ACCSCIENCE PUBLISHING

INNOSC Theranostics and Pharmacological Sciences

PERSPECTIVE ARTICLE

The crucial role of drug repositioning in tackling Chagas disease, sleeping sickness, and leishmaniasis

Exequiel O. J. Porta*

Department of Pharmaceutical and Biological Chemistry, School of Pharmacy, University College London, London, United Kingdom

Abstract

Neglected tropical diseases (NTDs), such as Chagas disease, human African trypanosomiasis (sleeping sickness), and leishmaniasis, disproportionately affect low-income populations in tropical and subtropical regions, leading to high morbidity and mortality rates. Consequently, these diseases, historically overlooked in global health agendas, perpetuate cycles of poverty and impede economic development. Drug repositioning, the repurposing of existing drugs for new therapeutic uses presents a promising strategy by reducing drug development time and cost while leveraging known safety profiles. However, despite its success in other therapeutic areas, this approach remains underutilized for NTDs due to challenges such as a limited drug pool, intellectual property barriers, regulatory complexities, and ethical concerns. Essential strategies to overcome these obstacles include expanding approved drug libraries, fostering multi-sector collaborations, streamlining regulatory processes, and adopting innovative funding models. Collaborative efforts among governments, pharmaceutical companies, research institutions, and non-profit health organizations are crucial to fully unlock the potential of drug repositioning. By working together as a united front, these stakeholders can ultimately transform NTD treatment and improve global health outcomes.

Keywords: Chagas disease; Drug repositioning; Drug repurposing; Leishmaniasis; Neglected tropical diseases; Parasitic diseases; Sleeping sickness

***Corresponding author:**
Exequiel O. J. Porta
(e.porta@ucl.ac.uk)

Citation: Porta EOJ. The crucial role of drug repositioning in tackling Chagas disease, sleeping sickness, and leishmaniasis. *INNOSC Theranostics and Pharmacological Sciences*. 2024;7(4):3721. doi: 10.36922/itps.3721

Received: May 21, 2024

Accepted: September 23, 2024

Published Online: October 15, 2024

1. Introduction

Neglected tropical diseases (NTDs) encompass a diverse group of diseases that predominantly afflict low-income populations in tropical and subtropical regions.[1] Historically, these diseases have been overlooked in global health priorities, receiving limited attention and funding. Among these, Chagas disease, sleeping sickness (human African trypanosomiasis [HAT]), and leishmaniasis are particularly notable for their significant morbidity and mortality rates.[2] Along with malaria, these parasitic diseases exert a profound impact on global health.[3] These diseases disproportionately affect millions in economically disadvantaged areas, resulting in substantial health and socioeconomic burdens (Figure 1).

Consequently, these illnesses perpetuate cycles of poverty and impede economic development in affected communities.[4] This critical situation, marked by the significant

