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Research Article

Drug Repurposing in the Era of Emerging Infectious Diseases

Reuben P Syiem[1]*, Namit Ray[2], Krishnamoorthi R [2] and Rajesh Kumar[2]

[1]*Senior Resident Doctor, Department of Pharmacology, NEIGRIHMS, Shillong, India*

[2]*Post Graduate Trainee, Department of Pharmacology, NEIGRIHMS, Shillong, India*

***Corresponding Author:** Reuben P Syiem, Senior Resident Doctor, Department of Pharmacology, NEIGRIHMS, Shillong, India.

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Abstract

Emerging infectious diseases (EIDs) pose significant challenges to global health, often resulting in substantial morbidity, mortality, and economic burden. The traditional drug development process, with its prolonged timelines and high costs, cannot adequately address the urgent need for effective therapeutics during outbreaks. Drug repurposing- leveraging approved drugs for new therapeutic uses, has emerged as a promising strategy to combat EIDs. This review discusses the principles, methodologies, and technologies driving drug repurposing, along with its successful applications in recent pandemics, such as COVID-19 and Ebola. Regulatory and ethical challenges are analyzed, emphasizing the importance of balancing speed with safety. Finally, future perspectives, including the role of artificial intelligence and global collaboration, are explored. Drug repurposing represents a vital tool in pandemic preparedness, offering the potential for rapid and cost-effective responses to emerging health threats.

Keywords: Drug Repurposing; Emerging Infectious Diseases; Pandemic Preparedness; High-throughput Screening; COVID-19; Artificial Intelligence; Therapeutics

Introduction

Emerging infectious diseases (EIDs) such as COVID-19, Zika, and Ebola represent a persistent global threat, characterized by their sudden outbreaks, rapid transmission, and often severe health outcomes [1]. Over the past two decades, the frequency of such outbreaks has increased, fueled by factors including globalization, urbanization, and climate change [2]. These diseases often outpace the traditional drug development pipeline, which can take an average of 10-15 years and costs approximately $2.6 billion to bring a new drug to market [3,4]. Consequently, the search for rapid, cost-effective therapeutic strategies has become a public health priority.

Drug repurposing, or drug repositioning, offers an efficient alternative to conventional drug discovery by identifying new uses for existing medications. Unlike traditional drug development, repurposing capitalizes on drugs with established safety profiles, significantly reducing the time and resources required to deliver treatments to patients [5]. This approach has gained traction in the wake of pandemics, where rapid therapeutic responses are critical. During the COVID-19 pandemic, drugs such as remdesivir and dexamethasone were repurposed with varying degrees of success, underscoring the potential and limitations of this strategy [6,7]. This review delves into the principles and methodologies of drug repurposing, examines successful applications, and addresses the challenges and future directions of this approach in the context of EIDs.

Principles of drug repurposing

Drug repurposing involves re-evaluating approved drugs or investigational compounds for new therapeutic indications. This strategy builds upon pre-existing knowledge of a drug's pharmacokinetics, pharmacodynamics, and safety profile, thereby reducing development risks and costs [8].

Types of drug repurposing

- **Target-based repurposing**: Focuses on identifying drugs that can interact with a specific molecular target implicated in a new disease [9].
- **Mechanism-based repurposing**: Explores drugs with mechanisms of action that may be beneficial in other diseases, such as immunomodulation or antiviral activity [10].
- **Phenotype-based repurposing**: Relies on observing the therapeutic effects of drugs in disease models without prior knowledge of their molecular targets [11].

Advantages

- **Reduced development time:** Safety and pharmacological data from previous applications enable faster progression to clinical trials [12].
- **Cost-effectiveness**: Avoids the high costs associated with de novo drug discovery [13].
- **Higher success rates**: Repurposed drugs often have better chances of clinical and regulatory success due to established safety profiles [14].

Methodologies driving drug repurposing

Advances in technology and computational biology have revolutionized drug repurposing, enabling the systematic identification of candidate drugs.

High-throughput screening (HTS)

HTS involves automated testing of large drug libraries to identify compounds with activity against specific biological targets or disease phenotypes [15]. For example, HTS was instrumental in identifying remdesivir as a candidate for COVID-19 treatment [6].

Artificial intelligence and machine learning

AI-driven approaches analyze vast datasets to predict drug-target interactions and identify repurposing opportunities. Machine learning models have been used to prioritize drugs for testing during pandemics, significantly accelerating discovery timelines [16].

Omics technologies

Omics tools, including genomics, proteomics, and transcriptomics, provide insights into disease mechanisms and potential therapeutic targets. These technologies have been pivotal in identifying repurposing candidates for diseases such as COVID-19 and Zika [17].

Real-world data (RWD)

Electronic health records and observational studies provide valuable data on off-label drug use, facilitating the identification of repurposing candidates [18].

Applications of drug repurposing in EIDS

Several repurposed drugs have demonstrated efficacy in combating EIDs, with notable examples from recent outbreaks.

COVID-19

- **Remdesivir**: Originally developed for Ebola, remdesivir was repurposed to inhibit SARS-CoV-2 replication. It received emergency use authorization based on its ability to shorten recovery time in hospitalized patients [6,19].
- **Dexamethasone**: This corticosteroid reduced mortality in severe COVID-19 cases by suppressing hyperinflammatory responses [7].
- **Baricitinib**: An immunomodulatory drug for rheumatoid arthritis, baricitinib was identified as a candidate through AI-based screening and demonstrated efficacy in reducing inflammation and viral replication [20].

Ebola virus disease

- **Favipiravir:** Originally developed for influenza, favipiravir was shown to inhibit Ebola virus replication *in vitro*, though clinical efficacy remains debated [21].

Zika virus

- **Chloroquine:** This antimalarial drug was repurposed for Zika due to its ability to inhibit viral replication, though further studies are needed to confirm its clinical utility [22].

Malaria

- **Ivermectin:** Repurposed to reduce malaria transmission by targeting mosquito vectors, ivermectin has shown potential as a complementary tool in malaria control programs [23].

Challenges in drug repurposing

Despite its promise, drug repurposing faces several challenges:

- **Regulatory Hurdles:** Regulatory pathways for repurposed drugs often require new clinical trials to demonstrate efficacy for the novel indication, prolonging approval timelines [24].
- **Supply Chain Issues**: Repurposing can lead to shortages of critical drugs for their original indications, as seen with hydroxychloroquine during the COVID-19 pandemic [25].
- **Ethical Considerations:** Off-label use raises ethical concerns, particularly in emergency settings where evidence may be limited. Ensuring informed consent and equitable access is critical [26].

Future perspectives

The future of drug repurposing lies in leveraging emerging technologies and fostering global collaboration. Key priorities include:

- **Integration of AI**: Expanding the use of AI to predict repurposing opportunities and optimize clinical trial designs [16].
- **Global Drug Libraries**: Developing comprehensive databases of approved drugs with detailed molecular and clinical data to facilitate rapid responses during pandemics [27].
- **Personalized Medicine**: Tailoring repurposed therapies to individual patients based on genetic and phenotypic profiles [28].

Conclusion

Drug repurposing offers a viable and cost-effective strategy for addressing the urgent therapeutic needs posed by EIDs. Advances in technology and global collaboration have enhanced its potential, as demonstrated during the COVID-19 pandemic. While challenges remain, the integration of AI, omics technologies, and real-world data will continue to drive innovation in this field. As the world faces the inevitability of future pandemics, drug repurposing will play a pivotal role in strengthening global health preparedness.

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