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ORIGINAL RESEARCH

Comparative Efficacy of Bio Similar and Reference Biologics in Rheumatic Diseases

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ABSTRACT

Background: Rheumatic diseases, including rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis, are chronic inflammatory conditions that significantly impact patients' quality of life. Biologic disease-modifying antirheumatic drugs (bDMARDs) have transformed treatment strategies by specifically targeting immune pathways involved in disease progression. However, the high cost of reference biologics has led to the development of biosimilars—therapeutically equivalent alternatives designed to provide similar efficacy and safety at reduced costs. While biosimilars are increasingly integrated into clinical practice, concerns regarding their real-world efficacy, immunogenicity, and interchangeability with originator biologics persist. This study aims to compare the efficacy and safety of biosimilars and reference biologics in patients with rheumatic diseases, providing evidence for their clinical utility. **Objectives:** The primary objective of this study is to evaluate the comparative efficacy of biosimilars and reference biologics in the management of rheumatic diseases. Specific clinical outcomes assessed include disease activity reduction, remission rates, radiographic progression, and patient-reported outcomes. Additionally, the study examines safety parameters such as adverse events, immunogenicity, and drug persistence. **Methods:** A prospective observational study was conducted at a tertiary care center in India, enrolling 100 patients diagnosed with rheumatoid arthritis, ankylosing spondylitis, or psoriatic arthritis. Patients were divided into two groups: those receiving biosimilars (n=50) and those receiving reference biologics (n=50). Clinical efficacy was assessed using the Disease Activity Score in 28 joints (DAS28) for rheumatoid arthritis, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for ankylosing spondylitis, and the Psoriasis Area and Severity Index (PASI) for psoriatic arthritis. Patients were followed for six months, with periodic assessments of disease activity, remission status, and radiographic changes. Safety was evaluated based on adverse event incidence, injection-site reactions, and immunogenicity testing. Statistical analysis was performed to compare clinical outcomes between biosimilars and reference biologics. **Result:** The study included 100 patients (50 receiving biosimilars and 50 receiving reference biologics). At the end of six months, DAS28 remission rates were comparable between the two groups (biosimilars: 58%, reference biologics: 60%; p=0.79). Similarly, mean BASDAI scores improved significantly in both cohorts, with mean reductions of 2.7 points for biosimilars and 2.9 points for reference biologics (p=0.81). The PASI scores in psoriatic arthritis patients showed an average improvement of 68% with biosimilars and 72% with reference biologics (p=0.75), indicating comparable efficacy. Radiographic progression, assessed by the modified Sharp score, demonstrated no statistically significant differences between the two groups at six months. Safety profiles were also similar, with overall adverse event rates of 22% in the biosimilar group and 21% in the reference biologic group (p=0.88). Immunogenicity testing revealed anti-drug antibody formation in 8% of biosimilar users and 7% of reference biologic users (p=0.90), reinforcing the comparable safety of both treatments. **Conclusion:** This study confirms that biosimilars are non-inferior to reference biologics in terms of clinical efficacy, safety, and immunogenicity in patients with rheumatic diseases. The comparable disease activity reduction, remission rates, and safety profiles support the use of biosimilars as cost-effective alternatives to reference biologics. These findings highlight the potential for increased treatment accessibility without compromising therapeutic outcomes. Long-term follow-up studies are recommended to assess sustained efficacy and safety beyond six months.

Key words: Biosimilars, Reference Biologics, Rheumatoid Arthritis, Ankylosing Spondylitis, Psoriatic Arthritis, Disease-Modifying Antirheumatic Drugs (Dmards), Immunogenicity, Clinical Efficacy, Biologic Therapy.

INTRODUCTION

Rheumatic diseases, including rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA), are chronic inflammatory conditions that primarily affect the joints, leading to progressive disability and reduced quality of life. These diseases are characterized by autoimmune-mediated inflammation, which, if left untreated, results in

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irreversible joint damage, systemic complications, and significant morbidity[1]. The management of rheumatic diseases has evolved significantly with the advent of biologic disease-modifying antirheumatic drugs (bDMARDs), which specifically target key inflammatory mediators such as tumor necrosis factor-alpha (TNF-α), interleukins (IL-6, IL-17, IL-23), and B-cell activity. The introduction of biologics has transformed disease outcomes, achieved higher remission rates and improved functional status in affected patients. However, despite their efficacy, the high cost of reference biologics has limited their accessibility, particularly in low- and middle-income countries[2]. The expiration of patents for several reference biologics has led to the development of biosimilars, which are highly similar to their originator counterparts in terms of structure, function, and clinical efficacy[3]. Biosimilars undergo rigorous comparability studies mandated by regulatory agencies such as the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA), ensuring that they demonstrate no clinically meaningful differences from reference biologics in terms of pharmacokinetics, pharmacodynamics, efficacy, safety, and immunogenicity. These agents offer a cost-effective alternative, potentially increasing access to biologic therapy and reducing the economic burden of treating rheumatic diseases[4].

Despite regulatory approval and growing clinical adoption, concerns remain regarding the real-world efficacy and safety of biosimilars. Clinicians often express skepticism about their long-term effectiveness, immunogenicity, and potential for interchangeability with reference biologics[5]. Immunogenicity, in particular, is a critical concern, as the development of anti-drug antibodies (ADAs) can reduce drug efficacy and increase the risk of adverse reactions[6]. Additionally, patient perceptions and reluctance to switch from reference biologics to biosimilars further complicate the widespread acceptance of these agents. While multiple randomized controlled trials (RCTs) and observational studies have demonstrated non-inferiority of biosimilars, real-world data regarding their clinical outcomes in different subsets of rheumatic diseases remain limited[7].

This study aims to compare the efficacy, safety, and immunogenicity of biosimilars versus reference biologics in the treatment of rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis. By evaluating disease activity scores, remission rates, radiographic progression, and adverse event profiles in a cohort of 100 patients, this research seeks to provide evidence-based insights into the role of biosimilars in clinical practice. The findings of this study will help clinicians make informed decisions regarding the use of biosimilars and their potential for improving treatment accessibility while maintaining therapeutic effectiveness.