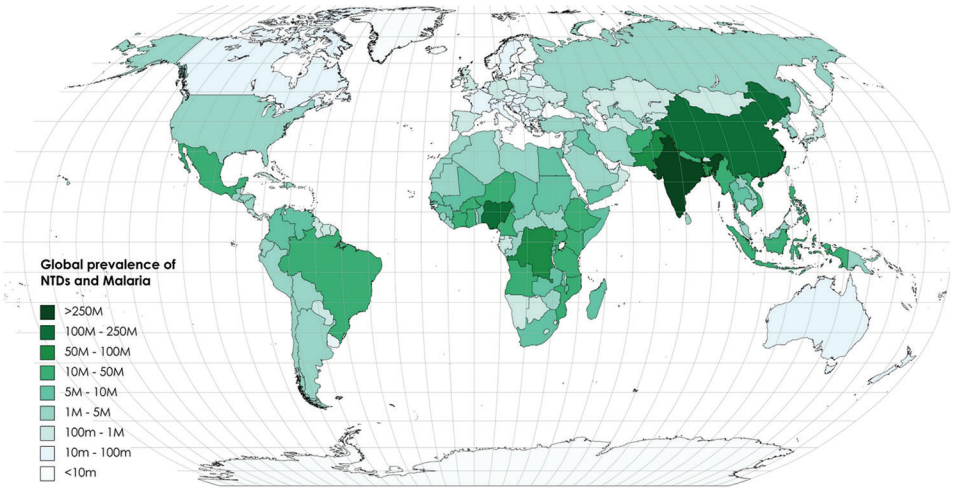

Figure 1. Global prevalence of parasitic neglected tropical diseases, specifically Chagas disease, sleeping sickness, and leishmaniasis, as well as malaria, based on the Global Burden of Disease Data (2019). Collectively, these conditions affect over 1.3 billion people worldwide. Data sourced from: Global Health Data Exchange (https://ghdx.healthdata.org/).

impact of NTDs and a glaring lack of effective and accessible treatments, underscores an urgent need for innovative health-care solutions and therapeutic strategies.[5] However, the development of new drugs for NTDs faces considerable challenges. Primarily, the limited financial incentives for pharmaceutical companies are a major obstacle since these diseases predominantly affect poorer regions with minimal market potential. In addition, the biological complexity of these parasitic diseases makes the development of specific and effective treatments a formidable task.[6]

2. The urgency of utilizing drug repositioning to combat NTDs

Drug repositioning, also known as drug repurposing, involves reevaluating existing drugs for new therapeutic uses.[7] This approach offers a promising alternative to traditional drug discovery by reducing both the cost and time required to bring a treatment to market.[8] Crucially, since the safety profiles of these drugs are already established, the risk of adverse effects is significantly minimized.[9] In the context of NTDs, drug repositioning may be more effective than *de novo* drug design, primarily due to its speed and cost-effectiveness. Repurposing existing drugs circumvents the lengthy and costly process of developing new drugs from scratch,[10] representing a crucial advantage when responding to urgent health needs in resource-limited settings, such as those typical of NTDs. Therefore, these advantages make drug repurposing a practical and efficient approach for addressing these diseases. For comparison, drug repurposing typically shortens the development timeline to 3 – 12 years, as opposed to 12 – 18 years for new drug development (*de novo*). It also reduces costs to US$ 0.4 – 0.8 billion, compared to US$ 1 – 2 billion for developing a new drug.

The potential of drug repositioning is well-documented in various contexts.[11-13] For instance, thalidomide, originally marketed as a sedative, found new purposes in treating multiple myeloma[14] and leprosy.[15] The literature is rich with examples of successful drug repositioning, notably in oncology and cardiovascular diseases.[16-18] Yet, paradoxically, this approach remains considerably underutilized in the realm of NTDs, despite its demonstrated potential in addressing parasitic diseases such as malaria.[19,20] A noteworthy example of the treatment of parasitic NTDs is the repositioning of miltefosine.[21] Initially developed as an anticancer agent, miltefosine made a significant impact in 2002 when it was repurposed as the first oral antileishmanial medication. This milestone in drug repositioning not only exemplifies the versatility of existing drugs but also highlights their potential to address challenging diseases beyond their original intended use. This example of repurposing has set a groundbreaking precedent, paving the way for more innovative and efficient therapeutic approaches in the fight against NTDs.

Although Chagas disease, HAT, and leishmaniasis present unique challenges, including complex life cycles of the causative parasites and diverse clinical manifestations, drug repositioning offers a viable solution to swiftly address these challenges by repurposing existing drugs with known antiparasitic properties.[22] For instance, collectively, the studies by Porta *et al.*,[23] Charlton *et al.*,[24] and Sbaraglini *et al.*[25] present a comprehensive overview of over 100 approved drugs that have been repurposed and are in various stages of development as antiparasitic treatments

for NTDs. Each of these drugs has the potential to evolve into new therapies aimed at eradicating these diseases. These efforts align with the World Health Organization's (WHO) 2021 – 2030 roadmaps for the elimination of NTDs,[26] emphasizing the global commitment to eradicate these illnesses.

