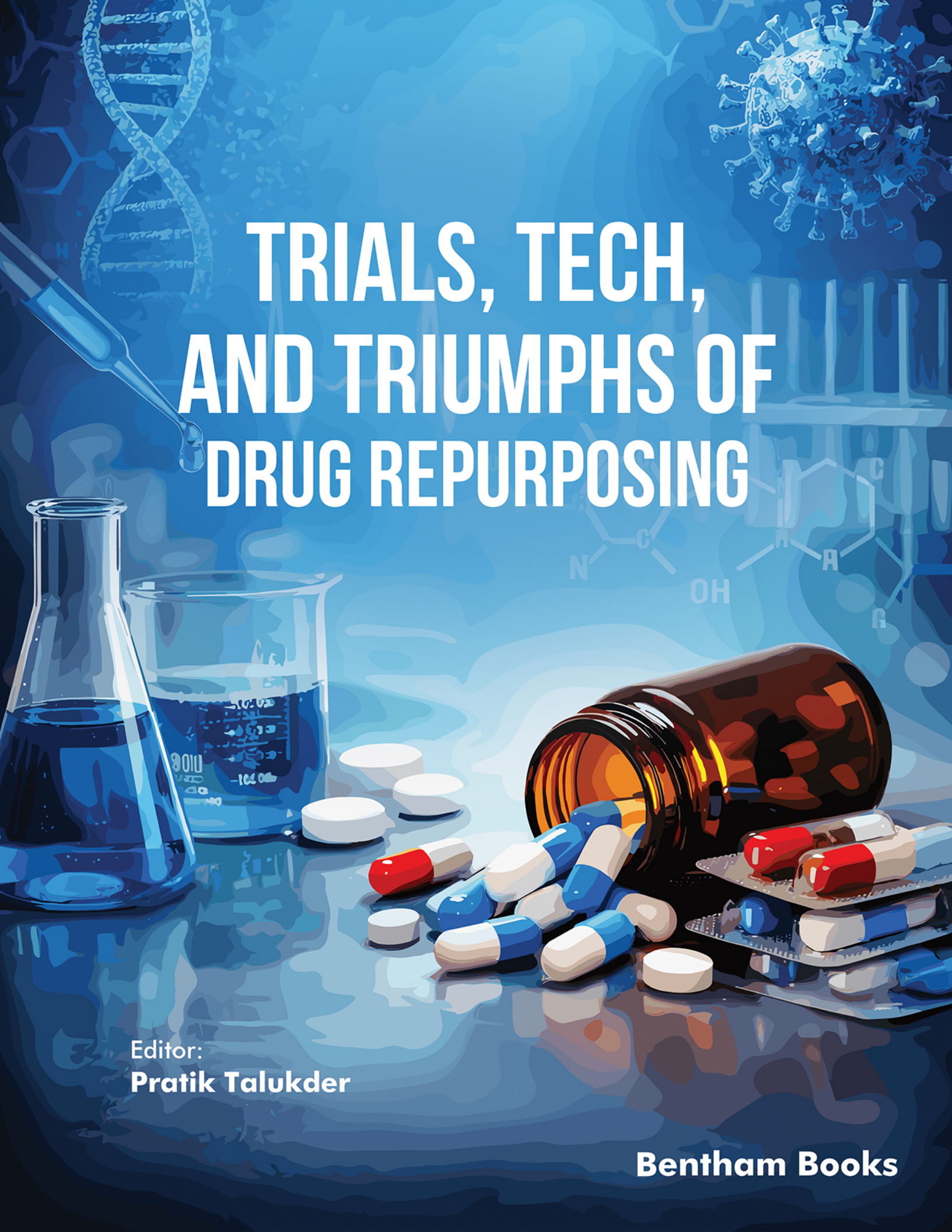
TRIALS, TECH,
AND TRIUMPHS OF
DRUG REPURPOSING
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Trials, Tech, and Triumphs of Drug Repurposing

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Trials, Tech, and Triumphs of Drug Repurposing

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FOREWORD

It gives me immense pleasure to write the book titled **Trials, Tech, and Triumphs of Drug Repurposing**, expertly edited by Dr. Pratik Talukder, which arrives at a pivotal moment for the biomedical sciences. In an era marked by escalating costs, prolonged development timelines, and unacceptably high rates of clinical failure, the traditional paradigm of de novo drug discovery is increasingly proving inadequate to meet urgent global healthcare needs. These constraints have compelled the biomedical research community to seek more pragmatic, efficient, and innovative strategies for therapeutic development. Among the most promising of these approaches is drug repurposing, which shifts the focus from discovering entirely new chemical entities to identifying novel clinical applications for existing, approved, or investigational drugs. Far from being a mere strategic adjustment, drug repurposing represents a fundamental evolution in how modern medicine addresses both persistent and emerging health challenges.

It is within this rapidly evolving and highly consequential scientific landscape that Trials, Tech, and Triumphs of Drug Repurposing, expertly edited by Dr. Pratik Talukder, makes a timely and substantive contribution. This volume offers a comprehensive and insightful examination of the scientific, technological, and translational dimensions of drug repurposing, seamlessly integrating foundational concepts with cutting-edge innovations. The book successfully bridges historical perspectives with contemporary methodologies, presenting a coherent narrative that reflects the maturity and growing significance of the field.

