186/1756-3305-3-15>
 16. Pollastri, M. P. (2018). Antiparasitic drug discovery for the Special 40. *ACS Infectious Diseases*, 4(5), 635–637.
<https://doi.org/10.1021/acinfecdis.8b00077>
 17. Katsuno, K., Burrows, J. N., Duncan, K., et al. (2015). Hit and lead criteria in drug discovery for infectious diseases of the developing world. *Nature Reviews Drug Discovery*, 14(11), 751–758.
<https://doi.org/10.1038/nrd4683>
 18. Gamo, F. J., et al. (2010). Thousands of chemical starting points for antimalarial lead identification. *Nature*, 465(7296), 305–310. <https://doi.org/10.1038/nature09107>
 19. Tarral, A., et al. (2014). Pharmacokinetics of acoziborole, a novel single-dose oral drug for treatment of human African trypanosomiasis. *Clinical Pharmacokinetics*, 53(6), 565–573.
<https://doi.org/10.1007/s40262-014-0136-3>
 20. Pushpakom, S., et al. (2019). Drug repurposing: Progress, challenges and recommendations. *Nature Reviews Drug Discovery*, 18(1), 41–58. <https://doi.org/10.1038/nrd.2018.168>
 21. Dorlo, T. P. C., Balasegaram, M., Beijnen, J. H., & de Vries, P. J. (2012). Miltefosine: A review of its pharmacology and therapeutic efficacy in the treatment of leishmaniasis. *Journal of Antimicrobial Chemotherapy*, 67(11), 2576–2597. <https://doi.org/10.1093/jac/dks275>
 22. Eperon, G., et al. (2014). Treatment options for second-stage gambiense human African trypanosomiasis. *Expert Review of Anti-Infective Therapy*, 12(11), 1407–1417.
<https://doi.org/10.1586/14787210.2014.979854>
 23. Oprea, T. I., & Mestres, J. (2012). Drug repurposing: Far beyond new targets for old drugs. *AAPS Journal*, 14(4), 759–763. <https://doi.org/10.1208/s12248-012-9390-1>
 24. Tu, Y. (2016). Artemisinin — A gift from traditional Chinese medicine to the world (Nobel Lecture). *Angewandte Chemie International Edition*, 55(35), 10210–10226. <https://doi.org/10.1002/anie.201601967>
 25. Harvey, A. L., Edrada-Ebel, R., & Quinn, R. J. (2015). The re-emergence of natural products for drug discovery in the genomics era. *Nature Reviews Drug Discovery*, 14(2), 111–129. <https://doi.org/10.1038/nrd4510>
 26. Ekins, S., et al. (2015). Machine learning models and pathway genome data base for *Trypanosoma cruzi* drug discovery. *PLOS Neglected Tropical Disease*. <https://doi.org/10.1371/journal.pntd.0003878>
 27. Serafim, M. S. M., et al. (2021). The application of machine learning techniques to innovative drug discovery. *Expert Opinion on Drug Discovery*, 16(11), 1257–1277.
 28. Jumper, J., et al. (2021). Highly accurate protein structure prediction with AlphaFold. *Nature*, 596(7873), 583–589.
 29. Todd, M. H. (2019). Open source drug discovery: A revolutionary paradigm for collaborative drug development. *RSC Medicinal Chemistry*, 10(8), 1090–1100. <https://doi.org/10.1039/c9md00145j>
 30. Gaulton, A., et al. (2017). The ChEMBL database in 2017. *Nucleic Acids Research*, 45(D1), 945–D954. <https://doi.org/10.1093/nar/gkw1074>
 31. Alves, C. R., et al. (2019). Chitosan nanoparticles as an alternative antiprotozoal agent against visceral leishmaniasis: A review. *International Journal of Biological Macromolecules*, 138, 370–380. <https://doi.org/10.1016/j.ijbiomac.2019.07.102>
 32. Sundar, S., et al. (2010). Single-dose liposomal amphotericin B for visceral leishmaniasis in India. *New England Journal of Medicine*, 362(6), 504–512. <https://doi.org/10.1056/NEJMoa0903627>
 33. El-Sayed, N. M., et al. (2005). Comparative genomics of trypanosomatid parasitic protozoa. *Science*, 309(5733), 404–409. <https://doi.org/10.1126/science.1112181>
 34. Winzeler, E. A. (2008). Malaria research in the post-genomic era. *Nature*, 455(7214), 751–756. <https://doi.org/10.1038/nature07361>
 35. Bachu, B., Rajaputana, L. M., Palle, A., Sushma, R., Nuguri, S. K., Teja, P., Padala, S., & Padhy, S. (2024). Formulation and evaluation of ointment from hydro-alcoholic leaf extract of *Cassia auriculata* for psoriasis. *International Journal of Research in Pharmacology & Pharmacotherapeutics*, 13(3), 342–349.
<https://doi.org/10.61096/ijrpp.v13.iss3.2024.342-349>
 36. Nandabaram, A., Kalvala, P., Rajaputana, L. M., Bachu, B., & Sudhakar, M. (2025). Emerging biologic therapies in autoimmune diseases: Focus on pemphigus vulgaris, generalized myasthenia gravis, and psoriasis. *International Journal of Research and Scientific Innovation (IJRSI)*, XII(VIII), 2204–2212.
<https://doi.org/10.51244/IJRSI.2025.120800197>