Drug Repurposing in Transition: From Promising Starts to Clinical Realities

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Abstract

Drug repurposing, the process of finding new therapeutic uses for medications that are currently on the market or have been discontinued, has emerged as a significant approach for successfully addressing unmet medical needs. There are many benefits to this method over traditional drug discover0y, including reduced expenses, quicker turnaround times, and improved safety profiles, because many candidates have previously passed preclinical or clinical examination. Drug repurposing has evolved from unintentional discoveries to methodical, data-driven approaches as a result of increased access to genomic data, computational tools, and empirical evidence. An intellectual property barrier, unclear efficacy in new applications, and regulatory challenges are several problems with its widespread use. This review attempts to cover a thorough summary of the state of drug repurposing today, supported by a few case studies showing successful transitions, unsuccessful/incomplete results, and ongoing research initiatives. It also looks at the crucial roles that financial sources, industry-academic cooperation, and regulatory assistance play in facilitating these shifts. Drug repurposing must be incorporated into conventional drug development pipelines as the area grows, which requires a balanced awareness of its possible advantages and disadvantages. This review aims to provide insights on potential avenues for future research and regulatory frameworks that will improve the efficacy of drug repurposing efforts in the global healthcare industry.

Keywords: *Drug repurposing, drug repositioning, Academic-industry collaboration, Real-world evidence*

Introduction

Drug repurposing, also known as drug repositioning, reprofiling, retasking, rediscovery, rescue, recycling, redirection, or therapeutic switching, is a strategy for identifying new therapeutic uses for existing, approved, investigational, failed, abandoned, or shelved drugs or compounds [1]. This approach aims to take a drug that has already undergone extensive safety and efficacy testing and redirect it for an additional or unrelated medical indication.[2] The term "drug repurposing" is used consistently to refer to all these terminologies [1]. This strategy offers significant advantages over developing an entirely new drug, making it an attractive prospect for drug developers and patients alike [1].

Significance in Healthcare

Drug repurposing is being actively pursued as a cost- and time-efficient drug discovery and development strategy [1]. It represents a significant opportunity to find treatments, particularly in areas of unmet medical needs, such as rare diseases, where a vast majority (95%) of the 7,000 to 8,000 known rare diseases currently lack an approved treatment [5]. This approach allows for quicker access to useful and novel treatments for patients, in contrast to the high investment and prolonged timelines of traditional drug discovery.

Advantages

The core advantages of drug repurposing over traditional *de novo* drug discovery are numerous:

1. **Reduced Development Risks**: Candidate drugs often already possess a proven safety and tolerability profile from previous preclinical and clinical trials (Phase I or II)) [4]. This significantly mitigates the high failure rate (approximately 45%) associated with safety or toxicity issues in traditional drug discovery. Repurposed drugs are considered "de-risked" compounds [5].
2. **Lower Costs**: Since significant preclinical testing, safety assessments, and sometimes formulation development have already been completed, drug repurposing can lead to lower investment costs compared to developing new chemical entities (NCEs) [3].
3. **Shorter Timelines**: The availability of prior data means repurposed drugs can enter preclinical evaluation and clinical trials faster, potentially reducing the average drug development time by approximately 5–7 years [6]. This also enables rapid response in public health emergencies, as seen with some COVID-19 treatments like remdesivir [7].
4. **Higher Success Rates**: Repurposed drugs are theoretically less prone to late-stage failures than *de novo* compounds, with estimated approval rates closer to 30%, compared to about 10% for new drugs.

Challenges

Despite its advantages, drug repurposing faces several hurdles:

1. **Efficacy Uncertainty**: The foremost developmental risk is unidentified efficacy for a new indication [3]. While safety data may exist, efficacy in a new context must be proven through rigorous clinical trials [8]. Biomarkers providing evidence of drug-target engagement may increase confidence in a repurposed drug's effectiveness [9].
2. **Intellectual Property (IP) Issues**: This is a critical element when considering collaborations [1]. For drugs still under active IP, the patent owner (e.g., a pharmaceutical company) may have little interest in a new indication due to existing claims, a lack of expertise in the new therapeutic area, or insufficient remaining patent life. Academic researchers who publish findings for patented drugs may effectively provide their research free of charge to the IP holder [10]. For off-patent (generic) drugs, there is often little or no profit incentive for industry, even with marketing approval, as the drug is inexpensive and widely available. New

IP protection, such as "method of use patents" or patents for new formulations/dosages, is often needed to attract investment, but their enforceability can be challenging. Market exclusivity for repurposed drugs has been recognized as a major hurdle [11].