The COVID-19 pandemic served as a profound global reminder of the urgency inherent in therapeutic development. When time is of the essence, the conventional drug discovery pipeline, which often extends beyond a decade, becomes impractical. During the pandemic, the rapid evaluation of existing drugs for novel antiviral indications compellingly demonstrated the power and feasibility of repurposing strategies. By leveraging established safety profiles, known pharmacokinetics, and existing manufacturing and regulatory infrastructures, drug repurposing enabled accelerated clinical responses and reinvigorated scientific and clinical interest in this approach. Crucially, this period marked a shift away from largely serendipitous discoveries toward a more systematic, data-driven, and technology-enabled discipline.

This volume distinguishes itself through its thoughtful and rigorous exploration of that evolution. It traces the historical roots of drug repurposing from classic examples such as aspirin and metformin to the forefront of modern methodologies driven by artificial intelligence, network pharmacology, and multi-omics technologies. The chapters provide in-depth analyses of the experimental and computational frameworks that underpin contemporary repurposing research, encompassing in vitro and in vivo validation alongside increasingly sophisticated in silico approaches. By integrating computational biology, bioinformatics, systems pharmacology, and machine learning with experimental sciences, the book convincingly presents drug repurposing as a truly interdisciplinary enterprise.

One of the notable strengths of this work lies in its strong translational and application-oriented focus. Beyond theoretical and methodological discussions, the volume explores high-impact therapeutic domains where drug repurposing has demonstrated exceptional promise. The detailed treatment of repurposing strategies for neurodegenerative disorders such as Parkinson's disease and frontotemporal dementia, rheumatic autoimmune conditions, and various cancers highlights both the versatility and clinical relevance of this approach. These case studies persuasively illustrate that drug repurposing is not merely a stopgap

solution, but rather a robust and sustainable pathway for tackling complex, multifactorial diseases that have long resisted conventional drug development efforts.

Dr. Talukder, together with a distinguished group of contributors, has curated a volume that will appeal to a wide and diverse readership. Students and researchers in biotechnology, pharmacology, and life sciences; computational and systems biologists; and clinicians engaged in translational and patient-centred research will all find substantial value in this work. The book strikes an effective balance between scientific rigor and accessibility, presenting complex concepts—such as molecular docking, phenotypic screening, and genomic signature matching, and data integration—with clarity, precision, and pedagogical care. Arriving at a pivotal moment in the evolution of pharmaceutical research, Trials, Tech, and Triumphs of Drug Repurposing captures both the remarkable successes and the persistent challenges that define the field. It thoughtfully addresses critical issues, including intellectual property constraints, regulatory considerations, and data integration challenges, while simultaneously highlighting emerging opportunities enabled by collaborative research frameworks, open-access databases, and advanced analytical technologies.

Written with clarity and scientific rigor, this book, containing seven chapters, will be invaluable to students, researchers, and clinicians across biotechnology, pharmacology, computational biology, and translational medicine. More than a scholarly reference, it serves as a forward-looking guide to smarter, faster, and more efficient therapeutic innovation. Dr. Talukder and his contributors are to be commended for delivering a timely, insightful, and highly relevant volume that is poised to shape the future of drug development. I wholeheartedly commend Dr. Pratik Talukder and all contributing authors for their significant contribution to the scientific literature.

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PREFACE

The last decade observed a pivotal shift from the conventional methods of research and development to the conglomerate effects of the applied fields of biological sciences. This shift emerged as a beam of hope for the pharmaceutical industry as the latest approach of “Drug Repurposing”, which seeks to reutilise existing drugs for treating new disorders. Since its inception to its current eminence in pharmaceutical research, this book navigates through the past, present, and future of drug repurposing. By delving deeper into the metamorphic abilities of this approach, readers will gain insights into its wide-ranging applications and how it can bridge the gap between the pace of drug development and rigorous research scrutiny. The journey of drug repurposing dates back centuries, with serendipitous discoveries leading to the realization of a drug's alternative therapeutic benefits. From aspirin's transition from pain relief to colorectal cancer prevention to amantadine’s evolution from an antiviral drug to a treatment for Parkinson’s disease, historical anecdotes underscore the inherent value in exploring existing drugs for new purposes.

This interdisciplinary book welcomes scientists, scholars, academicians, computational biologists, and medical personnel to converge their knowledge in developing the wide arena of drug repurposing. By eliminating the highly time-consuming screening of hit and lead compounds in pharmacology, drug repurposing addresses the unmet medical needs within a minimum time span. The field of drug repurposing is an amalgamation of both computational and experimental techniques encompassing procedures like genetic association, pathway mapping, retrospective clinical analysis, molecular docking, and binding assays to identify target molecules, phenotypic screening and others. Traditional drug discovery is associated with resource-intensive elements such as capital, multiple clinical phase trials, probable chances of failures and numerous false positive results. To overcome these challenges, drug repurposing has emerged as a strategic avenue in the contemporary landscape. "Reviving Hope" sheds light on recent success stories, innovative methodologies, and collaborative efforts, driving this approach to become a prevailing practice in the pharmaceutical industry. The salient features of drug repurposing involve modifying conventional drugs to better treat the present untreatable diseases. This caters to patient-specific treatment by designing personalized drugs, thereby ruling out chances of failure. This approach brings under one roof a wide range of applied biological and other sciences, including computational biology, artificial intelligence, genomic profiling, proteomics, pharmacology, systems biology, and immunological fields. By exploring the potential implications of these technological advancements, this book provides a glimpse into the transformative role drug repurposing is poised to play in shaping the future of medicine.

