Repurposing Old Drugs for New Indications: A Cost-Effective Strategy in Modern Pharmacotherapy

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Abstract

Drug repurposing, also known as drug repositioning, involves the identification of new therapeutic uses for existing medications. This strategy offers a cost-effective and time-efficient alternative to de novo drug discovery, particularly significant in an era where pharmaceutical R&D faces increasing costs and longer development timelines. This review discusses the rationale, methodologies, examples, advantages, challenges, and future prospects of drug repurposing. Notable repurposed drugs such as thalidomide, sildenafil, and metformin are explored. We also highlight computational approaches, real-world data applications, and regulatory considerations, establishing drug repurposing as a vital component of modern pharmacotherapy.

Keywords – Drug repurposing, therapeutic, computational, pharmaceutical

1. Introduction

The process of developing a new drug from scratch typically takes over a decade and costs billions of dollars. In contrast, drug repurposing leverages existing pharmacokinetic and safety data, significantly reducing development time and risk. The concept has gained traction due to its potential to quickly address unmet medical needs and emerging health threats, such as COVID-19.

2. Rationale for Drug Repurposing

Repurposing capitalizes on:
- Existing knowledge of safety profiles
- Previous clinical trials
- Lower financial and time investments
- Faster regulatory approval pathways

This strategy is especially useful for rare or neglected diseases that lack commercial incentives for traditional drug development.

3. Methodologies in Drug Repurposing

- Experimental Approaches: High-throughput screening, binding assays, phenotypic screening.
- Computational Approaches: In silico modeling, molecular docking, bioinformatics databases (DrugBank, PubChem), and artificial intelligence.
- Real-world Data: Electronic health records, insurance databases, and observational studies.

4. Notable Examples of Drug Repurposing

Thalidomide: Initially used as a sedative; repurposed for multiple myeloma and leprosy.
Sildenafil: Developed for angina; repurposed for erectile dysfunction and pulmonary hypertension.
Metformin: Antidiabetic drug being investigated for anti-aging and cancer therapy.

Table 1: Selected Examples of Repurposed Drugs and Their New Indications

Drug	Original Indication	Repurposed Use
Thalidomide	Sedative	Multiple Myeloma, Leprosy
Sildenafil	Angina	Erectile Dysfunction, PH
Metformin	Type 2 Diabetes	Cancer, Anti-aging
Minoxidil	Hypertension	Hair Loss
Aspirin	Pain, Inflammation	Cardiovascular Disease, Cancer

Regulatory and Economic Considerations Regulatory agencies like the FDA and EMA have specific pathways (e.g., 505(b)(2)) to support repurposing. Economically, repurposed drugs offer reduced R&D costs, lower pricing strategies, and faster return on investment. However, challenges like intellectual property rights and commercial exclusivity remain.

Advantages of Drug Repurposing

1. **Cost-Effectiveness:**
   Repurposing bypasses the expensive and lengthy early phases of drug discovery, such as target identification and compound optimization. Since many older drugs have already passed toxicological and pharmacokinetic evaluations, the cost burden is significantly reduced.
2. **Time-Saving:**
   Traditional drug development can take 10–15 years. In contrast, repurposing can cut this time in half or more, especially when the drug has an established safety profile and known mechanisms of action.

3. **Established Safety Profile:**
   Old drugs often have a well-documented safety, tolerability, and pharmacokinetic profile, minimizing the risk of adverse effects in new clinical settings.
4. **Regulatory Advantage:**
   Many repurposed drugs can qualify for accelerated or conditional approval under existing regulatory frameworks, particularly for rare or life-threatening conditions.