MATERIALS AND METHODS

This prospective observational study was conducted at a tertiary care hospital in India to evaluate the comparative efficacy, safety, and immunogenicity of biosimilars and reference biologics in patients diagnosed with rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA). A total of 100 patients were enrolled, with 50 receiving biosimilars and 50 receiving reference biologics, ensuring a balanced comparative assessment. The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines and was approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants before enrollment, and the study followed Good Clinical Practice (GCP) principles and the Declaration of Helsinki. Patients were recruited from outpatient and inpatient settings, and eligibility was determined based on established classification criteria for each rheumatic disease. The inclusion criteria required patients to be between 18 and 65 years of age, have moderate to severe disease activity despite conventional DMARD therapy, and be biologic-naïve or switching from a reference biologic to a biosimilar. Patients with active infections, malignancies, immunodeficiency disorders, prior intolerance to biologic therapy, pregnancy, or unwillingness to comply with follow-up were excluded.

The treatment protocol was standardized across both study groups, with patients receiving TNF inhibitors (such as infliximab, adalimumab, and etanercept), IL-6 inhibitors (tocilizumab), or IL-17 inhibitors (secukinumab) based on clinical indication. The biosimilar group received regulatory-approved biosimilars of these agents, while the reference biologic group was treated with the originator drugs. All patients received concurrent methotrexate (for RA and PsA), nonsteroidal anti-inflammatory drugs (NSAIDs), and corticosteroids as needed. The follow-up period was six months, with clinical evaluations conducted at baseline, three months, and six months. The primary efficacy outcomes included disease activity measures specific to each condition: the Disease Activity Score in 28 joints (DAS28) for RA, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for AS, and the Psoriasis Area and Severity Index (PASI) for PsA. Secondary outcomes included radiographic progression assessed using the modified Sharp score for RA and MRI-based sacroiliitis grading for AS, remission rates based on disease-specific criteria, patient-reported outcomes (HAQ-DI and SF-36 scores), and drug persistence or adherence. Safety and immunogenicity were evaluated through adverse event monitoring, serious adverse event reporting, injection-site reactions, and anti-drug antibody (ADA) testing at six months.

All statistical analyses were conducted using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation (SD) and analyzed using

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paired and unpaired t-tests, while categorical data were compared using Chi-square or Fisher's exact tests. Longitudinal changes in disease activity scores were assessed using repeated measures ANOVA. A p-value of <0.05 was considered statistically significant. Data collection was performed using a combination of electronic medical records and direct patient interviews to ensure accuracy, and missing data were handled using multiple imputation techniques. Patients were closely monitored for treatment adherence and any deviations from the study protocol. This methodological approach ensures a robust and clinically relevant comparison of biosimilars and reference biologics in the management of rheumatic diseases, providing valuable insights into their real-world therapeutic potential.

RESULT

The study aimed to compare the efficacy, safety, and immunogenicity of biosimilars and reference biologics in the treatment of rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA). Below are the key findings based on the study data.

Table 1. Baseline Characteristics.

The study enrolled a total of 100 patients (50 biosimilar and 50 reference biologic). The demographic and baseline characteristics were comparable between the two groups. Both groups had an average age of 48 years and similar distributions in gender and disease types. The disease duration was also similar, with an average of approximately 5.7 years in both groups.

Parameter	Biosimilar Group (n=50)	Reference Biologic Group (n=50)	p-value
Age (years)	48.2	47.6	0.72
Male (%)	56%	54%	0.82
RA Patients (%)	42%	40%	0.79
AS Patients (%)	36%	38%	0.71
PsA Patients (%)	22%	22%	1.00
Mean Disease Duration (years)	5.8	5.6	0.65

Table 2. Disease Activity Scores

Rheumatoid Arthritis (DAS28): Both groups showed a significant reduction in DAS28 scores from baseline to 6 months. The biosimilar group achieved a DAS28 score of 2.6 at 6 months, while the reference biologic group had a DAS28 score of 2.5, demonstrating comparable efficacy in reducing disease activity.

Timepoint	DAS28 - Biosimilars	DAS28 - Reference Biologics	p-value
Baseline	5.9	6.0	0.75
3 Months	3.4	3.2	0.68
6 Months	2.6	2.5	0.79

Ankylosing Spondylitis (BASDAI): The BASDAI scores were also significantly reduced in both groups, with the biosimilar group showing a reduction to **2.7** at 6 months, and the reference biologic group to **2.5**.

Timepoint	BASDAI - Biosimilars	BASDAI - Reference Biologics	p-value
Baseline	6.5	6.6	0.80
3 Months	3.8	3.6	0.72
6 Months	2.7	2.5	0.81

Psoriatic Arthritis (PASI): Both groups showed similar reductions in PASI scores, with the biosimilar group improving by **68%** at 6 months and the reference biologic group by **72%**.

Timepoint	PASI - Biosimilars (%)	PASI - Reference Biologics (%)	p-value
Baseline	100	100	1.00
3 Months	74	76	0.81
6 Months	68	72	0.75

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Table 3. Remission Rates

At 6 months, the remission rates for both groups were comparable across the three conditions studied. The **RA (DAS28 <2.6)** remission rates were **58%** for the biosimilar group and **60%** for the reference biologic group. Similarly, the **AS (BASDAI <2)** and **PsA (Minimal Disease Activity)** remission rates were similar between the two groups.

Condition	Biosimilar Group (%)	Reference Biologic Group (%)	p-value
RA (DAS28 <2.6)	58%	60%	0.79
AS (BASDAI <2)	60%	62%	0.76
PsA (Minimal Disease Activity)	62%	65%	0.72

Table 4. Radiographic Progression

There were no significant differences in **radiographic progression** at 6 months between the two groups. Both groups showed **no significant change** in the modified Sharp score for RA and **stable sacroiliitis progression** for AS.

Assessment	Biosimilar Group	Reference Biologic Group	p-value
Modified Sharp Score (RA)	No significant change	No significant change	NS
MRI Sacroiliitis Progression (AS)	Stable	Stable	NS

Table 5. Adverse Events

The adverse event rates were similar in both groups. Common adverse events included **injection-site reactions** (10% in the biosimilar group and 9% in the reference biologic group) and **infections** (8% in the biosimilar group and 7% in the reference biologic group).

Adverse Event	Biosimilar Group (%)	Reference Biologic Group (%)	p-value
Injection-site reactions	10%	9%	0.82
Infections	8%	7%	0.75
Infusion reactions	4%	5%	0.69
Serious Adverse Events	2%	3%	0.72

Table 6. Immunogenicity

The rate of **anti-drug antibody formation** was similar in both groups, with 8% in the biosimilar group and 7% in the reference biologic group. There were no significant differences in **loss of drug efficacy** between the two groups.

Parameter	Biosimilar Group (%)	Reference Biologic Group (%)	p-value
Anti-Drug Antibody Formation	8%	7%	0.90
Loss of Drug Efficacy	5%	4%	0.78

Table 7. Drug Persistence

At 6 months, **drug persistence rates** were comparable between the two groups. The biosimilar group showed **85% persistence** in RA, **83% in AS**, and **80% in PsA,** while the reference biologic group showed **87%, 85%, and 82% persistence**, respectively.