Aim:

1. Learn in depth how repurposed medications can be a viable answer by leveraging well-known compounds for new indications, avoiding the costs and delays of developing new cancer treatments.

2. Discover how cutting-edge approaches, such as molecular docking for effective drug-protein interaction prediction, high-throughput screening, computational modeling, and signature-based tactics that take advantage of gene expression patterns, are propelling advances in drug repurposing.

3. Find ways to work together and conduct multidisciplinary research in the area of medication repurposing to promote creativity and hasten the development of new treatments.

4. Explain the various molecular pathways through which repurposed medications impact cancer, including the induction of apoptosis, the suppression of angiogenesis, the modification of the cell cycle, and the disruption of cancer cell metabolism.

5. Learn more about the potential uses of drug repurposing to improve patient outcomes, meet unmet medical needs, and change the pharmaceutical industry.

Scope:

The impetus behind this book stems from a recognition of the untapped potential inherent in existing drugs and the urgent need to overcome the barriers hindering their repurposing. The budding success of drug repurposing is characterized by its high speed, specificity, and transformative impact in the realm of healthcare. This new age technique has come in handy in treating various incurable neurodegenerative ailments such as Parkinson's disease and Alzheimer's disease, as well as other life-threatening disorders such as cancer, with minimal side effects and high-yielding outcomes. With the combination and sharing of multidisciplinary knowledge from intersecting fields of biological and technological sciences, such as medicine and clinical sciences, pharmacology, computational biology, bioinformatics, and drug discovery, the emergence of drug repurposing has been possible. However, the concept of drug repurposing faces ethical and legal challenges, funding restrictions, strict regulatory frameworks, and limited market exposure. Nonetheless, drug repurposing has been continuing to overcome these hurdles through rigorous research and development, casting aside all prior ethical concerns. Drug repurposing involves the use of new-age technologies, and understanding of drug-protein interactions through molecular docking, and subsequent changes in cell lines through phenotypic screening. By employing molecular markers, drug signatures can be matched to design patient-specific, customized treatment regimens. The results obtained from practicing the various technological aids can be used for future treatment procedures and to alleviate and strengthen the backbone of the healthcare system.

The prominence of drug repurposing came into the spotlight during the COVID-19 pandemic, in the course of which, repurposed drugs were utilized to treat comorbidities. Prior to this, repurposed drugs were widely used to treat cancer. Conventional cancer drugs are associated with multiple side effects, low survival rates, and an inability to arrest cancer progression due to the development of drug resistance. This highlighted the need for the development of new and improved cancer drugs. However, investigating new drugs is time-consuming as it requires the screening of potential drug candidates, stringent clinical trials, approval of associated ethical and legal bodies, and a proper marketing strategy. Hence, the focus shifted towards a less resource-intensive alternative – drug repurposing. With its progress, studies and research have shown drug repurposing to be beneficial in treatment regimens of neurodegenerative diseases – Parkinson's and Alzheimer's disease. This book entails the chronology of events that led to the establishment of drug repurposing as a poignant practice in the healthcare system. Further, it elicits the details of the interdisciplinary fields that led to its discovery. By compiling insights from leading experts, synthesizing the latest research findings, and offering practical guidance for researchers, clinicians, and policymakers, this book aims to catalyze further progress in drug repurposing and contribute to the collective effort to advance global health outcomes.

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CHAPTER 1

The Triumphant Journey of Drug Repurposing: *In Vitro*, *In Vivo* and *In Silico* Approaches

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Abstract: Drug repurposing, also known as drug repositioning, can be defined as a process of identifying pharmacological indications from existing approved drugs and the application of newly developed drugs to the treatment of diseases other than the drug's intended for therapeutic uses. Given the high attrition rates, substantial costs, and slow pace of new drug discovery and development, the repurposing of existing drugs is increasingly becoming an attractive proposition because it involves the use of de-risked compounds, with potentially lower overall development costs and shorter development timelines. The pharmaceutical industry has long used internal networking and disease-related phenotypic assays to explore the potential of new drugs in different disease areas. Drug repositioning is not a new concept. Many medications, whether in development or on the market, have been repurposed for new indications based on clinical observations (*e.g.*, sildenafil) or improved knowledge of their mechanism of action (*e.g.*, thalidomide). The initial drug repurposing was mainly through serendipity. Later, with time and advancements in technology, scientists started using various methods, like *in vivo* and *in vitro*, to repurpose drugs. There are two approaches for repurposing. The first approach, the traditional method, is experiment-based, while the other, the most recent one, is *in silico*-based approach. The experiment-based method is also called the activity-based method, which mainly focuses on screening of original drugs for unused pharmacological signs based on experimental measures. It includes *in vitro* or *in vivo* model building without the need for any basic data on the target protein. In contrast, the *in silico* method involves the use of bioinformatics, computational biology, and modern AI tools to screen huge databases of drug and chemical libraries. This method is time and labor-effective and reduces the risk of failure; this is the reason why it gained popularity and success in drug delivery programs. Thus, in this paper, we will delve into the developmental progression of successful drug repurposing over time.