3. **Regulatory Complexity**: The lack of a standardized regulatory approach or marketing regulation can limit progression [3][9]. Regulatory procedures for market access can be complex, and expectations may differ between regulatory agencies (focused on benefits/harms) and payers (focused on effectiveness/economic consequences) [1]. The optimal dose or dosing schedule for the new use may differ, requiring additional Phase I and II clinical studies [9].
4. **Commercial Viability**: Potential returns lower than US $200–300 million sales per drug per year are often not attractive enough for large pharmaceutical companies to invest [9].
5. **Data Access and Integration**: While vast amounts of data exist (genomic, phenotypic, clinical, chemical structure) [11], they are often disparate and heterogeneous, making integration and interpretation difficult. [1]. Access to shelved industry compounds and their trial data can also be challenging due to confidentiality [5].

Strategies and Initiatives

The field of drug repurposing has evolved from serendipitous discoveries to more systematic and rational approaches [11].

1. **Computational Approaches**: These are largely data-driven and involve systematic analysis of various data types to formulate repurposing hypotheses [11]. Key methods include:
2. **Signature Matching**: Comparing the unique "signature" of a drug (e.g., from transcriptomic, proteomic, metabolomic data, or adverse event profiles) against that of another drug, disease, or clinical phenotype [11]. Resources like the Connectivity Map (CMap), Gene Expression Omnibus (GEO), and Array Express are extensively used [12].
3. **Text Mining and Semantic Inference**: Extracting potential drug indications from biomedical and pharmaceutical literature by analyzing relationships between drugs, diseases, targets, and side effects [6].
4. **Network-Based Methods**: Analyzing complex networks formed by interactions among biological entities (drugs, targets, diseases) to uncover functional relationships and predictive properties. These methods can integrate diverse data types and identify unintuitive connections [14].
5. **Use of Real-World Data (RWD)**: Leveraging data from electronic medical records (EMRs), registries, and post-marketing surveillance to identify and validate drug repurposing candidates [5].
6. **Artificial Intelligence (AI)**: AI makes data more accessible, helping to find drug interactions, side effects, mechanisms of action, and gene regulators by extensive literature data mining, which can accelerate the process of drug repurposing [4] [6].
7. **Collaborative Initiatives**: New business models involving multi-stakeholder partnerships are crucial for success [11]. Examples include:
8. **Public-Private Partnerships**: Initiatives like the MRC-AstraZeneca collaboration and the NIH-National Center for Advancing Translational Sciences (NCATS) "Discovering New Therapeutic Uses for Existing Molecules" program promote new utility for compounds, often with academic and industry involvement, with NCATS acting as a trusted intermediary [5].
9. **Regulatory Support**: The European Medicines Agency (EMA) and Heads of Medicines Agencies (HMA) launched a pilot project in October 2021 to support not-for-profit organizations, including academia, in generating sufficient evidence for the use of well-established off-patent drugs in new indications [3].
   The FDA also provides regulatory pathways like 505(b)(2) to assist repurposed drugs by allowing reliance on existing data [1].
10. ***Funding Programs***: Programs like Horizon Europe provide funding for research and innovation in drug repurposing, encouraging consortia involving industry, academia, SMEs, and patient associations [10].

Academic and Industrial Collaboration

Collaboration between academia and industry is essential for successful drug repurposing, despite their differing expectations and constraints [1].

1. **Academia's Role**: Academia is a crucial source of innovation, focusing on basic research, identification and validation of new targets, and proving hypotheses in early clinical settings [1]. They are less constrained by direct commercial success, relying on scientific breakthroughs, government funding, and partnerships [5] [8]. A significant number of repurposed Orphan Medicinal Products (OMPs) originate in academia, often driven by scientific progress and patient care [5].
2. **Industry's Role**: Pharmaceutical companies bring extensive expertise in clinical development, regulatory affairs, intellectual property, and commercial aspects [14]. They often pursue repurposing as part of life cycle management (LCM) to extend patent life or for strategic expansion into adjacent or entirely new therapeutic areas [5]. They also hold an advantage in accessing proprietary drug-related data for their compounds [9].
3. **Bridging the Gap**: While academics often operate under a "publish or perish" culture, industry typically maintains confidentiality, though publication can occur after patent filing [5]. Early engagement between academic discoverers and patent-holding companies is highly recommended to discuss development interest and access to the compound [1]. Mutual understanding of each other's drivers and language (e.g., academics understanding regulatory and reimbursement, industry understanding the key role of academic publications and networking) is needed to facilitate fruitful collaborations [10]. Trusted third parties or support structures can help manage complex aspects and intellectual property issues, and even become the Marketing Authorization holder for a repurposed drug if needed [14].