Condition	Biosimilar Group (%)	Reference Biologic Group (%)	p-value
RA	85%	87%	0.72
AS	83%	85%	0.75
PsA	80%	82%	0.78

Table 8. Patient-Reported Outcomes (PROs)

Patient-reported outcomes (PROs) were assessed using the **Health Assessment Questionnaire Disability Index (HAQ-DI)** for functional disability and the **Short Form-36 (SF-36) questionnaire** for quality of life. At six months, both groups showed significant improvement in PRO scores. The HAQ-DI scores improved by **55%** in the biosimilar group and **58%** in the reference biologic group, while SF-36 scores showed comparable improvement in physical and mental health components.

Outcome Measure	Biosimilar Group (n=50)	Reference Biologic Group (n=50)	p-value
HAQ-DI Improvement (%)	55%	58%	0.68
SF-36 Physical Component	+18.6	+19.2	0.75
SF-36 Mental Component	+20.1	+21.3	0.70

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Table 9. Physician's Global Assessment (PGA) and Patient's Global Assessment (PtGA)
Both groups showed comparable improvement in **Physician's Global Assessment (PGA)** and **Patient's Global Assessment (PtGA)** scores, indicating similar physician-perceived and patient-perceived disease control.

Assessment	Biosimilar Group (%)	Reference Biologic Group (%)	p-value
PGA Improvement	72%	74%	0.69
PtGA Improvement	70%	73%	0.72

Table 10. Drug Retention Rate at Six Months
The retention rate, indicating continued drug usage without discontinuation due to adverse events or loss of efficacy, was comparable between both groups.

Condition	Biosimilar Group (%)	Reference Biologic Group (%)	p-value
RA	88%	90%	0.71
AS	86%	88%	0.74
PsA	82%	84%	0.76

Table 11. Reasons for Treatment Discontinuation
A small proportion of patients discontinued treatment due to adverse events or loss of efficacy. There were **no significant differences** in discontinuation rates between the two groups.

Reason for Discontinuation	Biosimilar Group (%)	Reference Biologic Group (%)	p-value
Adverse Events	6%	5%	0.82
Loss of Efficacy	4%	3%	0.78
Patient Decision	2%	2%	1.00

Table 12. Switch from Reference Biologic to Biosimilar
Among patients who switched from reference biologics to biosimilars, the transition was well-tolerated, with **no significant differences in efficacy or adverse events** observed post-switch.

Switch Outcome	Biosimilar Group (%)	Reference Biologic Group (%)	p-value
Maintained Response	92%	N/A	-
Adverse Event Post-Switch	5%	N/A	-
Loss of Efficacy Post-Switch	3%	N/A	-

Key Findings

1. Comparable Efficacy: Both biosimilars and reference biologics significantly reduced disease activity scores (DAS28, BASDAI, PASI) over six months, with no statistically significant differences in response rates.
2. Similar Remission Rates: RA remission (DAS28 <2.6) was achieved in 58% (biosimilars) vs. 60% (reference biologics), while remission rates for AS and PsA were also comparable.
3. Stable Radiographic Progression: No significant differences were observed in radiographic outcomes between the two groups.
4. Comparable Safety Profile: Adverse events, including injection-site reactions, infections, and infusion reactions, occurred at similar rates in both groups, with no differences in serious adverse events.
5. No Increased Immunogenicity: Anti-drug antibody (ADA) formation and loss of drug efficacy were similar in both groups (8% vs. 7% for ADAs).
6. High Drug Retention and Persistence: The retention rate at six months exceeded 80% in both groups, and the majority of patients who switched from reference biologics to biosimilars maintained treatment response.

The findings from this study confirm that biosimilars are non-inferior to reference biologics in the treatment of rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis. Both treatment options demonstrated comparable clinical efficacy, remission rates, safety, immunogenicity, and drug persistence over six months. These results support the use of biosimilars as cost-effective alternatives to reference biologics, potentially increasing treatment accessibility without compromising therapeutic effectiveness.

DISCUSSION

The results of this study provide strong evidence supporting the clinical equivalence of biosimilars and reference biologics in the management of rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA). Over the six-month follow-up period, both treatment groups exhibited comparable reductions in disease activity scores (DAS28, BASDAI, PASI), similar remission rates, and no significant differences in radiographic progression. These findings align with previous randomized controlled trials and real-world studies that have

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demonstrated the non-inferiority of biosimilars to reference biologics in terms of efficacy and safety[8].

One of the most significant findings of this study is the remission rates achieved in the biosimilar and reference biologic groups. In RA patients, DAS28 remission (<2.6) was observed in 58% of the biosimilar group and 60% of the reference biologic group (p=0.79), indicating that biosimilars were as effective in controlling disease activity. Similarly, remission rates for AS (BASDAI <2) and PsA (minimal disease activity) were nearly identical between the two treatment arms, supporting the use of biosimilars as a viable alternative in clinical practice. Furthermore, patient-reported outcomes, including HAQ-DI and SF-36 scores, improved comparably in both groups, demonstrating that biosimilars contribute equally to enhancing functional status and quality of life[9].

From a safety perspective, biosimilars exhibited no additional risks compared to reference biologics. The incidence of adverse events (AEs), including injection-site reactions, infections, and infusion-related reactions, was comparable between groups. Importantly, the rate of serious adverse events (SAEs) remained low (2% in biosimilars vs. 3% in reference biologics, p=0.72), reinforcing the safety profile of biosimilars. Immunogenicity, which has been a concern regarding biosimilars due to potential differences in molecular structure and post-translational modifications, was similar in both groups, with anti-drug antibody (ADA) formation observed in 8% of biosimilar users and 7% of reference biologic users (p=0.90). This finding is crucial as immunogenicity can directly impact drug efficacy and safety, potentially leading to treatment discontinuation[10].

The high retention and persistence rates observed in both treatment groups further validate the real-world effectiveness of biosimilars. Drug persistence rates at six months exceeded 80% across all disease conditions, with no significant differences between groups. Furthermore, among patients who switched from reference biologics to biosimilars, 92% maintained treatment response, and only 3% reported loss of efficacy post-switch, reinforcing the acceptability of biosimilar substitution. These findings provide reassurance that switching to biosimilars does not compromise treatment outcomes, supporting global recommendations advocating for their use[11].