Keywords: Activity-based method, Drug repositioning, *In vitro*, *In vivo*, *In silico* approach.

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Pratik Talukder (Ed.)

INTRODUCTION

Drug repurposing, also known as drug repositioning or drug reprofiling, is the process of finding alternative therapeutic applications for currently existing medications. They are used for medical purposes beyond their original indications [1]. Although there have been significant improvements in drug detection techniques, creating brand-new medications still faces several challenges. Finding novel uses for already-approved medicines is one way that drug repurposing serves as a potential solution for reducing these difficulties. With the increasing population and rising life expectancy, the list of required drugs also increases. Unfortunately, the original and conventional process of finding drugs takes a very long time and is not at all cost-effective. Therefore, finding a novel therapeutic application for a previously approved medication for another condition is defined as drug repurposing, a technique used to speed up the medicine discovery process [2].

Since ancient times, the concept of drug repurposing has been prevalent. For example, in ancient Egypt, opium was initially discovered for pain relief but was later used as a sedative and anaesthetic. In the same way, the usage of the ephedra plant for treating a variety of illnesses is mentioned in ancient Chinese scriptures [3]. The repurposing of willow bark for pain and fever treatment eventually led to the development of aspirin. Thus, from the beginning, only drug repurposing has been highly valuable. As technology advanced, the methods of drug repurposing evolved, although many discoveries still occur serendipitously [4].

In recent years, methods led by artificial intelligence (AI), machine learning, and bioinformatics have shown new possibilities for speeding up the process of drug re-profiling. These technologies have significantly enhanced the capacity to identify expanded function for prevailing drugs, making the process more efficient and effective [5]. Large-scale data on protein molecules and their interactions with other macromolecules and metabolites, as well as genome-wide gene expression profiles, are being produced by advances in genomics technologies. In order to better organize and comprehend this complicated data and aid researchers in their knowledge of the complex biological processes involved, molecular interaction networks provide a useful tool [6].

COVID-19 has drawn significant attention to drug repurposing and highlighted its importance more than ever before. While drug repurposing existed prior to the pandemic, it did not receive the same level of focus. The urgent need to speed up the drug discovery process and the need to find solutions to the increasing health threat highlight the importance of identifying new applications for existing medicines. This urgency pushed drug repurposing to the forefront of medical

research and treatment strategies during the pandemic [7]. Recently, a number of high-profile programs have been launched to identify new therapeutic areas for already existing medications. Recent initiatives by NIH-NCATS and AstraZeneca-MRC collaborations focus on drug repurposing by funding academic research to explore new uses for existing clinical compounds. Innovative pharmaceutical companies, like Lilly and AstraZeneca, are making their compound libraries, which are available to the scientific community. These efforts aim to deepen the understanding of disease mechanisms and identify new clinical uses for existing drugs, potentially accelerating the development process compared to creating new chemical entities [8]. In the modern era, drug repurposing has experienced substantial progress, with the integration of diverse *in vitro*, *in vivo*, and *in silico* approaches. Recent years have witnessed the emergence of methods driven by artificial intelligence, machine learning, and bioinformatics, which have opened up new avenues for accelerating drug reprofiling [5]. The various steps and time involved in the entire process are shown in Fig. (**1**).

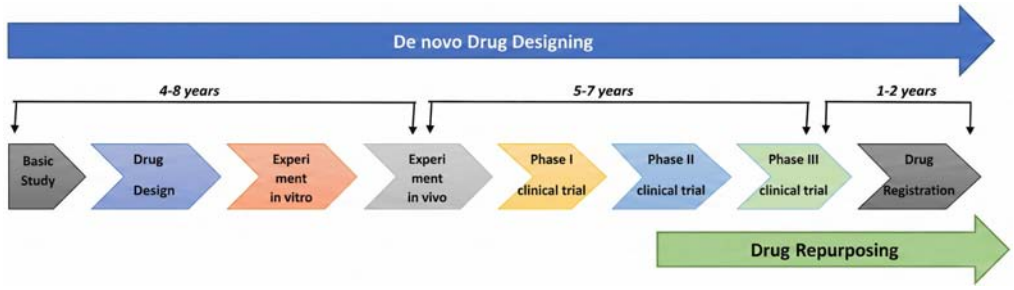

Fig. (1). Timeline of drug development.

IMPORTANCE

With the growing population and rising life expectancy, the demand for new drugs to treat various diseases has also increased. Consequently, the need to address this increased demand for medications has become more urgent [5]. Unfortunately, the traditional method of drug discovery takes a very long time for the drug to be manufactured and be available in the market. In addition to the long duration required for drug discovery, this process is also associated with substantial financial costs. Often, even after reaching the human trial stage, a drug may exhibit side effects, leading to its rejection, thereby resulting in the loss of the entire investment involved in the process.