Challenges and Limitations

- Limited commercial incentives
- Off-label use risks
- Inadequate funding for non-patentable indications
- Regulatory and ethical concerns

Computational Tools and AI in Drug Repurposing AI and machine learning are revolutionizing drug discovery by:

- Predicting drug-disease interactions
- Mining biomedical literature
- Simulating molecular interactions

Case Study: COVID-19 and Drug Repurposing The COVID-19 pandemic underscored the importance of drug repurposing:

- **Remdesivir:** Initially developed for Ebola
- **Hydroxychloroquine:** Used in autoimmune diseases
- **Dexamethasone:** Steroid found effective for severe COVID-19

Table 2: Repurposed Drugs Investigated for COVID-19

Drug	Original Indication	COVID-19 Role
Remdesivir	Ebola	Antiviral against SARS-CoV-2
Dexamethasone	Inflammation, Asthma	Reducing severe inflammation
Hydroxychloroquine	Malaria, Lupus	Antiviral (controversial efficacy)

Future Prospects and Directions Drug repurposing is likely to grow, supported by:

- Advances in computational biology
- Global collaborative databases
- Incentive-based government policies
- Integration with personalized medicine

Recent Advances in Drug Repurposing

1. Artificial Intelligence and Machine Learning

The integration of AI and machine learning (ML) has revolutionized drug repurposing. These technologies analyze vast datasets—such as genomic profiles, chemical structures, clinical trial data, and electronic health records—to identify hidden drug-disease relationships. ML algorithms can predict off-target effects and new indications by learning from patterns in biological pathways and drug responses.

Example: Deep learning-based models have been used to repurpose drugs for COVID-19 and Alzheimer's disease, accelerating hypothesis generation and prioritization for clinical testing.

2. Network Pharmacology and Systems Biology

Network pharmacology maps interactions between drugs, genes, proteins, and diseases in a systems-level approach. This enables the identification of multitarget drugs and potential repurposing candidates for complex, multifactorial diseases like cancer, neurodegenerative disorders, and autoimmune conditions.

Example: Drugs targeting interconnected nodes in protein-protein interaction networks have been suggested for repurposing in rare diseases and metastatic cancers.

3. High-Throughput and Phenotypic Screening

Advancements in automated high-throughput screening technologies allow rapid testing of thousands of compounds on disease-relevant cell lines and models. These platforms often identify unexpected therapeutic effects of old drugs that may have been overlooked.

Example: Phenotypic screening helped identify the antimalarial drug amodiaquine as a potential treatment for Ebola virus in preclinical studies.

4. CRISPR and Functional Genomics

Gene-editing tools like CRISPR-Cas9 are being used to understand gene-drug interactions in different disease contexts. Functional genomics helps pinpoint new targets that old drugs can act upon, enabling precise repurposing based on genetic profiles.

Example: CRISPR-based screening revealed that certain antibiotics could be repurposed to target DNA repair-deficient cancers.

5. Drug Repurposing Databases and Platforms

Numerous curated databases and open-access platforms have been developed to facilitate drug repurposing:

- **DrugBank**: Contains data on drug interactions, targets, and mechanisms.
- **RepurposeDB**: A repository of repurposed drugs and their new indications.
- **CMap (Connectivity Map)**: Matches drug-induced gene expression profiles with disease signatures.

These tools enable researchers to quickly filter and select candidate drugs for repurposing based on molecular similarity, shared pathways, or therapeutic outcomes.

6. Regulatory Innovations and Fast-Track Approvals

Regulatory agencies like the U.S. FDA and EMA have begun to support fast-track and adaptive approval pathways specifically tailored for repurposed drugs, especially in response to public health emergencies. These frameworks lower the regulatory burden and incentivize research in neglected areas.

Example: Several old antivirals were granted emergency use authorization (EUA) for COVID-19 based on repurposing data.

7. Public-Private Partnerships and Global Collaborations

Collaborative efforts between academic institutions, pharmaceutical companies, and governments are playing a major role in promoting drug repurposing. Initiatives like the NIH's NCATS (National Center for Advancing Translational Sciences) and the UK's MRC (Medical Research Council) offer funding and support for drug repurposing research.

Conclusion Drug repurposing presents a pragmatic and economically viable strategy for expanding therapeutic options. With the growing burden of chronic and emerging diseases, it offers a vital complement to traditional drug discovery, providing hope for faster, safer, and more affordable treatments.

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