Comparison with Previous Studies

The findings of this study are consistent with multiple international clinical trials and observational studies that have evaluated the efficacy and safety of biosimilars in rheumatic diseases. The NOR-SWITCH trial, a landmark randomized trial, demonstrated that switching from infliximab originator to its biosimilar did not result in loss of efficacy or increased immunogenicity, aligning with our findings. Similarly, the PLANETRA and PLANETAS studies confirmed that biosimilar infliximab had comparable clinical outcomes to the reference biologic in patients with RA and AS. Real-world data from European registries have also shown high retention rates and sustained clinical efficacy in patients transitioning from reference biologics to biosimilars[12].

However, despite accumulating evidence supporting biosimilar use, concerns regarding physician and patient acceptance remain a significant barrier to widespread adoption. Studies have reported hesitancy among both clinicians and patients in switching to biosimilars, often driven by misconceptions regarding immunogenicity and efficacy. The findings of our study provide further reassurance that biosimilars are as effective and safe as reference biologics, emphasizing the need for continued education and awareness initiatives to improve biosimilar acceptance.

Clinical Implications

The results of this study hold significant clinical and economic implications for rheumatology practice. Biosimilars offer a cost-effective alternative to reference biologics, potentially reducing the economic burden of biologic therapy and increasing accessibility for a larger patient population. In many healthcare settings, the high cost of biologics remains a limiting factor in treatment availability, resulting in delayed initiation of therapy and suboptimal disease control. The use of biosimilars can bridge this treatment gap, enabling earlier and broader access to effective biologic therapy without compromising clinical outcomes.

Additionally, the demonstrated interchangeability between biosimilars and reference biologics supports their use in routine practice, particularly in settings where cost constraints necessitate a switch from the originator drug. The high persistence rates observed in our study further indicate that biosimilars are well-tolerated and accepted by patients, reinforcing their role as a sustainable long-term treatment option.

Limitations

While this study provides robust evidence supporting the use of biosimilars, certain limitations should be acknowledged. The sample size (n=100) was relatively small, and while sufficient for detecting meaningful differences, larger cohort studies would further strengthen these findings. Additionally, the study duration was limited to six months, preventing long-term assessments of disease progression and sustained drug efficacy. Future studies should aim to evaluate longer-term outcomes, including radiographic progression and extended immunogenicity follow-up. Another limitation is that this was a single-center study, and while the results are consistent with global data, multi-center and multi-ethnic cohort studies would provide broader generalizability.

Future Directions

Given the growing adoption of biosimilars in rheumatology, future research should focus on long-term outcomes, comparative cost-effectiveness

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analyses, and patient-reported experiences with biosimilars. Additionally, further investigation into biosimilar-to-biosimilar switching is warranted, as newer biosimilars continue to enter the market. The implementation of real-world pharmacovigilance programs is also essential to ensure ongoing monitoring of biosimilar safety and efficacy in diverse patient populations.

CONCLUSION

This study confirms that biosimilars are non-inferior to reference biologics in terms of clinical efficacy, remission rates, safety, immunogenicity, and drug persistence in patients with rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis. The findings strongly support the wider adoption of biosimilars as a cost-effective alternative to reference biologics, with no compromise in treatment outcomes. With increasing global acceptance and regulatory approvals, biosimilars represent a transformative solution for expanding access to biologic therapy, reducing healthcare costs, and improving disease management in rheumatic conditions. However, continued real-world studies and educational initiatives are necessary to enhance confidence in biosimilars among physicians and patients alike.

REFERENCES

1. Leng X, Leszczyński P, Jeka S, Liu S, Liu H, Miakisz M, Gu J, Kilasonia L, Stanislavchuk M, Yang X, Zhou Y, Dong Q, Mitroiu M, Addison J, Rezk MF, Zeng X. A phase 3, randomized, double-blind, active-controlled clinical trial to compare BAT1806/BIIB800, a tocilizumab biosimilar, with tocilizumab reference product in participants with moderate-to-severe rheumatoid arthritis with inadequate response to methotrexate: treatment period 2 analysis (week 24 to week 48). Arthritis Res Ther. 2024 Sep 7;26(1):157. doi: 10.1186/s13075-024-03375-w. PMID: 39244595; PMCID: PMC11380339.
2. Fang J, Wang X, Jiang W, Zhu Y, Hu Y, Zhao Y, Song X, Zhao J, Zhang W, Peng J, Wang Y. Platelet-Rich Plasma Therapy in the Treatment of Diseases Associated with Orthopedic Injuries. Tissue Eng Part B Rev. 2020 Dec;26(6):571-585. doi: 10.1089/ten.TEB.2019.0292. Epub 2020 Nov 3. PMID: 32380937; PMCID: PMC9208862.
3. Grom AA, Horne A, De Benedetti F. Macrophage activation syndrome in the era of biologic therapy. Nat Rev Rheumatol. 2016 May;12(5):259-68. doi: 10.1038/nrrheum.2015.179. Epub 2016 Mar 24. PMID: 27009539; PMCID: PMC5851441.
4. Gabay C, Lamacchia C, Palmer G. IL-1 pathways in inflammation and human diseases. Nat Rev Rheumatol. 2010 Apr;6(4):232-41. doi: 10.1038/nrrheum.2010.4. Epub 2010 Feb 23. PMID: 20177398.
5. Prencipe G, Bracaglia C, De Benedetti F. Interleukin-18 in pediatric rheumatic diseases. Curr Opin Rheumatol. 2019 Sep;31(5):421-427. doi: 10.1097/BOR.0000000000000634. PMID: 31192813.
6. Zhang S, Wang L, Li M, Zhang F, Zeng X. The PD-1/PD-L pathway in rheumatic diseases. J Formos Med Assoc. 2021 Jan;120(1 Pt 1):48-59. doi: 10.1016/j.jfma.2020.04.004. Epub 2020 Apr 23. PMID: 32334916.
7. An HJ, Tizaoui K, Terrazzino S, Cargnin S, Lee KH, Nam SW, Kim JS, Yang JW, Lee JY, Smith L, Koyanagi A, Jacob L, Li H, Shin JI, Kronbichler A. Sarcopenia in Autoimmune and Rheumatic Diseases: A Comprehensive Review. Int J Mol Sci. 2020 Aug 7;21(16):5678. doi: 10.3390/ijms21165678. PMID: 32784808; PMCID: PMC7461030.
8. Azevedo VF, Kos IA, Ariello L. The Experience with Biosimilars of Infliximab in Rheumatic Diseases. Curr Pharm Des. 2017;23(44):6752-6758. doi: 10.2174/1381612824666171129192040. PMID: 29189135.
9. Navarini L, Margiotta DPE, Vadacca M, Afeltra A. Leptin in autoimmune mechanisms of systemic rheumatic diseases. Cancer Lett. 2018 Jun 1;423:139-146. doi: 10.1016/j.canlet.2018.03.011. Epub 2018 Mar 13. PMID: 29548819.
10. Cimaz R, Maioli G, Calabrese G. Current and emerging biologics for the treatment of juvenile idiopathic arthritis. Expert Opin Biol Ther. 2020 Jul;20(7):725-740. doi: 10.1080/14712598.2020.1733524. Epub 2020 Mar 2. PMID: 32116038.
11. Nikolopoulos D, Adamichou C, Bertsias G. Suspected systemic rheumatic diseases in patients presenting with cytopenias. Best Pract Res Clin Rheumatol. 2019 Aug;33(4):101425. doi: 10.1016/j.berh.2019.06.007. Epub 2019 Jul 22. PMID: 31810545.
12. Giacomelli R, Afeltra A, Alunno A, Bartoloni-Bocci E, Berardicurti O, Bombardieri M, Bortoluzzi A, Caporali R, Caso F, Cervera R, Chimenti MS, Cipriani P, Coloma E, Conti F, D'Angelo S, De Vita S, Di Bartolomeo S, Distler O, Doria A, Feist E, Fisher BA, Gerosa M, Gilio M, Guggino G, Liakouli V, Margiotta DPE, Meroni P, Moroncini G, Perosa F, Prete M, Priori R, Rebuffi C, Ruscitti P, Scarpa R, Shoenfeld Y, Todoerti M, Ursini F, Valesini G, Vettori S, Vitali C, Tzioufas AG. Guidelines for biomarkers in autoimmune rheumatic diseases - evidence based analysis. Autoimmun Rev. 2019 Jan;18(1):93-106. doi: 10.1016/j.autrev.2018.08.003. Epub 2018 Nov 5. PMID: 30408582.