Therefore, it is imperative to make a concerted effort to integrate drug repositioning into NTD research and to advance the stages of development and clinical trials of repositioned drugs, specifically targeting these parasitic diseases. Achieving this goal requires increased funding, robust international collaboration, and effective public–private partnerships to facilitate the identification and development of repurposed drugs.[27]

3. Limitations of drug repositioning and mitigation strategies

Despite its significant potential, drug repositioning faces several limitations that hinder its application.[12,23] A significant challenge is the limited pool of drugs available for repurposing. Most existing drugs were developed for diseases prevalent in high-income countries, which may not directly translate to effective treatments for NTDs. This limitation reduces the likelihood of finding suitable candidates for repositioning. In addition, intellectual property and financial considerations pose substantial hurdles. Patents on existing drugs may restrict their use for new indications, creating legal and financial barriers. Moreover, the financial incentives for pharmaceutical companies to invest in NTDs are limited due to the low market potential in affected regions.

Regulatory challenges further complicate the drug repositioning process. Each repurposed drug must undergo rigorous clinical trials to ensure efficacy and safety for the new indication, making the regulatory pathway as complex and lengthy as that for new drug development.[28] This process can be time-consuming and costly. Repositioned drugs often target well-known molecular mechanisms, making the patients susceptible to drug resistance, particularly when the molecular targets are conserved across species (*e.g.*, humans and parasites); this challenge is not exclusive to repositioned therapies. Newly developed drugs face similar risks of resistance. To mitigate these risks, both repositioned and new drugs require careful monitoring and, where appropriate, the use of adaptive treatment strategies, such as combination therapies (*vide infra*). Ethical considerations also play a crucial role, particularly when conducting clinical trials in vulnerable populations. Ensuring informed consent and equitable access to the benefits of such trials can be challenging, necessitating robust ethical frameworks to address these concerns.

To mitigate all these risks, several strategies can be employed.[29] Expanding the drug repositioning pipeline by including compounds from diverse therapeutic areas can enhance the discovery of potential candidates. Encouraging open-access databases and fostering collaborations between academia, industry, and non-profit organizations are essential steps in this direction (*vide infra*). Addressing intellectual property challenges requires the active involvement of governments and international organizations to facilitate agreements that overcome patent barriers. Creating patent pools and offering incentives for companies to share intellectual property can help mitigate legal and financial obstacles. In addition, extending market exclusivity for repositioned drugs can provide financial incentives for pharmaceutical companies.

Streamlining regulatory pathways specifically for drug repositioning can accelerate the approval process. Regulatory agencies can establish dedicated frameworks recognizing the lower risk profile of repurposed drugs due to existing safety data, implementing conditional approvals and adaptive licensing to expedite access to these therapies. Innovative funding models, such as public–private partnerships and advanced market commitments, can attract investment in drug repositioning for NTDs. Leveraging financial instruments such as social impact bonds and global health funds can provide the necessary resources to support clinical trials and development efforts.

Combining repositioned drugs with existing therapies can enhance their efficacy and mitigate the risk of resistance. Research should focus on identifying synergistic drug combinations and exploring novel delivery methods to improve treatment outcomes. Continuous monitoring of resistance patterns and adaptive treatment protocols are essential to ensure long-term effectiveness. Establishing robust ethical frameworks for conducting clinical trials in vulnerable populations is critical. Ensuring transparency, informed consent, and community engagement can build trust and promote equitable access to the benefits of drug repositioning. Collaborating with local health authorities and stakeholders can help align trial designs with the needs and priorities of affected communities.

By proactively addressing these limitations through targeted mitigation strategies, we can fully realize the potential of drug repositioning. This approach offers a pragmatic and efficient pathway to develop new therapies for NTDs, accelerating the availability of effective treatments and aligning with global health goals to improve outcomes for millions affected by these debilitating diseases.

4. Successful implementation of drug repositioning for NTDs

The successful implementation of drug repositioning, along with other strategies, relies heavily on the collaborative and synergistic efforts of all stakeholders involved. The efforts of various consortia and initiatives, including public–public and public–private partnerships, are crucial in advancing the repurposing of compounds through clinical trials.[30] Such collaborative approaches pave the way for more effective therapies against NTDs, offering hope for improved health care in endemic regions.