Drug repurposing offers several advantages over the conventional drug invention procedure. With the advancement of *in silico* tools and the involvement of existing drugs that have already undergone extensive trials and clinical testing, the

CHAPTER 2

Evolution in the Method of Drug Repurposing - Past, Present, and Future, A Chronological Doctrine Journey

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Abstract: Drug repurposing is a method that is used to explore alternative therapeutic usages of compounds that are abandoned during the research period and also prolong the use of pharmaceuticals currently in use. Drug repurposing process is considered to be a critical approach, especially in the case of rare genetic disorders, where the conventional drug development process is costly and time-consuming, considering the uncommon nature of the diseases. Although drug repurposing is not a new concept, it has gained popularity over the past decade due to the substantial benefits it provides to the pharmaceutical industry. From 1991 to 2000, there was a substantial decline in the rates occurring during Phase II studies, which examined the effectiveness and safety criteria of medication candidates. Therefore, many tactics such as collaborations, acquisitions, and the use of modern technologies were used to optimise the drug development process, but had very little impact. Given these interferences, repurposing of drugs looks like a potential way to overcome these barriers during the drug development process. Drug repurposing can be used to re-examine promoted drugs, inhibited drugs, and drug contenders that were dropped during the clinical phase for various reasons. In recent times, computational methods have played a crucial part in repurposing drugs, as they provide researchers with methods and tools for incorporating data available on diseases, targets, and drugs, which can later be used to shed light on previously undiscovered processes. Drug repurposing has had a major impact on neglected diseases as effective treatments were not available in the past.

Keywords: Computational biology, Drug repurposing, Genetic disorders, Marketed drugs, Rare diseases.

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INTRODUCTION

Drug repurposing is a method that identifies alternative uses for compounds that act like drugs but may have been unsuccessful during drug development. Drug repurposing process, which is recognized as drug repositioning or drug reprofiling, was also used to extend the usage of existing drugs [1, 2]. Drug repurposing is considered an essential technique, especially in cases of uncommon genetic disorders for which the typical method of drug discovery may be time-consuming and costly [3]. Drug repurposing processes have gained popularity in recent years due to their significant applications and benefits in the medicinal industry, because it is facing difficulties due to the decreasing quantity of NMEs accepted globally each year [1]. The years 1991 and 2000 witnessed an increase in attrition rates during the second stage of trials, as in this stage, potential drug candidates are examined for their efficacy and safety [4]. Therefore, various other techniques, such as collaborations, acquisitions, and utilisation of cutting-edge technology, were used to safeguard and enhance the drug discovery process; however, with minimal success. Considering all these difficulties, drug repurposing is beginning to show promise as a potential way to overcome barriers in the drug development process [5]. This strategy is useful to reinvestigate withdrawn drugs, drug candidates, and marketed drugs that were discontinued during the stages of clinical development due to commercial or efficacy motives, although not because of safety.

The drug repurposing process began by chance, but as interest from various pharmaceutical firms increased and advancements in bioinformatics and cheminformatics strategies advanced, it has become an advanced data-driven method. An example of this data-driven strategy is the repurposing of imatinib, an ABL kinase inhibitor that was first approved for chronic myelogenous leukaemia but was later repurposed for systemic macrocytosis [6]. Topiramate, an anticonvulsant sulfamate-based drug that was generally registered for prophylaxis of migraine and epilepsy, was later repurposed and gained FDA approval. A study on bipolar and migraine disorders depicted loss of weight as a detrimental impact of topiramate [7]. Topiramate's effect on weight loss was further investigated through thorough proof of concept and clinical studies [8 - 10]. Topiramate was not approved for monotherapy due to its detrimental effects [11]. Furthermore, it was observed that when used alongside phentermine, an anti-obesity drug, at low doses in controlled-release formulations, topiramate effectively treated obesity [12]. Drug repurposing is based on the reality that: i) a drug can operate on various targets, ii) two different types of illnesses may have comparable molecular structures, and iii) a target can have pleiotropic impacts on molecular effects. Computational techniques, data analytics, and screening platforms are

capable of predicting previously unknown drug-disease target relationships [13 - 16].

Computational methods, including bioinformatics, systems biology, cheminformatics, and network biology, play an essential part in drug repurposing by combining all available data on targets, drugs, and diseases, which allows for a clear understanding of unknown mechanisms in short periods of time [17 - 19]. The number of drug repurposing articles published monthly has been increasing rapidly [20]. A new journal, Drug Repurposing, has been launched to address the growing number of papers on drug repurposing. Many academic institutions, government organisations, and non-profit organisations have supported and adopted the drug repurposing approach. There has also been a significant upsurge of drug repurposing companies over the past few years. Drug repurposing has a significant impact on neglected and rare diseases that lack feasible treatments [21]. In this chapter, we discuss the problems of developing and regulating repurposed medications.