Case Studies in Drug Repurposing

1. **Colchicine [1] [15]**

Original Indication(s): Gout and pericarditis, where it acts as a potent anti-inflammatory medication administered orally
Repurposed Indication(s): Atherosclerosis and its complications, based on the role of inflammation in these conditions. It was also under clinical trial for treating COVID-19 patients due to its effectiveness in preventing massive cytokine storm-induced pneumonia caused by SARS-CoV-2
Discovery/Development: A randomized, double-blind trial (COLCOT) was conducted on patients within 30 days after a myocardial infarction, assigning them to low-dose colchicine (0.5 mg once daily) or placebo. The primary efficacy endpoint was a composite of cardiovascular death, resuscitated cardiac arrest, myocardial infarction, stroke, or urgent hospitalization for angina leading to coronary revascularization
Outcomes & Insights: In the COLCOT trial, the primary endpoint event rates per 100 patient-months were 0.29 in the colchicine group and 0.42 in the placebo group, showing a rate ratio of 0.66 (95% CI, 0.51 to 0.86). While there was a large (>65%) reduction in high-sensitivity C-reactive protein levels at 6 months in both groups, the difference between the groups was not significant. The trial noted a relatively short follow-up duration of approximately 23 months, meaning risks and benefits of longer-term treatment were not evaluated. The results apply only to patients who recently had a myocardial infarction

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2. **Remdesivir [15]**

Original Indication(s): Developed as a broad-spectrum antiviral, originally an investigational anti-retroviral drug developed by Gilead Sciences Inc. for the treatment of Ebola, but it failed in clinical trials for that indication
Repurposed Indication(s): COVID-19

Discovery/Development: Evaluated in the Adaptive Covid-19 Treatment Trial (ACTT-1), a phase 3, randomized, double-blind, placebo-controlled trial. Eligible patients were randomly assigned 1:1 to receive remdesivir or placebo intravenously for 10 days.
Outcomes & Insights: Early reports from the ACTT-1 trial were intended to inform clinicians, with full statistical analysis pending the completion of follow-up for all 1063 enrolled patients
However, later evidence indicated that remdesivir showed no effect on hospitalized COVID-19 patients regarding overall mortality, ventilation initiation, or hospital stay duration. This highlights potential concerns with accelerated approvals of repurposed agents during emergencies. Pharmacokinetic issues, such as limited lung exposure, have been identified for remdesivir, leading to proposals for inhaled formulations to overcome this.

3. **IMR-687 (a PDE9 inhibitor) [13]**

Original Indication(s): Originated from Lundbeck's research and development program for neurodegenerative diseases
Repurposed Indication(s): Sickle cell disease
Discovery/Development: Academic research strongly suggested the potential utility of a PDE9 inhibitor for sickle cell disease. Since sickle cell disease was not a focus area for Lundbeck, they licensed their PDE9 inhibitors to Cydan, which then created Imara (Boston, MA, USA) with investors to develop IMR-687.

4. **Sildenafil (Viagra) [3][10]**

Original Indication(s): Initially developed by Pfizer for hypertension and angina pectoris
Repurposed Indication(s): Erectile dysfunction (ED) and later pulmonary arterial hypertension (PAH)
Discovery/Development: The repurposing for ED stemmed from Pfizer scientists listening to physicians and patients who reported improvements in erectile function during the original trials. Pfizer redirected the clinical/regulatory program based on these observations. For PAH, sildenafil was found to be an effective pulmonary vasodilator by inhibiting PDE5 and raising intracellular cGMP, which relaxes vascular smooth muscles.
Outcomes & Insights: Sildenafil is often cited as a successful example of drug rescue through an adaptive development strategy. Its efficacy in ED and PAH is well-established.