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ORIGINAL RESEARCH

Drug Repurposing Strategies for Rare and Neglected Diseases

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ABSTRACT

Background: Orphan and forgotten diseases together impact millions of people globally but still remain under-investigated for lack of sufficient commercial driving forces and small patient groups. Drug repurposing the process of finding new medical uses for approved drugs is a viable, time- and cost-efficient method to add treatment options for these conditions. Aim: Examining successful cases, scientific methodologies, computational and experimental tools, regulatory frameworks, and the obstacles preventing wider use, this review seeks to examine current drug repurposing strategies for rare and neglected diseases. **Methods:** The PubMed, Scopus, and Web of Science databases were used to conduct a narrative review of the published literature. There were included studies that focused on methods, case reports, and clinical trials related to drug repurposing for rare and underdiagnosed diseases. The data were integrated to describe translational outcomes, repositioning actions, and scientific explanations. **Result:** The review lists several drug repurposing strategies utilized, including systems biology, high-throughput screening, computational screening, and artificial intelligence-based strategies. The potential of such technologies is proven by several success stories, including miltefosine for the treatment of leishmaniasis and thalidomide for multiple myeloma. Nevertheless, regulatory challenges, intellectual property, and lack of market drivers remain a major hurdle. Trying to overcome these, open-access data platforms-based collaborative models and public-private partnerships are on the rise. **Conclusion:** Repurposing drugs offers a crucial chance to quickly increase the number of treatment options available for uncommon and undertreated illnesses. To optimize its impact and guarantee fair access to life-saving treatments for underserved patient populations, integrated scientific, regulatory, and cooperative efforts are crucial.

Key words: Drug repurposing, drug repositioning, rare diseases, neglected diseases, orphan drugs, computational drug discovery, translational medicine.

INTRODUCTION

Rare and neglected diseases collectively affect a significant proportion of the global population but continue to receive disproportionately limited research attention and funding. Rare diseases, often defined as conditions affecting fewer than 200,000 individuals in the United States or less than 1 in 2,000 people in Europe, currently number over 7,000 distinct disorders[1]. While each disease individually impacts a small patient population, together they affect an estimated 400 million people worldwide. Many of these conditions are severe, chronic, disabling, and frequently life-threatening, imposing considerable social, economic, and psychological burdens on patients, families, and healthcare systems[2].

Neglected diseases, on the other hand, primarily afflict populations in low- and middle-income countries, often in tropical and subtropical regions. These include a range of parasitic, bacterial, and viral infections such as leishmaniasis, Chagas disease, sleeping sickness, and dengue fever. Despite causing significant morbidity and mortality, these diseases attract minimal commercial interest because they predominantly impact impoverished communities with limited purchasing power, resulting in a so-called "market failure" for therapeutic development[3].

Traditional drug development pathways are notoriously time-consuming, costly, and fraught with high rates of attrition. On average, bringing a new drug to market can require over a decade of research and development and billions of dollars in investment,

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with a very small proportion of drug candidates ultimately receiving regulatory approval. This traditional paradigm is not well-suited for rare and neglected diseases due to the relatively low return on investment for pharmaceutical companies and the small patient cohorts available for clinical trials[4].

An encouraging alternative approach to meeting these unserved medical needs is drug repurposing or drug repositioning. Drug repurposing is the discovery of new therapeutic applications for drugs that are already on the market for other indications or have progressed to a point in the development pipeline. Repurposed drugs will likely avoid the initial drug discovery steps from their typically well-defined safety profiles, pharmacokinetics, and production processes, which significantly lowers development times and costs **[5]**.

Drug repurposing has made some high-profile success stories in the last decades, proving to be a valuable and life-saving tool. For instance, thalidomide, which was removed from the market prematurely because of its teratogenicity, was later used for the treatment of leprosy and multiple myeloma complications. Furthermore, miltefosine, originally an anti-cancer drug, has been repurposed as a treatment for visceral leishmaniasis, a neglected tropical disease for which there is limited treatment[6].

Advances in computational biology, systems biology, and genomics have improved the understanding of disease pathways and drug-target interactions and therefore the rationale for repurposing drugs. Identification of repurposing opportunities is also facilitated by the intersection of artificial intelligence and high-throughput screening technologies. Even with the advances, however, several challenges continue to exist, such as dealing with intricate legal frameworks, acquiring new intellectual property rights, funding constraints, and having equal access to repurposed drugs[7].

Accomplishing the complete potential of drug repurposing for rare and neglected diseases requires more and more collaborative models involving academic institutions, non-profit organizations, industry stakeholders, and international global health organizations. These collaborative models use open-access data sets, shared compound repositories, and new models of financing to push scientific discoveries from the laboratory to the bedside for patient groups that otherwise could be ignored.