A notable example of successful collaboration in drug repositioning is demonstrated by the Drugs for Neglected Diseases initiative (DNDi). DNDi's translational research program effectively repurposed fexinidazole, originally developed as a broad-spectrum anti-infective agent in the 1970s, for the treatment of Chagas disease. Fexinidazole, selected from over 700 nitroheterocyclic compounds, was initially repositioned by DNDi for sleeping sickness,[31] before being repurposed for the treatment of Chagas disease. This achievement highlights the critical role of collaborative efforts in advancing drug repositioning initiatives.

Building upon such successful collaborations, countries with robust research capacities, advanced pharmaceutical industries, and significant resources are well-positioned to take a leading role in the implementation of drug repositioning strategies. By forming partnerships with low- and middle-income countries, non-governmental organizations, and global health agencies, these nations can significantly bolster the global fight against NTDs. While international collaborations can face challenges such as resource disparities and regulatory differences, establishing standardized protocols and shared goals can mitigate these issues.

To ensure the success of drug repositioning for NTDs, stakeholders must go beyond scientific collaboration; it necessitates a supportive policy environment, strategic involvement from the pharmaceutical industry, proactive participation from research and academic institutions, and robust engagement from international health organizations and public and non-profit entities (Figure 2). Collectively, acting as a united front, these stakeholders contribute to a cohesive and comprehensive framework that facilitates the advancement of drug repositioning for NTDs, overcoming challenges, accelerating the development of effective therapies, and ultimately improving health outcomes in regions burdened by these diseases.

4.1. Policy recommendations

To facilitate the widespread adoption of drug repositioning for NTDs, specific policy measures are essential. Governments should prioritize funding for NTD research and establish regulatory frameworks that expedite the approval process for repurposed drugs. Streamlined regulatory pathways can significantly reduce the time and cost involved in bringing repositioned drugs to market, enhancing their accessibility to those in need.

In addition to government funding and supportive policies, regulatory bodies such as the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have developed mechanisms to fast-track drug approvals to meet urgent medical needs.

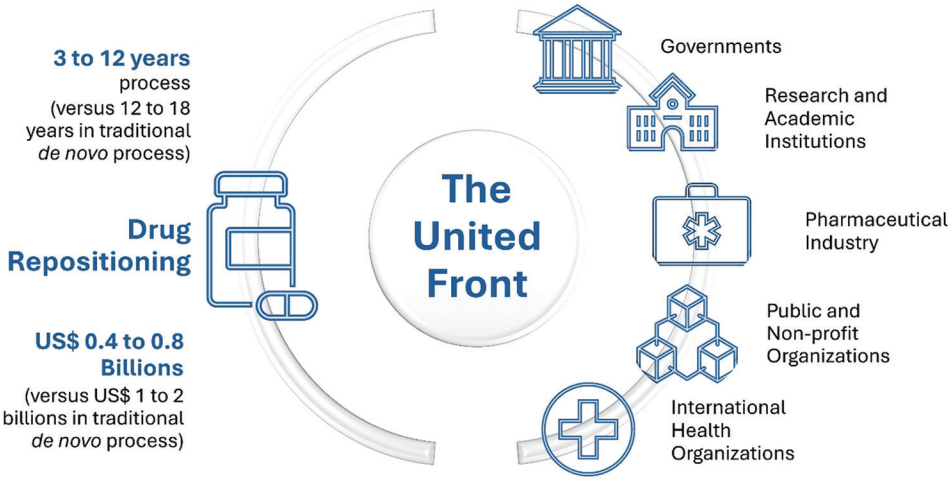

Figure 2. A collaborative partnership between governments, pharmaceutical industry, academic and research institutions, public and non-profit organizations, and health organizations is essential to unlock the full potential of drug repositioning. This cooperation will enhance treatments for neglected tropical diseases and transform global health outcomes.

