Chapter 4

Drug Repurposing: A Modern Approach to Drug Discovery

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Abstract

Drug repurposing, also known as drug repositioning, involves identifying new therapeutic uses for existing drugs. This approach offers a faster, safer, and more cost-effective alternative to traditional drug discovery, which is often time-consuming and expensive. Since repurposed drugs have already been tested for safety and pharmacokinetics, they can be rapidly advanced into clinical trials. Several well-known drugs, such as aspirin, sildenafil, and thalidomide, have successfully been repurposed for new indications. Repurposing can be done using experimental methods or computer-based technologies, including artificial intelligence and large drug databases. The COVID-19 pandemic highlighted the importance of drug repurposing in emergencies, with drugs like Remdesivir and Dexamethasone playing crucial roles. Despite its advantages, challenges such as limited profitability, and the need for further testing remain. With growing access to biomedical data and advanced computational tools, drug repurposing is poised to become a key strategy in modern medicine.

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1. Introduction

Drug repurposing, or repositioning, is the process of finding new therapeutic uses for existing drugs. Unlike traditional drug discovery, which is time-consuming and costly, repurposing offers a faster and more economical approach since safety and pharmacological data are already available. Successful examples such as aspirin, sildenafil, and thalidomide demonstrate its potential, while the COVID-19 pandemic further highlighted its value with drugs like Remdesivir and Dexamethasone. With advances in computational tools and artificial intelligence, drug repurposing is emerging as a vital strategy to meet unmet medical needs in modern healthcare.

2. Importance of Drug Repurposing

The conventional pathway for drug development takes 10–15 years and requires billions of dollars in investment. Despite this, many drug candidates fail during clinical trials due to safety or efficacy concerns. Repurposing offers a practical solution by using compounds with established safety records, thereby reducing risk and time to market. Examples of drug repurposing has been given in Table 1.

Table 1: An example of successful Drug Repurposing

Drug	Existing use	Use after Repurposing
Aspirin	Pain and fever relief	Prevention of blood clots/MI
Sildenafil	Hypertension /Angina	Erectile dysfunction

3. Methodologies in Drug Repurposing

- Experimental Approaches: Laboratory-based studies, including in vitro and in vivo testing, to assess drug activity against new disease targets.
- Computational Approaches: Use of AI, molecular docking, network pharmacology, and big data analytics to predict novel drug-disease associations. These tools help in screening vast databases such as Drug Bank, PubChem, and Repurpose DB.

4. Types of Drug Repurposing

a) On-target repurposing: It refers to a type of drug repurposing where the existing drug targets the same biological pathway or molecular target in the new indication as it did in the original indication. The drug's mechanism of action remains the same, but it is used to treat a different disease or condition.

b) Off-target repurposing: It refers to a type of drug repurposing where the existing drug is found to have therapeutic effects for a new indication through a different biological pathway or molecular target than its original mechanism of action. In this case, the drug's new therapeutic effect is attributed to interactions with unintended targets or pathways.

5. Benefits of Drug Repurposing

Drug repurposing, also known as drug repositioning, offers significant advantages in modern pharmaceutical research and development. Unlike the traditional drug discovery process, which is time-consuming, costly, and carries a high risk of failure, drug repurposing makes use of existing drugs with known safety profiles

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to identify new therapeutic indications. This approach reduces the overall cost of development, as preclinical safety studies and Phase I clinical trials are often minimized or bypassed, thereby saving years of research and millions of dollars.

Another key benefit is the reduction of risk. Since repurposed drugs already have well-established pharmacokinetics, pharmacodynamics, and toxicity data, the uncertainty associated with their development is considerably lower compared to novel drug candidates. This accelerates the timeline from laboratory research to clinical application, making effective treatments available to patients much faster.

6. Challenges in Drug Repurposing

6.1 Patent and Intellectual Property Issues

One of the major challenges is securing intellectual property rights for repurposed drugs. Since many candidate drugs are already off-patent, companies face difficulties in obtaining exclusivity. This reduces commercial incentives for large-scale investment. As a result, research may remain limited despite strong therapeutic potential.

6.2 Regulatory and Approval Barriers

Even though the safety of an approved drug is established, new indications require regulatory approval. Authorities often demand additional preclinical and clinical evidence to ensure safety and efficacy in the new disease area. This can prolong timelines and increase costs. Thus, the expected advantage of faster market entry may be reduced.

6.3 Limited Knowledge of Drug Mechanisms

Many existing drugs have complex or poorly understood mechanisms of action. This makes it difficult to identify suitable new therapeutic targets. Without clear mechanistic insights, the chances of failure in repurposing increase. Consequently, this uncertainty slows down research progress.

7. Drug Repurposing During COVID-19

The outbreak of COVID-19 posed an urgent global health emergency, where rapid identification of effective treatments was essential. Developing a new drug or vaccine typically takes years, but the pandemic demanded immediate therapeutic solutions. In this context, drug repurposing became a highly valuable strategy, as it allowed researchers to investigate already approved or clinically tested drugs for new use against SARS-CoV-

In severe cases, the disease triggered a inflammatory state known as a “cytokine storm.” To address this, immunomodulators and anti-inflammatory drugs like dexamethasone, tocilizumab, and baricitinib were repurposed to reduce immune activation and improve survival rates. Similarly, anticoagulants were used to manage COVID-associated blood clotting disorders.

This global effort highlighted both the strengths and challenges of repurposing. On one hand, it significantly reduced development timelines by bypassing early safety studies. On the other, it revealed limitations, as not all drugs demonstrated consistent clinical efficacy despite promising laboratory results.