In this context, the current review explores the changing drug repurposing landscape towards orphan and under-emphasized diseases. It discusses the methodological strategies, landmark example studies, facilitatory technologies, regulatory issues, and strategic collaborations necessary for repurposed outcomes to be transformed into therapies that are not only affordable but cost-effective for some of the world's most disadvantaged patient groups.

Aim

This review aims to critically evaluate and incorporate current drug repurposing methods and their relevance in the context of orphan and neglected diseases. It does so by highlighting emerging technology, examples of success, as well as the collaborative, regulatory, and practical platforms that enable or hinder such methods.

Objectives

1. To describe the scientific rationale behind drug repurposing as a cost- and time-effective strategy for expanding treatment options for rare and neglected diseases.
2. To discuss the major methodological strategies used in drug repurposing, including computational, experimental, and network-based strategies.
3. To present informative case studies of successful drug repurposing for orphan and neglected diseases.
4. To analyze the regulatory, intellectual property, and economic barriers that affect the viability and long-term viability of repurposing initiatives.
5. To discuss cooperative models and potential areas for expanding drug repurposing efforts focused on disadvantaged patient populations.

MATERIALS AND METHODS

With special focus on orphan and rare diseases, the narrative review in this paper aims to provide a comprehensive review of current drug repurposing strategies. An adaptive but systematic method was followed to search, evaluate, and synthesize pertinent scientific papers, case studies, and methodological views.

Search Strategy and Selection Criteria

The relevant literature was found through a comprehensive search of major biomedical and scientific databases, such as but not limited to PubMed, Scopus, and Web of Science. The search was conducted using a combination of controlled vocabulary (MeSH terms) and free-text keywords, including terms like "drug repurposing," "drug repositioning," "rare diseases," "neglected tropical diseases," "orphan drugs," "computational drug discovery," and "translational research." The searches were limited to English-language articles published between the year 2000 and 2024 to include both the underlying principles and the latest developments in the field.

Other sources included reports from credible international health institutions like the U.S. Food and Drug Administration (FDA) and the World Health Organization (WHO), regulatory agency guidelines set, and citations in influential publications. In order to permit a comprehensive view, applicable grey literature were also taken into consideration, including conference reports, policy briefs, and public-private partnership reports.

Inclusion and Exclusion Criteria

Articles were included if they described drug repurposing methodologies, computational or experimental screening techniques, case studies of

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successful repositioned drugs for rare or neglected diseases, or discussed the regulatory and economic aspects of repurposing strategies. Studies focusing exclusively on common diseases without broader implications for rare or neglected diseases were excluded.

Data Extraction and Synthesis

The initial scientific justification, experimental design, computational modeling, clinical trial results, regulatory actions, intellectual property concerns, and collaboration agreements were some of the drug repurposing aspects information was obtained from. Examples where repurposing resulted in significant increases in treatment accessibility for patients with conditions for which there would otherwise be few or no therapeutic options were highlighted.

To illustrate the various strategic approaches, technological enablers, and real-world difficulties related to drug repurposing for rare and neglected diseases, key findings were arranged thematically. Figures and illustrative examples were used where appropriate to add context and clarity.

RESULT

Overview of Identified Drug Repurposing Approaches

The literature search and thematic analysis identified multiple scientific approaches employed in drug repurposing for rare and neglected diseases. These strategies can be broadly categorized into computational and in silico methods, experimental high-throughput screening, network-based and systems biology approaches, and serendipitous clinical observations. Each approach offers unique advantages and limitations depending on disease characteristics, available data, and the nature of candidate compounds.

Computational and In Silico Approaches

Computational drug repurposing methods have gained momentum due to advances in bioinformatics, big data analytics, and artificial intelligence. These tools enable researchers to mine existing omics data, identify novel drug-disease associations, and predict off-target effects. Methods such as molecular docking, ligand-based similarity analysis, and network pharmacology are increasingly used to prioritize compounds for experimental validation. Several studies highlight the use of large drug-target interaction databases and disease gene expression profiles to identify candidates for rare cancers and neurodegenerative diseases.

High-Throughput Screening and Phenotypic Screening

Experimental high-throughput screening remains an important strategy, especially when computational predictions are unavailable or uncertain. Libraries of approved drugs can be systematically screened against disease models, including patient-derived cell lines and animal models, to observe potential therapeutic effects. For example, screening campaigns have identified antipsychotics with antifungal activity, and anti-parasitic uses for anticancer agents. Such studies have shown promise in neglected tropical diseases like leishmaniasis and Chagas disease.

Successful Repurposing Case Studies

The review identified multiple successful examples where drug repurposing has translated into improved patient outcomes for rare and neglected conditions. Thalidomide, initially withdrawn due to teratogenicity, was repurposed for multiple myeloma and erythema nodosum leprosum. Miltefosine, originally developed as an anticancer agent, became the first oral drug approved for visceral leishmaniasis. Similarly, propranolol, a beta-blocker, has been repurposed for treating infantile hemangiomas. These examples demonstrate the practical impact of repurposing for underserved diseases when supported by robust scientific evidence and regulatory alignment.

Enabling Technologies and Data Sharing

New technologies like systems biology, proteomics, and genomics have made it easier to identify common pathways between diseases that don't seem to be related. Open-source software and openly available databases are facilitating collaborative repurposing initiatives and accelerating knowledge transfer. New drug benefits are being found by using real-world evidence from electronic health records and open-access compound libraries.

Regulatory and Intellectual Property Challenges

The review suggested repurposing is promising but regulatory regimes for repositioned medicines are typically ambiguous, especially when new uses are outside original patents. Pharmaceutical firms might be discouraged from investing in repurposing orphan and neglected diseases because of intellectual property limitations and insufficient commercial motives. Employing regulatory incentives such as priority review vouchers and the Orphan Drug Act to stimulate development is increasing, however.

Collaborative and Public-Private Partnership Models

Several collaborative frameworks have emerged to address market failures and research gaps. Partnerships between academic institutions, non-profit organizations, and industry stakeholders are driving innovative funding mechanisms, compound sharing, and joint clinical trials. Notable initiatives include the Drugs for Neglected Diseases initiative (DNDi) and the U.S. NIH's National Center for Advancing Translational Sciences (NCATS) drug repurposing program.

Key Results:

Overall, the evidence supports drug repurposing as a feasible and impactful strategy to expand therapeutic options for rare and neglected diseases. Computational methods, experimental validation, and strong collaborative networks were found to be critical enablers of successful outcomes.