The FDA offers programs such as Fast Track (to expedite the review of drugs for serious conditions with unmet medical needs), Priority Review (which reduces the FDA review period from ten to six months), and Accelerated Approval (allowing earlier approval based on surrogate endpoints).[32] Similarly, the EMA has introduced the PRIME (Priority Medicines) scheme,[33] offering early and enhanced support to medicines that target unmet medical needs, including those for NTDs. The PRIME program provides early and continuous support to developers of promising drugs, ensuring faster access for patients. These streamlined approval pathways are particularly vital for repurposing drugs, as they accelerate the development and availability of critical treatments, ensuring faster access to affordable therapies for NTDs. Therefore, implementing such regulatory mechanisms globally is essential to accelerate and address the urgent medical needs posed by NTDs through drug repositioning.

4.2. The role of the pharmaceutical industry

The pharmaceutical industry has a pivotal role in embracing social responsibility by investing in research and forming public–private partnerships to unlock the potential of drug repositioning for NTDs. By collaborating with academic institutions and global health organizations, pharmaceutical companies can significantly contribute to developing cost-effective therapies for NTDs, thereby addressing both public health needs and market gaps. These partnerships are particularly crucial in low- and middle-income countries, where the burden of NTDs is highest, and access to affordable treatments is most urgently needed. In these regions, pharmaceutical companies can play a transformative role by ensuring that medical innovations are accessible and affordable. Through these efforts, the pharmaceutical sector can bridge the gap between innovation and access, ensuring that repositioned drugs reach the populations most in need. Furthermore, pharmaceutical companies can leverage their expertise in drug development, manufacturing, and distribution to ensure that repositioned drugs are produced efficiently, meet quality standards, and are delivered promptly to regions in need. By participating in shared intellectual property agreements and open-access research initiatives, the industry can further reduce costs, foster innovation, and accelerate drug development timelines. In addition, pharmaceutical companies play a pivotal role in advocating for regulatory reforms that streamline the approval process for repositioned drugs, thereby making treatments available more rapidly to those in need. By embracing these roles, the pharmaceutical industry can significantly contribute to combating NTDs, ultimately improving global health outcomes and fulfilling their social responsibility.

4.3. Research and academic institutions

Research and academic institutions play a crucial role in driving innovation in drug repositioning. Interdisciplinary collaboration (bringing together experts from multidisciplinary fields such as biology, chemistry, and computer science) and international partnerships are essential for advancing the scientific understanding of NTDs and identifying potential drug candidates. Institutions should focus on innovative research methodologies such as high-throughput screening, which allows rapid testing of thousands of compounds against disease targets, artificial intelligence, and computational modeling, which can predict drug-target interactions and accelerate the identification of promising candidates.[34]

In addition, these institutions play a key role in building scientific capacity in low-income regions by providing training for local researchers and fostering South–South collaborations (partnerships between developing countries). For example, the Global Network for NTDs (a network formed by researchers from Argentina, Brazil, India, Pakistan, the United Kingdom, and Uruguay) has advanced NTD research through shared resources and expertise.[35] This not only strengthens the local infrastructure for NTD research but also enriches the global scientific community by incorporating diverse perspectives and expertise. Moreover, research and academic institutions are pivotal in conducting pre-clinical and clinical trials necessary to evaluate the safety and efficacy of repositioned drugs. By fostering strong partnerships with industry and governmental bodies, they can accelerate the translation of laboratory discoveries into real-world treatments, bridging the gap between research and application and ensuring that scientific discoveries become accessible therapies. By leading innovation and capacity building, research and academic institutions ensure that drug repositioning efforts remain at the forefront of scientific advancement.

4.4. International health organizations

International health organizations, such as the WHO, play a pivotal role in coordinating global efforts to address NTDs through drug repositioning. By advocating for equitable resource distribution and raising the profile of NTDs through initiatives such as the "Uniting to Combat NTDs" campaign,[36] these organizations can help mobilize the necessary resources and support for repositioning efforts. Moreover, they play a critical role in setting global health priorities, establishing guidelines, and fostering cross-border collaborations to share knowledge and resources.