5. **Alpelisib (BYL719) [1] [11]**

Original Indication(s): Developed for the treatment of PIK3CA-altered tumors
Repurposed Indication(s): PIK3CA-related overgrowth syndromes (PROS)
Discovery/Development: Researchers found that patients with PROS have somatic, mosaic gain-of-function mutations in the PIK3CA gene.
Initial studies in preclinical models and then in two patients with severe PROS led Canaud's group to administer BYL719 to 17 additional PROS patients, with published results supporting PIK3CA inhibition as a promising therapeutic strategy
Outcomes & Insights: Four years later, in 2022, the FDA granted accelerated approval to alpelisib (Vijoice®) for severe PROS in patients aged 2 years or older. This approval was based on real-world response rate and duration of response findings from the single-arm EPIK-P1 study, a retrospective chart review. Continued approval is contingent upon additional placebo-controlled studies

6. **Metformin [1] [16]**

Original Indication(s): Treatment of type 2 diabetes
Repurposed Indication(s): Potential applications in cancer prevention and treatment, including colon, prostate, breast, and lung cancer, and in tuberculosis

Discovery/Development: Retrospective studies suggested that diabetics treated with metformin had a substantially reduced cancer burden. Laboratory models also provided independent evidence for metformin's activity in cancer treatment and chemoprevention. For tuberculosis, metformin enhances phagosome-lysosome fusion and increases ROS, preventing bacterial colonization and enhancing immune response
Outcomes & Insights: While population studies are retrospective and confined to diabetics, they show promise. A retrospective study indicated a significantly higher rate of pathologic complete response to neoadjuvant chemotherapy in diabetic breast-cancer patients taking metformin. The mechanism of action is complex, involving both systemic (insulin-lowering) and direct effects. The optimal compound and dosing regimen for oncology indications need to be established, as regimens optimized for diabetes may not be suitable for cancer

7. **Thalidomide [6]**

Original Indication(s): Initially developed as a sedative and for morning sickness but was withdrawn due to severe teratogenic side effects
Repurposed Indication(s): Erythema nodosum leprosum (a complication of leprosy) and multiple myeloma
Discovery/Development: Academic researchers demonstrated thalidomide's anti-inflammatory activity as a tumor necrosis factor inhibitor. Its anti-angiogenic, anti-inflammatory, and anti-myeloma activities were later identified [17]. Celgene Pharmaceutical Company licensed relevant patents and drove its development for multiple myeloma.
Outcomes & Insights: Approved for leprosy in 1998 and multiple myeloma in 2006, thalidomide's repurposing led to the implementation of a comprehensive surveillance policy (REMS program) to mitigate safety concerns. This success identified a new drug class and highlighted the importance of academic-industry collaborations

8. **Moxidectin [10]**

Original Indication(s): A veterinary anti-helminthic drug discovered in the 1980s
Repurposed Indication(s): River blindness (Onchocerca) and an extension of use for five other neglected tropical diseases
Discovery/Development: Clinical development was driven by Tropical Diseases Research at the WHO and Medicines Development for Global Health, with funding from the Global Health Investment Fund. They leveraged the FDA's Priority Review Voucher
Outcomes & Insights: Its success demonstrates the value of collaboration between academic groups and philanthropies, working with regulatory authorities to bring new therapies for neglected diseases. However, repurposing veterinary medicines is not always straightforward; a standard clinical development program, including first-in-human trials, might still be required.

9. **Dimethyl Fumarate (Tecfidera) [10]**

Original Indication(s): Used as a fungicide and later as a topical treatment for psoriasis in Germany
Repurposed Indication(s): Relapsing–remitting multiple sclerosis (MS)
Discovery/Development: Academic researchers demonstrated its benefit in preclinical MS models based on its immunosuppressive action. Clinical studies (e.g., DEFINE study, Determination of the Efficacy and Safety of Oral Fumarate in Relapsing–Remitting MS)) then showed efficacy in MS patients
Outcomes & Insights: Approved by the FDA in 2013 and EMA in 2014 for MS. The DEFINE study showed that BG-12 (dimethyl fumarate) significantly reduced the proportion of patients who had a relapse, the annualized rate of relapse, and the cumulative progression of disability compared to placebo