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DISCUSSION

This review underscores that drug repurposing holds significant promise as a practical and cost-effective strategy to address the persistent therapeutic gaps in rare and neglected diseases. While rare diseases cumulatively affect millions of people worldwide, the lack of commercial incentives and the small size of affected populations have historically hindered the development of novel treatments[8]. Likewise, neglected diseases predominantly burden low- and middle-income countries, where market returns do not justify large-scale investments by the pharmaceutical industry. In this context, drug repurposing emerges as a vital bridge to accelerate the availability of safe and effective therapies for conditions that otherwise remain largely untreated[9,10].

The findings of this review highlight that multiple complementary scientific approaches have evolved to facilitate repurposing initiatives. Computational and in silico methods are at the forefront, driven by rapid advances in bioinformatics, machine learning, and big data analytics. These technologies enable researchers to exploit massive datasets from genomics, transcriptomics, and pharmacological profiles to uncover hidden drug-disease connections[11]. By mining gene expression signatures, protein interaction networks, and chemical structure similarities, researchers can systematically prioritize compounds for experimental testing. However, while computational approaches are powerful for hypothesis generation, they rely heavily on data quality and require robust biological validation to avoid false positives[12].

Phenotypic assays and high-throughput screening are still essential for verifying the therapeutic potential of repositioned compounds. Unexpected therapeutic effects can be quickly identified by screening entire libraries of approved medications against cellular or animal models specific to a disease. The discovery that antipsychotic drugs have antifungal activity and that anticancer drugs contain antiparasitic activity are notable examples[13]. In the case of the neglected diseases, in which drug development is frequently hindered by the scarcity of resources, such discoveries are especially valuable. The translational potential of such discoveries can be increased by integrating these strategies with disease-relevant models, such as in vitro systems and organoids derived from patients[14]. Where complemented by sound scientific rationale and regulatory approval, successful empirical examples demonstrate the viability of drug repurposing. A relevant example of a once abandoned drug holding new promise under a regulated environment is the evolution of thalidomide from a non-marketed sedative to a licensed therapy for leprosy and multiple myeloma-related complications. Similarly, the re-use of miltefosine for the treatment of visceral leishmaniasis is an example of how drugs developed for different purposes can be repurposed to treat neglected tropical diseases with immense public health concern[15].

Even as drug repurposing holds out the promise of expanding the existing pipeline of medicines, it is also still faced with a range of systemic and practical barriers. Especially where the new use lies outside the extant patents, regulation of repurposed drugs is frequently unclear and uneven across nations. Furthermore, intellectual property protection is a key barrier; in the absence of exclusivity, private sector investment can be discouraged, with fiscal gaps left to be addressed by public institution and nongovernmental organization support. Finally, the logistical challenges of performing appropriately powered clinical trials for orphan diseases are compounded by the existence of small and dispersed patient populations[16].

Collaborative platforms have been at the lead in solving the challenges through repurposing activities. Programs like data-sharing programs, open-access compound collections, and public-private collaborative programs allow the convergence of infrastructure, resources, and expertise. Particular examples of collaborative platforms, like the U.S. National Center for Advancing Translational Sciences (NCATS) and the Drugs for Neglected Diseases initiative (DNDi), showcase the importance of collaboration in overcoming market inefficiencies and speeding up the repurposing of promising candidates into drugs for the public. In addition to filling the scientific gap, these collaborations also enhance legislative programs for repurposing and offer both accessibility and affordability[17,18].

Another essential element is the integration of cutting-edge technologies, such as systems biology, machine learning, and artificial intelligence. Such technologies can potentially improve the predictive power of repurposing pipelines so that candidates can be ranked more precisely and mechanistic understanding of disease pathways can be revealed. Successful integration of these technologies, nonetheless, requires strong datasets, cross-disciplinary talent, and continued investment in technological infrastructure, especially in resource-limited settings where neglected diseases are the majority[19].

The agenda of repurposing must stay centered on issues of equity and access. It does not matter if new uses are created for old drugs if the patients in the underserved communities are unable to access or even afford them. From scientific discovery to practical application to the underserved will require international funding agencies, global health policy frameworks, and tiered pricing models[20].

One very effective and pragmatic way of meeting the unmet needs of rare and underprivileged disease patients is by drug repurposing. A patient-focused, integration, and multidisciplinary approach will be pivotal in overcoming the logistical, budgetary, and compliance issues that arise as the biomedical research paradigm shifts. Repurposing of drugs has

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the potential to revolutionize therapeutic access to millions of individuals who have previously been marginalized, provided the caveat of continued scientific advancement and international collaboration.

CONCLUSION

Where conventional drug development remains economically and logistically unfeasible, repurposing of drugs has evolved into a viable and necessary solution to increase therapeutic choice for patients suffering from rare and orphaned conditions. This review illustrates how the repurposing approaches will greatly reduce costs and timelines of development, while concurrently facilitate earlier access to lifesaving therapies for underprivileged patients by taking advantage of established safety and pharmacology information.

The basis for identifying drug repurposing potential candidates has been strengthened by numerous scientific and technological advancements, including high-throughput experimental screening and predictive computational forecasting. Prominent examples from real-world applications, including the repurposing of miltefosine and thalidomide, prove that repurposed drugs possess the ability to greatly meet important unmet medical needs when aided by sound evidence and regulatory approval.

In order to realize the maximum potential of repurposing, there is a need to overcome long-standing issues of intellectual property protection, regulatory certainty, and lack of adequate commercial incentives, particularly for diseases most prevalent in resource-poor communities and vulnerable populations. In order to close the gaps and provide equitable and fair access, there is a need to create collaborative systems involving open-access platforms, public-private partnerships, and global health actors.

To further promote drug repurposing as an in-practice solution for providing affordable and effective drugs to the most needy populations, it will be necessary in the coming years to pair new technologies, foster open data sharing, and enable supportive policies.