Through initiatives such as the WHO's Roadmap for NTDs (which outlines strategies for the control, elimination, and eradication of 20 prioritized NTDs) these

organizations align the efforts of governments, research institutions, and private industry toward common goals. Furthermore, by supporting local health-care systems, training health-care professionals, and ensuring access to affordable therapies (including repositioned drugs) international health organizations directly improve health outcomes in affected communities.

International health organizations, with their oversight and global reach, are well-positioned to promote regulatory harmonization across countries. By streamlining the approval process for repositioned drugs, they ensure faster delivery to those in need. By leveraging their extensive networks and resources, these organizations play an essential role in uniting stakeholders and advancing the fight against NTDs through effective drug repositioning strategies.

4.5. Public and non-profit organizations

Public and non-profit organizations play a vital role in raising awareness about NTDs and supporting fundraising efforts for research into drug repositioning. Grassroots campaigns and public education initiatives can generate the political and financial support needed to advance these projects. Moreover, these organizations act as crucial intermediaries, bridging the gap between affected communities, policymakers, and researchers. By advocating equitable access to treatments and promoting global partnerships, they ensure that drug repositioning efforts are tailored to the specific needs of low-income regions, directly addressing the challenges faced by these communities.

In addition, they often lead advocacy initiatives that pressure governments and international bodies to prioritize NTD research, allocate funding, and streamline regulatory pathways for repositioned drugs. Organizations such as Médecins Sans Frontières[37] and the Bill and Melinda Gates Foundation[38] have launched campaigns and funded projects that significantly contribute to NTD research and drug repositioning efforts. Their sustained advocacy and influence help maintain momentum in the fight against NTDs, fostering a more inclusive and collaborative global health agenda that prioritizes neglected communities.

5. Conclusion

Drug repositioning has emerged as a pivotal strategy in the battle against NTDs, offering the potential to rapidly deliver effective treatments for these devastating diseases. As we look to the future, harnessing this approach will be crucial in changing the landscape of NTD treatments and bringing hope to millions affected. Achieving success requires collective action from governments, the pharmaceutical industry, research institutions, international health organizations, and public and non-profit organizations: a united front. This collaborative effort should involve governments aligning regulations to support expedited drug approvals; pharmaceutical companies sharing intellectual property and resources; and research institutions advancing innovative drug repositioning techniques. International health organizations must coordinate funding and implementation efforts, whereas public and non-profit organizations raise awareness and advocate equitable access to treatments. By joining forces and leveraging drug repositioning, this united front can significantly transform the treatment landscape for NTDs, bringing effective and accessible therapies to millions in impoverished regions. Given the urgency of this cause, immediate collaborative action is imperative to develop rapid, cost-effective solutions that will ultimately improve global health. Our greatest strength lies in unity; by working together, we can transform the fight against NTDs and bring hope to millions.

Acknowledgments

The author extends gratitude to the Global Network for Neglected Tropical Diseases, of which he is a proud member.

Funding

This study is supported by the Medical Research Council (MRC) of the United Kingdom for the fellowship award.

Conflict of interest

The author declares no competing interests.

Author contributions

This is a single-authored article.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Not applicable.

References

1. WHO. World Health Organization; 2024. Available from: https://www.who.int/health-topics/neglected-tropical-diseases [Last accssed on 2024 Oct 12].
2. Porta EOJ, Ballari MS, Carlucci R, *et al*. Systematic study

of 1,2,3-triazolyl sterols for the development of new drugs against parasitic Neglected Tropical Diseases. *Eur J Med Chem*. 2023;254:115378.

doi: 10.1016/j.ejmech.2023.115378

3. Previti S, Di Chio C, Ettari R, *et al*. Dual inhibition of parasitic targets: A valuable strategy to treat malaria and neglected tropical diseases. *Curr Med Chem*. 2022;29(17):2952-2978.

doi: 10.2174/0929867328666210810125309

4. Magalhães AR, Codeço CT, Svenning JC, *et al*. Neglected tropical diseases risk correlates with poverty and early ecosystem destruction. *Infect Dis Poverty*. 2023;12(1):32.