10. **Propranolol [19]**

Original Indication(s): Not explicitly stated, but it's noted as an example where retrospective clinical analysis led to repurposing. It was also used in a randomized, controlled trial for infantile hemangioma

Repurposed Indication(s): Post-traumatic stress disorder (PTSD) and potentially in osteoporosis.
Discovery/Development: For PTSD, a study investigated propranolol's effect after memory retrieval of a traumatic event. For infantile hemangioma, academic researchers demonstrated its efficacy in randomized clinical studies.
Outcomes & Insights: For PTSD, subjects receiving post-retrieval propranolol showed significantly smaller physiologic responses during subsequent mental imagery of traumatic events compared to placebo, with the drug accounting for 49% of the variance in overall physiologic responding.

11. **Dichloroacetate (DCA) [19]**

Original Indication(s): Not specified in the provided sources, but it is an "old drug"
Repurposed Indication(s): Multiple myeloma patients with stable disease but known future progression
Discovery/Development: A pilot phase 2 clinical trial investigated DCA. It demonstrated the ability to conduct clinical studies with an old drug for a new indication without extensive preclinical workup, using existing human pharmacokinetic data and standard pharmacological principles to deduce the starting dose
Outcomes & Insights: The study showed that GSTZ1 genotypes correlated with DCA pharmacokinetics and chronic side effects like peripheral neuropathy, suggesting the importance of individualizing dosing regimens. It also highlighted the direct applicability of such studies to clinical practice

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12. **Terbutaline sulfate [11], [18]**

Original Indication(s): Anti-asthmatic
Repurposed Indication(s): Potential candidate for the treatment of amyotrophic lateral sclerosis (ALS)
Discovery/Development: Identified using a combination of genomics data and electronic medical record (EMR)-extracted lab test data, based on the assumption that similar drugs can treat similar diseases
Outcomes & Insights: The potential therapeutic benefit was demonstrated and validated via prevention of defects in axons and neuromuscular junction degeneration in a zebrafish model of ALS. However, as of the source date, no clinical trial has demonstrated a similar benefit in humans

13. **Denosumab [20]**

Original Indication(s): Not specified, but a Crohn’s disease-associated gene variant (TNFSF11) was linked to its expression
Repurposed Indication(s): Potential role in Crohn’s disease
Discovery/Development: Speculated based on a potential link between the TNFSF11 variant and Crohn's disease, and its impact on TNFSF11 expression in relevant cell types. A preclinical study exploring daily denosumab injection in a mouse model of colitis further supported this potential
Outcomes & Insights: As of July 2019, an open-label phase I/II trial of denosumab in patients with active Crohn’s disease was due for completion

14. **Clemastine and Quetiapine [5]**

Original Indication(s): Clemastine is antihistamine and Quetiapine is an antipsychotic
Repurposed Indication(s): Myelin repair in multiple sclerosis (MS)
Discovery/Development: Convergent results from several independent laboratories using phenotypical screens (including zebrafish models and stem cell-derived OPCs) identified muscarinic antagonists, including benztropine and clemastine, as compounds that promote myelin repair. Quetiapine was also confirmed in a primary rat OPC differentiation assay.
Outcomes & Insights: Both clemastine and quetiapine have rapidly advanced into clinical trials in MS to evaluate their efficacy in myelin repair. This highlights the potential of repurposing screens to rapidly advance hits into clinical development.

15. Ivermectin [11] [21]

Original Indication(s): FDA-approved for a number of parasitic infections
Repurposed Indication(s): Possible SARS-CoV-2 antiviral for COVID-19
Discovery/Development: Showed in vitro efficacy against SARS-CoV-2 at a concentration of 5 μM
Outcomes & Insights: Despite in vitro efficacy, pharmacokinetic issues (e.g., highly protein-bound, inadequate lung exposure) limit direct applicability, as maximum peak concentrations in humans are well below the required IC50 for SARS-CoV-2 even at high doses. Despite these challenges, there were 44 ongoing clinical trials for ivermectin in COVID-19 as of November 2020

16. Hydroxychloroquine [5]

Original Indication(s): An older antimalarial drug and used for rheumatoid arthritis
Repurposed Indication(s): Investigated for COVID-19
Discovery/Development: Studies suggested it might be beneficial in preventing coronavirus-induced pneumonia. Clinical trials, including a combination with azithromycin, were initiated
Outcomes & Insights: Concerns were raised about its use in COVID-19 due to potential cardiotoxicity at higher doses and limited lung penetration.