Significance of Drug Repurposing

A new drug has been developed recently, and to enter the market, stringent rules and regulations must be followed. Therefore, to recognize a drug and develop it further requires a substantial investment, mostly in the form of various physicochemical properties that are incorporated as chemical entities and in the intricacy of scaling up production [22 - 24]. This restriction further permits academic centres and pharmaceutical industries to rapidly utilise already permitted medicines for new suggestions, that is not available for patients with that particular disease. It shows a decent start toward repurposing if the studied molecules flop and fail to demonstrate their efficacy for a predetermined indication. It can be further revived for innovative indications that are ultimately transformed into feasible therapies, mainly useful in cases of rare diseases, which face a lack of adequate resources and the challenges of diagnosis and treatment [25, 26]. For example, some bacterial infections, rare cancers, and autoimmune disorders are not genetic and are also idiopathic in nature, which cause various challenges in treatment [27]. The process of drug repurposing, comparatively a shorter, less expensive method, in which an impactful therapy for patients can be brought into an existing development procedure, a traditional discovery. Additionally, these methods actually overcome the inflated cost; therefore, the cost of the drugs for patients decreases, which ultimately reduces the original cost of the therapy [26].

During the examination of a new molecule, due to the unavailability of efficient data and safety information, there is a high probability of failure in the drug

CHAPTER 3

Methodologies in Drug Repurposing: From Phenotypic Screening to Molecular Docking

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Abstract: Sometimes, due to some genetic mutations in pathogens and other circumstances, they become resistant to the existing drugs and become virulent to a certain kind of species, or specifically, humans. Then, during that time, to fight against that mutant pathogen, we need to develop another effective drug asap, which is nearly impossible. Because designing a drug requires a significant investment and a long time as a set of trials is conducted over a long period. This is the reason why fatal cases will be outnumbered. For this reason, scientists actually discovered another approach to using existing drugs to cure a novel disease. One drug could be used not only to treat one disease but also to cure many diseases when combined with other drugs. This chapter covers many methods for repurposing medications. There are many methods for testing drugs' ability to cure diseases and their effects in cell lines and animal models, such as phenotypic screening and target-based approaches. Molecular docking can predict the drug ligand or drug protein interaction, which actually helps us understand the pharmacological activity of the drug and pharmacodynamics of the drug, and gives us a way of treating a disease related to it. Besides, there are many techniques by which we can assess the effects of a drug not only on a particular disease but also on other diseases.

Keywords: Computational biology, Drug repurposing, Genome-Wide Association Studies, Molecular docking, Phenotypic screening.

INTRODUCTION

Drug repurposing is a strategy for finding new therapeutic applications for medications already on the market that have been used to treat other diseases. Researchers actually discovered another approach to using existing drugs to cure a novel disease. Because in the case of Thalidomide, it was originally developed as a sedative, it was found out later that it can be used to treat diseases like leprosy

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or multiple myeloma, which is one type of cancer. So here we can see that one drug can be used not only to treat one disease but also to cure other diseases. And sometimes it can cure certain diseases when used in combination with other drugs [1]. For example, Aspirin was found to be a pain reliever, and it has been used as a pain reliever for a long period of time, but later we found out that it could help in preventing heart attacks. The reason behind this is that it can act as a blood thinner. So it is a huge benefit to have a drug like this, which has multiple effects on multiple diseases. We could give another example of Sildenafil Citrate, which is also developed to treat hypertension and angina, and was serendipitously found to be effective for erectile dysfunction [1]. Drug repurposing has been recommended as a way to develop treatments that take less time and cost less [2]. When a drug enters our body, it binds to receptors for which it is designed. Before the invention of computational models and software, drug repurposing required extensive trial-and-error experimentation. With major advancements in computational technology in the biological field, drug repurposing can now be performed using computational modeling. Large amounts of data collected from previous experiments are integrated into software systems, which can analyze drug–receptor binding potential for novel diseases, allowing research to progress much faster than previously possible. There are two approaches: the drug-centric approach and the disease-centric approach. The drug-centric approach focuses on finding new applications for existing drugs, while the disease-centric approach aims to discover more effective treatment strategies for specific diseases [3]. Through these methods, researchers have conducted extensive studies to identify new potential treatment options. Their work highlights the potential of computational approaches to expand the therapeutic applications of existing drugs [4].

Two technical advancements have enabled the widespread application of *in silico* drug repurposing technology. Extensive high-throughput data have been collected from genomics, proteomics, chemoproteomics, and phenomics [5]. Genomics analyzes genetic material; proteomics examines protein expression; chemoproteomics explores small-molecule–protein interactions; and phenomics links genetic variations to traits. This integrated data supports the identification of new therapeutic targets.

Information on disease characteristics and medication profiles has expanded to include pathway maps. Drug repurposing has led to the identification of promising candidates, some of which are currently in clinical trials. These drugs have the potential to treat both common and rare illnesses, making repurposing a crucial pathway for drug development. However, technological, administrative, and structural challenges continue to limit progress in drug repurposing.

This review covers numerous techniques for drug repurposing using a large dataset. We examine the difficulties involved and explore potential solutions through public–private collaborations in medication repurposing.