doi: 10.1186/s40249-023-01084-1

5. Chami GF, Bundy DAP. More medicines alone cannot ensure the treatment of neglected tropical diseases. *Lancet Infect Dis*. 2019;19(9):e330-e336.

doi: 10.1016/S1473-3099(19)30160-4

6. Weng HB, Chen HX, Wang MW. Innovation in neglected tropical disease drug discovery and development. *Infect Dis Poverty*. 2018;7(1):67.

doi: 10.1186/s40249-018-0444-1

7. Jourdan JP, Bureau R, Rochais C, Dallemagne P. Drug repositioning: A brief overview. *J Pharm Pharmacol*. 2020;72(9):1145-1151.

doi: 10.1111/jphp.13273

8. Pushpakom S, Iorio F, Eyers PA, *et al*. Drug repurposing: Progress, challenges and recommendations. *Nat Rev Drug Discov*. 2019;18(1):41-58.

doi: 10.1038/nrd.2018.168

9. Low ZY, Farouk IA, Lal SK. Drug repositioning: New approaches and future prospects for life-debilitating diseases and the COVID-19 pandemic outbreak. *Viruses*. 2020;12(9):1058.

doi: 10.3390/v12091058

10. Kulkarni VS, Alagarsamy V, Solomon VR, Jose PA, Murugesan S. Drug repurposing: An effective tool in modern drug discovery. *Russ J Bioorg Chem*. 2023;49(2):157-166.

doi: 10.1134/S1068162023020139

11. Hua Y, Dai X, Xu Y, *et al*. Drug repositioning: Progress and challenges in drug discovery for various diseases. *Eur J Med Chem*. 2022;234:114239.

doi: 10.1016/j.ejmech.2022.114239

12. Talevi A, Bellera CL. Challenges and opportunities with drug repurposing: Finding strategies to find alternative uses of therapeutics. *Expert Opin Drug Discov*. 2020;15(4):397-401.

doi: 10.1080/17460441.2020.1704729

13. Islam S, Wang S, Bowden N, Martin J, Head R. Repurposing existing therapeutics, its importance in oncology drug development: Kinases as a potential target. *Br J Clin Pharmacol*. 2022;88(1):64-74.

doi: 10.1111/bcp.14964

14. Latif T, Chauhan N, Khan R, Moran A, Usmani SZ. Thalidomide and its analogues in the treatment of Multiple Myeloma. *Exp Hematol Oncol*. 2012;1(1):27.

doi: 10.1186/2162-3619-1-27

15. Teo S, Resztak KE, Scheffler MA, *et al*. Thalidomide in the treatment of leprosy. *Microbes Infect*. 2002;4(11):1193-202.

doi: 10.1016/s1286-4579(02)01645-3

16. Abdelsayed M, Kort EJ, Jovinge S, *et al*. Repurposing drugs to treat cardiovascular disease in the era of precision medicine. *Nat Rev Cardiol*. 2022;19(11):751-764.

doi: 10.1038/s41569-022-00717-6

17. Xia Y, Sun M, Huang H, Jin WL. Drug repurposing for cancer therapy. *Signal Transduct Target Ther*. 2024;9(1):92.

doi: 10.1038/s41392-024-01808-1

18. Hijazi MA, Gessner A, El-Najjar N. Repurposing of chronically used drugs in cancer therapy: A chance to grasp. *Cancers* (*Basel*). 2023;15(12):3199.

doi: 10.3390/cancers15123199

19. Porta EOJ, Bofill Verdaguer I, Perez C, *et al*. Repositioning Salirasib as a new antimalarial agent. *Medchemcomm*. 2019;10(9):1599-1605.

doi: 10.1039/c9md00298g

20. Pessanha de Carvalho L, Kreidenweiss A, Held J. Drug repurposing: A review of old and new antibiotics for the treatment of malaria: Identifying antibiotics with a fast onset of antiplasmodial action. *Molecules*. 2021;26(8):2304.