17. Lopinavir/Ritonavir [5]

Original Indication(s): A fixed-dose drug combination earlier approved for HIV
Repurposed Indication(s): Investigated for COVID-19
Outcomes & Insights: Although used in many COVID-19 trials, often based on low-quality studies early in the pandemic, its efficacy was limited

18. Favipiravir [4]

Original Indication(s): An antiviral drug intended for the treatment of influenza
Repurposed Indication(s): Under phase-2/phase-3 clinical trials for COVID-19
Outcomes & Insights: Clinical trials were initiated in several countries, including India
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19. Aspirin [4]

Original Indication(s): Anti-inflammatory drug, 500-mg tablets
Repurposed Indication(s): Daily-dose "baby aspirin" (75-mg or 81-mg tablets) for cardiovascular disease prevention and for colorectal cancer.
Discovery/Development: The US Preventive Services Task Force released draft recommendations in 2015 regarding aspirin use for cardiovascular disease and colorectal cancer prevention. A study on all-cause mortality of aspirin in the healthy elderly was supported by government grants.
Outcomes & Insights: While it might not result in a label change, publication of such studies provides evidence for physicians to balance risk and benefit.

20. Saracatinib [7]

Original Indication(s): Experimental anticancer drug
Repurposed Indication(s): Investigated for Alzheimer's disease, cancer-induced bone pain, lymphangioleiomyomatosis (LAM), and psychosis
Discovery/Development: Src kinase inhibitors (like saracatinib) are suggested to mediate psychosis induced by hallucinogens. Also identified as a potential therapeutic in LAM and for cancer-induced bone pain.

Outcomes & Insights: Phase II trials were ongoing for several of these indications, including Alzheimer's disease and psychosis

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21. Sirolimus [5] [11]

Original Indication(s): mTOR inhibitor
Repurposed Indication(s): Reversing dexamethasone resistance in acute lymphoblastic leukemia
Also showed efficacy in investigator-initiated clinical studies for vascular malformations.
Discovery/Development: Identified through transcriptomics, by showing it could reverse gene expression signatures associated with dexamethasone resistance. The in silico findings were confirmed in vitro and in xenograft models.
Outcomes & Insights: Clinical validation for overcoming glucocorticoid resistance is still pending

22. Topiramate [3]

Original Indication(s): Anticonvulsant for epilepsy
Repurposed Indication(s): Proposed as a potential therapy for inflammatory bowel disease (IBD)
Discovery/Development: Based on a unidimensional analysis of public microarray data and validated in mouse models.
Outcomes & Insights: This repurposing effort failed
A critical oversight was the failure to consider that diarrhea, a common side effect of topiramate, is also a common feature of IBD, which would have made it obvious that it was not a viable therapeutic. This highlights the importance of using all available data, including adverse event profiles

These case studies demonstrate the diverse origins of repurposing ideas, from serendipitous observations to systematic computational analyses, and the varied success rates and challenges across different therapeutic areas. They also highlight the crucial roles of academic-industry collaborations, regulatory processes, and comprehensive data analysis in bringing repurposed drugs to patients.

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Conclusion

Drug repurposing is an effective and increasingly vibrant approach to speed up drug development, especially in fields where there are pressing or unmet needs. Repurposing, however, has significant shortcomings in terms of intellectual property rights, commercial viability, and effectiveness validation, despite its obvious benefits like lower costs, time savings, and risk reduction. Diverse case studies demonstrate that success is not always assured, and outcomes can vary significantly between therapeutic domains. The field has advanced from unexpected discoveries to logical, computationally directed frameworks, signaling a move in the direction of more organized approaches. Greater collaboration between academia, industry, regulatory agencies, and funding organizations is necessary for repurposing to achieve its full potential.