The future of drug repurposing looks promising, driven by advancements in bioinformatics, genomics, and artificial intelligence. These technologies enable the systematic analysis of large datasets to identify potential drug-disease interactions and predict new uses for existing drugs. Collaborations between academic institutions, pharmaceutical companies, and regulatory bodies are also crucial to overcoming challenges and accelerating the repurposing process.

Drug repurposing signifies a pragmatic and innovative technique to drug development, providing substantial benefits in terms of expenses, time, and risk reduction. Leveraging existing pharmacological knowledge provides a viable pathway to new treatments for a broad spectrum of diseases. As the healthcare landscape continues to evolve, drug repurposing is poised to play an increasingly significant role in addressing unmet medical needs and improving patient outcomes.

Investigating the Benefits of Drug Repurposing

Drug innovation is an intricate, costly, time-consuming, and often unsuccessful procedure. A drug development typically takes 12-15 years. As the medicine advances through the regulatory approval process, which precedes clinical phases, and is finally approved for marketing by the relevant regulatory agencies, the expenditure required to procure it increases significantly. Moreover, studies from complex animal and cellular models have limited clinical translation [6]. In recent years, drug repurposing has become a prominent strategy for accelerating drug development. Drug repurposing can help uncover new treatment opportunities for existing drugs beyond their original medical indications [7]. Repurposing existing medicines and chemicals for new therapeutic applications offers numerous advantages compared to the traditional innovative drug development process. These manufactured pharmaceuticals have already been proven safe for human use.

Drug repurposing has many advantages over traditional drug manufacturing. It reduces the time to market to 5-10 years, compared to 12-15 years for new drug development. The cost has been reduced from $35-75 million to $1.5-2.5 billion for developing a new drug from scratch. Regulatory approval methods are now faster due to existing safety data, resulting in a lower overall risk for established clinical data. This process increases the likelihood of success and return on investment. Also, it provides deeper insights into how diseases work, which later leads to more effective therapeutic options.

CHAPTER 4

Biological Insights into Neurodegenerative Disorders and the Use of Drug Repurposing for Their Treatment

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Abstract: Frontotemporal dementia is a type of frontotemporal degeneration disease that includes various forms of dementia, characterized by a considerable disintegration of the front and side pieces of grey matter in the brain in both sexes. Most of the people suffering from this disease demonstrate a gradual change in their behaviour or language disorders. Signs and symptoms often have their onset in the late adult years, usually between the ages of 45 and 65, but may occur before or after this. There are currently no effective or approved symptomatic treatments for FTD, although some off-label medications and behavioural methods may be used. Frontotemporal dementia (FTD) is a striking illness since it is a type of dementia that has no cure. This nature of the impairment exists as a consequence of brain deterioration. It results in a kind of brain lesion that cannot heal. As there is no cure or drug available for FTD, research is ongoing. A drug repurposing strategy can accelerate drug development and reduce costs and timeframes. Recent advancements in the understanding of FTD's pathophysiology, including protein aggregation, neuroinflammation, and synaptic dysfunction, have opened avenues for repurposing drugs initially developed for other conditions such as neuropsychiatric disorders, metabolic diseases, and cancer. Within the realm of FTD, various compounds that include antipsychotics, antidepressants, and kinase inhibitors possess potential therapeutic effects, and research works are ongoing to evluate them . Identifying multiple compounds as potential FTD targets may disrupt a few pathways that contribute to the range leading to tau protein aggregation, as well as TDP-43 pathology, in preclinical and clinical experiments.

Keywords: Cauopathy, Drug repurposing, Frontotemporal dementia, Neuroprotection, TDP-43.

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INTRODUCTION

Drug repurposing is the utilisation of already approved or previously used drugs for a new disease indication. It is obviously faster and cheaper than traditional ways of drug discovery since earlier information regarding the safety of drugs is available. Drug repurposing may necessitate that a new clinical trial be done, or a very small-scale trial, with the drug effects observed in different diseases. For instance, there are some drugs targeting cancer which were initially prescribed for some completely different ailments. Neurodegenerative diseases can be described as any illness that develops due to the steady loss of any function of the nervous system. In this type of disease, the neurons are often affected and destroyed. They are responsible for many disabilities of the human body, including the ability to move, remember, think and feel [1]. Consequently, when neurons are damaged, several biological processes in the body gradually change. Among the neurodegenerative diseases, the one that has been identified is called Frontotemporal Dementia. It is a neurodegenerative disorder involving the frontal and parietal lobes of the brain. These are two of the major divisions of the human brain. This region of the brain, located at the anterior part of the brain, is responsible for carrying out higher-order brain functions, including planning and decision-making, personality, *etc* [2]. The temporal lobe is located on the temporal sides of the brain and is concerned with hearing, memory, and emotion. Compared to Alzheimer's disease, which is associated with older persons, FTD is more common in those younger than 65 years and therefore a prime cause of early-onset dementia. This condition results in a gradual decline in behaviour, personality, language, and motor skills, significantly affecting daily functioning and quality of life. BVPTD is a type of disorder that affects a person's behaviour, language, and decision-making abilities. It is the third most common form of dementia with Lewy bodies, and it is a leading cause of early-onset dementia. FTD was first described by Dr Arnold Pick in 1892. Later on, Dr Alois Alzheimer recognised the link between Pick bodies and the disease, and the term Pick's disease was used to describe it. However, in 1982, another doctor described a subtype of the disease that affected a person's language use, now known as primary progressive aphasia [3].