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8. Repurposing Natural Products or Herbal Drugs:

Repurposing refers to identifying new pharmacological actions or therapeutic indications of already known herbal drugs or natural compounds. Many herbs have multiple bioactive constituents that act on different molecular targets, making them promising candidates for drug repurposing. Unlike synthetic drugs, natural products often possess a broad spectrum of biological activities such as anti-inflammatory, antioxidant, antimicrobial, anticancer, and immunomodulatory properties.

1. Curcumin (from turmeric): traditionally used for inflammation, now explored for anticancer and neuroprotective roles.

2. Resveratrol (from grapes): initially valued for cardioprotective effects, later studied for anti-aging and anticancer applications.

3. Artemisinin (from Artemisia annua): known as an antimalarial, now investigated for anticancer and antiviral properties.

9. Role of Technology in Drug Repurposing

Technology plays a crucial role in accelerating and refining the process of drug repurposing. With advancements in computational biology, bioinformatics, and artificial intelligence, researchers can rapidly identify new therapeutic uses for existing drugs. Drug repurposing mainly relies on three key methods: computational, experimental, and data-driven approaches. The computational (in-silico) method uses molecular docking, bioinformatics, and virtual screening to predict how existing drugs may interact with new biological targets, making the process faster and more cost-effective. The experimental or phenotypic screening method involves testing drugs directly on cell cultures or animal models to observe unexpected therapeutic benefits, providing strong biological evidence but often being time-consuming and costly

10. Case Studies of Failed Drug Repurposing Attempts:

1. Hydroxychloroquine for COVID-19: Hydroxychloroquine, an antimalarial and anti-inflammatory drug, was widely investigated as a potential treatment for COVID-19 during the pandemic. Early computational and in-vitro studies suggested antiviral activity, but large-scale clinical trials (e.g., WHO Solidarity Trial) demonstrated no significant benefit in reducing mortality or disease progression. Safety concerns, such as cardiac toxicity, further limited its use, making this one of the most well-known failed repurposing attempts.

2. Bevacizumab (Avastin) for Breast Cancer: Bevacizumab, an anti-VEGF monoclonal antibody used in colon and lung cancers, was granted accelerated approval for metastatic breast cancer. However, follow-up clinical trials showed minimal improvement in overall survival and raised safety issues like hypertension and bleeding. As a result, the FDA revoked approval for this indication, marking it a failed repurposing attempt.

11. Future of Drug Repurposing

The future of drug repurposing is highly promising as it integrates modern technology, big data analytics, and personalized medicine to accelerate drug discovery. With the rising costs and long timelines of traditional drug development, repurposing offers a faster, safer, and more economical alternative. Advances in artificial intelligence (AI), machine learning, and bioinformatics will enable precise prediction of new drug–target interactions, while network pharmacology and systems biology will help in understanding complex diseases where multi-target therapies are required. The use of real-world evidence

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(RWE), electronic health records, and pharmacovigilance databases will provide deeper insights into hidden therapeutic potentials of existing drugs. Furthermore, the growing emphasis on natural products and herbal medicines opens new opportunities for discovering multi-functional agents, especially for chronic and lifestyle-related disorders. In the future, repurposing strategies are expected to align closely with personalized and precision medicine, ensuring that drugs are tailored to genetic, proteomic, and metabolic profiles of patients. With global collaboration, digital health platforms, and regulatory support, drug repurposing will continue to expand as a sustainable and innovative pathway for addressing unmet medical needs and emerging health crises.

12. Artificial Intelligence in Target Identification

Artificial Intelligence (AI) has revolutionized the identification of drug targets by enabling rapid analysis of complex biological data. Traditionally, target discovery relied on labor-intensive laboratory research, but AI-driven approaches integrate genomics, proteomics, transcriptomics, and clinical data to reveal novel targets with greater accuracy. Machine learning algorithms can uncover hidden disease–gene or drug–protein associations, while natural language processing (NLP) extracts valuable insights from scientific literature, patents, and clinical trial reports. Network pharmacology models powered by AI further help in mapping disease pathways and prioritizing drug targets.

1. DeepMind's AlphaFold → Accurately predicts 3D structures of proteins, which is critical for identifying binding sites and new drug targets.

2. BenevolentAI → Uses machine learning and biomedical data mining to discover disease-associated targets; notably identified a potential target pathway for amyotrophic lateral sclerosis (ALS).

3. IBM Watson for Drug Discovery → Applies NLP and deep learning to analyze biomedical literature and patient data, suggesting novel cancer immunotherapy targets.

13. Conclusion

Drug repurposing has become a vital approach in the pharmaceutical field, offering a faster and safer path to discover new therapeutic applications of existing drugs. It significantly reduces time, cost, and risk compared to conventional drug development. With the support of modern technologies like artificial intelligence, bioinformatics, molecular docking, and network pharmacology, the process of identifying novel drug–disease associations has become more efficient. Repurposing has already shown success in several fields, from oncology to infectious diseases, and even in managing global health emergencies such as COVID-19. At the same time, failed attempts highlight the importance of rigorous validation, clinical trials, and careful safety assessment. Challenges related to intellectual property rights, regulatory guidelines, and commercial viability still remain barriers to wider adoption. However, the growing focus on personalized medicine and integration of real-world data will further strengthen the potential of this strategy. Herbal and natural products also provide a vast resource for future repurposing research due to their multi-target activities. Ultimately, drug repurposing represents not just a cost-effective alternative but also an innovative and sustainable solution to meet unmet medical needs.

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