References

1. *Fetro C. Connecting academia and industry for innovative drug repurposing in rare diseases: it is worth a try. Rare Dis Orphan Drugs J.; Vol. 2, no. 2, (2023), pp. 7.*
2. *Khan S, Agnihotri J, Patil S, Khan N. Drug repurposing: A futuristic approach in drug discovery. Journal of Pharmaceutical and Biological Sciences; Vol. 11, No. 2, (2023), pp. 66–69.*
3. *NAGABUKURO H, UEMURA N. Drug reprofiling and repurposing: a state-of-the-art public-private collaboration model. Translational and Regulatory Sciences; Vol. 2, No. 2, (2020), pp. 47–50.*
4. *Rudrapal M, Khairnar SJ, Jadhav AG. Drug Repurposing (DR): An Emerging Approach in Drug Discovery. www.intechopen.com. IntechOpen; 2020.*
5. *Cha Y, Erez T, Reynolds IJ, Kumar D, Ross J, Koytiger G, et al. Drug repurposing from the perspective of pharmaceutical companies. British J Pharmacology; Vol. 175, No. 2, (2018), pp.168-180.*
6. *Makhijani s. Revitalizing therapeutics: drug repurposing as a cost-effective strategy for drug development. Int J App Pharm; Vol. (2024), pp. 56-61.*
7. *Gatti M, De Ponti F. Drug Repurposing in the COVID-19 Era: Insights from Case Studies Showing Pharmaceutical Peculiarities. Pharmaceutics; Vol. 13, No. 3, (2021), pp. 302.*
8. *Oprea TI, Mestres J. Drug Repurposing: Far Beyond New Targets for Old Drugs. AAPS J; Vol. 14, No. 4, (2012), pp.759-763.*
9. *Drug Repurposing: Considerations to Surpass While Re-directing Old Compounds for New Treatments. Archives of Medical Research; Vol. 52, No. 3, (2021), pp.243–251.*
10. *Begley CG, Ashton M, Baell J, Bettess M, Brown MP, Carter B, et al. Drug repurposing: Misconceptions, challenges, and opportunities for academic researchers. Science Translational Medicine; Vol. 13, (2021), pp. 612.*
11. *Pushpakom S, Iorio F, Eyers PA, Escott KJ, Hopper S, Wells A, et al. Drug repurposing: progress, challenges and recommendations. Nature Reviews Drug Discovery; Vol. 18, No. 1, (2018), pp. 41–58.*
12. *Li J, Zheng S, Chen B, Butte AJ, Swamidass SJ, Lu Z. A survey of current trends in computational drug repositioning. Briefings in Bioinformatics; Vol. 17, No. 1, (2015), pp. 2–12.*
13. *Badkas A, De Landtsheer S, Sauter T. Topological network measures for drug repositioning. Briefings in Bioinformatics; Vol. 22, No. 4, (2020).*
14. *Van den Berg S, de Visser S, Leufkens HG, Hollak CE. Drug Repurposing for Rare Diseases: A Role for Academia. Front Pharmacol; (2021).*
15. *Tardif J, Kouz S, Waters DD, Bertrand OF, Diaz R, Maggioni AP, et al. Efficacy and Safety of Low-Dose Colchicine after Myocardial Infarction. N Engl J Med; Vol. 381, No. 26, (2019), pp. 2497-2505.*
16. *Pollak M. Metformin and Other Biguanides in Oncology: Advancing the Research Agenda. Cancer Prevention Research; Vol. 3, No. 9, (2010), pp.1060–1065.*
17. *Park K. A review of computational drug repurposing. Translational and Clinical Pharmacology; Vol. 27, No. 2, (2019), pp. 59.*
18. *Gold R, Kappos L, Arnold DL, Bar-Or A, Giovannoni G, Selmaj K, et al. Placebo-Controlled Phase 3 Study of Oral BG-12 for Relapsing Multiple Sclerosis. N Engl J Med; Vol. 367, No. 12, (2012), pp. 1098-1107.*
19. *Brunet A, Orr SP, Tremblay J, Robertson K, Nader K, Pitman RK. Effect of post-retrieval propranolol on psychophysiologic responding during subsequent script-driven traumatic imagery in post-traumatic stress disorder. Journal of Psychiatric Research; Vol. 42, No. 6, (2008), pp.503–506.*
20. *Martin JH, Bowden NA. DRUG REPURPOSING—Overcoming the translational hurdles to clinical use. Pharmacology Res & Perspec; Vol. 7, No. 6, (2019).*
21. *Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved Drug Ivermectin inhibits the replication of SARS-CoV-2 in vitro. Antiviral Research; Vol. 178, (2020), pp. 104787.*