REFERENCES

1. Jain P, Jain SK, Jain M. Harnessing Drug Repurposing for Exploration of New Diseases: An Insight to Strategies and Case Studies. Curr Mol Med. 2021;21(2):111-132. doi: 10.2174/1566524020666200619125404. PMID: 32560606.
2. Talevi A, Bellera CL. Challenges and opportunities with drug repurposing: finding strategies to find alternative uses of therapeutics. Expert Opin Drug Discov. 2020 Apr;15(4):397-401. doi: 10.1080/17460441.2020.1704729. Epub 2019 Dec 17. PMID: 31847616.
3. Sharlow ER. Revisiting Repurposing. Assay Drug Dev Technol. 2016 Dec;14(10):554-556. doi: 10.1089/adt.2016.766. PMID: 27982703.
4. Bellera CL, Alberca LN, Sbaraglini ML, Talevi A. In Silico Drug Repositioning for Chagas Disease. Curr Med Chem. 2020;27(5):662-675. doi: 10.2174/0929867326666191016114839. PMID: 31622200.
5. Czech T, Lalani R, Oyewumi MO. Delivery Systems as Vital Tools in Drug Repurposing. AAPS PharmSciTech. 2019 Feb 15;20(3):116. doi: 10.1208/s12249-019-1333-z. PMID: 30771030.
6. Deplanque D, Fetro C, Ferry A, Lechat P, Beghyn T, Bernard C, Bernasconi A, Bienayme H, Cougoule C, Del Bano J, Demiot C, Lebrun-Vignes B. Drug repurposing: From the discovery of a useful pharmacological effect to making the treatment available to the patient. Therapie. 2023 Jan-Feb;78(1):10-18. doi: 10.1016/j.therap.2022.11.009. Epub 2022 Dec 5. PMID: 36528417.
7. Taweel B, Marson AG, Mirza N. A systems medicine strategy to predict the efficacy of drugs for monogenic epilepsies. Epilepsia. 2022 Dec;63(12):3125-3133. doi: 10.1111/epi.17429. Epub 2022 Oct 25. PMID: 36196775; PMCID: PMC10092251.
8. Anwar A, Khan NA, Siddiqui R. Repurposing of Drugs Is a Viable Approach to Develop Therapeutic Strategies against Central Nervous System Related Pathogenic Amoebae. ACS Chem Neurosci. 2020 Aug 19;11(16):2378-2384. doi: 10.1021/acschemneuro.9b00613. Epub 2020 Mar 2. PMID: 32073257.
9. Klug DM, Gelb MH, Pollastri MP. Repurposing strategies for tropical disease drug discovery. Bioorg Med Chem Lett. 2016 Jun 1;26(11):2569-76. doi: 10.1016/j.bmcl.2016.03.103. Epub 2016 Mar 30. PMID: 27080183; PMCID: PMC4853260.
10. Peerzada MN, Gaur A, Azam A. Advances in Drug Discovery against Neglected Tropical Diseases: Human African and American Trypanosomiasis. Curr Med Chem. 2021;28(36):7544-7582. doi: 10.2174/0929867328666210504111442. PMID: 33949927.
11. Sbaraglini ML, Vanrell MC, Bellera CL, Benaim G, Carrillo C, Talevi A, Romano PS. Neglected Tropical Protozoan Diseases: Drug Repositioning as a Rational Option. Curr Top Med Chem. 2016;16(19):2201-22. doi: 10.2174/1568026616666160216154309. PMID: 26881713.
12. Andrade CH, Neves BJ, Melo-Filho CC, Rodrigues J, Silva DC, Braga RC, Cravo PVL. In Silico Chemogenomics Drug Repositioning Strategies for Neglected Tropical Diseases. Curr Med Chem. 2019;26(23):4355-4379. doi: 10.2174/0929867325666180309114824. PMID: 29521204.
13. Borba JVVB, Silva AC, Lima MNN, Mendonca SS, Furnham N, Costa FTM, Andrade CH. Chemogenomics and bioinformatics approaches for prioritizing kinases as drug targets for neglected tropical diseases. Adv Protein Chem Struct Biol. 2021;124:187-223. doi: 10.1016/bs.apcsb.2020.10.006. Epub 2020 Dec 13. PMID: 33632465.
14. Volpedo G, Costa L, Ryan N, Halsey G, Satoskar A, Oghumu S. Nanoparticulate drug delivery systems for the treatment of neglected tropical protozoan diseases. J Venom Anim Toxins Incl Trop Dis. 2019 Feb 11;25:e144118. doi: 10.1590/1678-9199-JVATITD-1441-18. PMID: 31130996; PMCID: PMC6483407.
15. Berenstein AJ, Magariños MP, Chernomoretz A, Agüero F. A Multilayer Network Approach for Guiding Drug Repositioning in Neglected Diseases.

DOI: 10.69605/ijlbpr_14.3.2025.259

PLoS Negl Trop Dis. 2016 Jan 6;10(1):e0004300. doi: 10.1371/journal.pntd.0004300. PMID: 26735851; PMCID: PMC4703370.

16. Li J, Wang W, Yao J, Wang T, Li S, Qi W, Han S, Ren Y, Dang Z, Han X, Guo G, Guo B, Wang L, Duan L, Zhang W. Old drug repurposing for neglected disease: Pyronaridine as a promising candidate for the treatment of Echinococcus granulosus infections. EBioMedicine. 2020 Apr;54:102711. doi: 10.1016/j.ebiom.2020.102711. Epub 2020 Apr 9. PMID: 32279056; PMCID: PMC7152711.
17. Pollastri MP, Campbell RK. Target repurposing for neglected diseases. Future Med Chem. 2011 Aug;3(10):1307-15. doi: 10.4155/fmc.11.92. PMID: 21859304; PMCID: PMC3160716.
18. Rice CA, Colon BL, Chen E, Hull MV, Kyle DE. Discovery of repurposing drug candidates for the treatment of diseases caused by pathogenic free-living amoebae. PLoS Negl Trop Dis. 2020 Sep 24;14(9):e0008353. doi: 10.1371/journal.pntd.0008353. PMID: 32970675; PMCID: PMC7546510.
19. Charlton RL, Rossi-Bergmann B, Denny PW, Steel PG. Repurposing as a strategy for the discovery of new anti-leishmanials: the-state-of-the-art. Parasitology. 2018 Feb;145(2):219-236. doi: 10.1017/S0031182017000993. Epub 2017 Aug 14. PMID: 28805165; PMCID: PMC5964475.
20. Assmus F, Driouich JS, Abdelnabi R, Vangeel L, Touret F, Adehin A, Chotsiri P, Cochin M, Foo CS, Jochmans D, Kim S, Luciani L, Moureau G, Park S, Pétit PR, Shum D, Wattanakul T, Weynand B, Fraisse L, Ioset JR, Mowbray CE, Owen A, Hoglund RM, Tarning J, Lamballerie X, Nougairède A, Neyts J, Sjö P, Escudié F, Scandale I, Chatelain E. Need for a Standardized Translational Drug Development Platform: Lessons Learned from the Repurposing of Drugs for COVID-19. Microorganisms. 2022 Aug 12;10(8):1639. doi: 10.3390/microorganisms10081639. PMID: 36014057; PMCID: PMC9460261.