doi: 10.3390/molecules26082304

21. Machado PR, Ampuero J, Guimarães LH, *et al*. Miltefosine in the treatment of cutaneous leishmaniasis caused by *Leishmania braziliensis* in Brazil: A randomized and controlled trial. *PLoS Negl Trop Dis*. 2010;4(12):e912.

doi: 10.1371/journal.pntd.0000912

22. Klug DM, Gelb MH, Pollastri MP. Repurposing strategies for tropical disease drug discovery. *Bioorg Med Chem Lett*. 2016;26(11):2569-2576.

doi: 10.1016/j.bmcl.2016.03.103

23. Porta EOJ, Kalesh K, Steel PG. Navigating drug repurposing for Chagas disease: Advances, challenges, and opportunities. *Front Pharmacol*. 2023;14:1233253.

doi: 10.3389/fphar.2023.1233253

24. Charlton RL, Rossi-Bergmann B, Denny PW, *et al*. Repurposing as a strategy for the discovery of new anti-leishmanials: The-state-of-the-art. *Parasitology*. 2018;145(2):219-236.

doi: 10.1017/S0031182017000993

25. Sbaraglini ML, Vanrell MC, Bellera CL, *et al*. Neglected tropical protozoan diseases: Drug repositioning as a rational option. *Curr Top Med Chem*. 2016;16(19):2201-2222.

doi: 10.2174/1568026616666160216154309

26. Casulli A New global targets for NTDs in the WHO roadmap 2021-2030. *PLoS Negl Trop Dis*. 2021;15(5):e0009373.

doi: 10.1371/journal.pntd.0009373

27. Engels D, Zhou XN. Neglected tropical diseases: An effective global response to local poverty-related disease priorities. *Infect Dis Poverty.* 2020;9(1):10.

doi: 10.1186/s40249-020-0630-9

28. Begley CG, Ashton M, Baell J, *et al*. Drug repurposing: Misconceptions, challenges, and opportunities for academic researchers. *Sci Transl Med*. 2021;13(612):eabd5524.

doi: 10.1126/scitranslmed.abd5524

29. Weth FR, Hoggarth GB, Weth AF, *et al*. Unlocking hidden potential: Advancements, approaches, and obstacles in repurposing drugs for cancer therapy. *Br J Cancer*. 2023;130:703-715.

doi: 10.1038/s41416-023-02502-9

30. Ma Z, Augustijn K, De Esch I, Bossink B. Public-private partnerships influencing the initiation and duration of clinical trials for neglected tropical diseases. *PLoS Negl Trop Dis.* 2023;17(11):e0011760.

doi: 10.1371/journal.pntd.0011760

31. Torreele E, Bourdin Trunz B, Tweats D, *et al*. Fexinidazole--a new oral nitroimidazole drug candidate entering clinical development for the treatment of sleeping sickness. *PLoS Negl Trop Dis.* 2010;4(12):e923.

doi: 10.1371/journal.pntd.0000923

32. FDA. *The United States Food and Drug Administration*; 2024. Available from: https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review [Last accssed on 2024 Oct 12].

33. *EMA. European Medicines Agency*; 2024. Available from: https://www.ema.europa.eu/en/human-regulatory-overview/research-development/prime-priority-medicines [Last accssed on 2024 Oct 12].

34. Hernandez HW, Soeung M, Zorn KM, *et al*. High throughput and computational repurposing for neglected diseases. *Pharm Res.* 2018;36(2):27.

doi: 10.1007/s11095-018-2558-3

35. *A Global Network for Neglected Tropical Diseases*; 2024. Available from: https://ntd-network.org [Last accssed on 2024 Oct 12].

36. *Uniting to Combat NTDs*; 2024. Available from: https://unitingtocombatntds.org [Last accssed on 2024 Oct 12].

37. *Médecins Sans Frontières*; 2024. Available from: https://www.msf.org [Last accssed on 2024 Oct 12].

38. *Bill & Melinda Gates Foundation*; 2024. Available from: https://www.gatesfoundation.org [Last accssed on 2024 Oct 12].