Abnormal proteins accumulating in the brain primarily cause damage in FTD. Two important proteins implicated are Tau and TDP-43. Normally, these proteins ensure normal functions in brain cells. But in FTD, they get either misfolded or placed at locations where deposits should not normally form. This starts damaging and eventually killing brain cells (neurons) in the frontal and temporal lobes. As a consequence, the brain starts shrinking around these areas that control behaviour, decision-making,

speech, and emotions. This buildup of abnormal protein classes helps to define the particular subtype of FTD, *e.g.*, tauopathies and TDP-43 proteinopathies. Consequently, abnormal protein action is largely responsible for the continued worsening of symptoms observed in patients with FTD. The World Health Organisation suggests that the number of people affected with dementia is expected to double every 20 years, with a projected 115.4 million cases in 2050. In a study that looked at early-onset dementia, which is when symptoms appear, before the age of 65, frontotemporal dementia was reported to be the second or third most prevalent type of neurodegenerative disorder in all the studies. The reviews showed that the disease's prevalence ranged from 3% to 26%. However, it is worth admitting that many patients with FTD are not even diagnosed correctly [4].

Behavioural Variant Frontotemporal Dementia

Frontotemporal dementia, which often manifests early in life, is one of the most common neurodegenerative diseases and is characterized by profound changes in personality, behavior, and social conduct. It primarily affects the anterior part of the brain, which is responsible for high-level executive functions, such as judgment, error prevention, and decision-making. As these areas deteriorate, individuals experience difficulty regulating their emotions effectively. So people have trouble controlling their emotions really well. The control function allows a person to suppress their emotions within themselves. Consequently, bvFTD makes a person apathetic, because the person cannot feel emotional sensations, not because he makes an effort to suppress such emotions. Family members and caregivers often notice these behavioural changes before the affected person recognises them, leading to a gradual but profound impact on daily life [5]. Both tau and TDP-43 are abnormally accumulated in the brain and may hamper normal functioning when bvFTD occurs. Genetics may also account for several cases of familial bvFTD, because they could share mutations. Clinically, bvFTD is diagnosed through detailed psychiatric evaluation, neuropsychological tests, and MRI or PET scans. In fact, these very tools help to distinguish bvFTD from the other neurodegenerative processes, being very specialised in specific topographies of brain atrophy [6]. Today, there is no treatment; only symptom relief and comfort are ensured for those affected. Pharmacological drugs improve some of the behavioural symptoms; the other non-pharmacological methods of behavioural therapy and caregiver support are also essential for the improvement of patients. The progress of research in bvFTD is very promising, and it investigates molecular mechanisms underlying the disorder, identifies triggering early biomarkers, and even aims for the development of more specific treatment

CHAPTER 5

Drug Repurposing to Improve the Treatment of Rheumatic Autoimmune Inflammatory Diseases

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Abstract: The past century has been marked by intense efforts, both in the pharmaceutical industry and academia, to provide new treatments to individuals suffering from various RAIDs, which often occur by 'borrowing' treatments that have been previously used in one RAID or in some completely different disease, a process called drug repurposing. In spite of typical clinical symptoms and immunological dysregulation, the disease pathophysiology and phenotype differ widely among RAIDs, and a lack of information about their causation has made the repurposing of medications for RAIDs difficult. Nonetheless, the last century has been marked by many 'waves' of repurposing. Earlier drug repurposing happened in academia and was motivated by incidental findings or apparent disease similarities, which were often affected by the popularity and availability of scientific therapeutic classes. Since the late 19th century, the majority of biological medicines have been created for one or several RAIDs and subsequently evaluated in combination, with variable degrees of success. Over the last two decades, data-driven drug repurposing has been witnessed, which is distinguished by signature-based techniques that depend on genetics and molecular biology. In addition, many data-driven strategies use computational modelling and machine learning to combine various data sources. These repurposing phases have jointly led to breakthroughs in the treatment of various RAIDs.

Keywords: Computational modelling, Drug repurposing, Machine learning, RAIDs, Targeted therapies.

INTRODUCTION

For the past half-century, the strategies of drug discovery have shifted, driven by a better understanding of disease biology, enabling higher-quality targeted therapies for various conditions [1 - 6]. Although therapeutic response remains inadequate

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for patients with various RAIDs, there are limited targeted therapies available for patients with several other RAIDs [7 - 11], which require new procedures in drug development. It is basically difficult to give treatment to RAIDs due to their heterogeneity and chronicity, as well as due to a lack of proper information about their aetiology. While discovering *de novo* drugs for a disease is very costly and a delicate technique, repurposing drugs can lead to new therapies for RAIDs more quickly with less risk.

Drug repurposing describes the assessment of already accepted and rejected drugs in new indications and also enhances a functional process for integrating new therapeutic options into the treatment of relevant and appropriate diseases. The demand for repurposing, also known as retasking, retooling, reprofiling, or repositioning [12], refers to the partial decrease in cost and time compared with *de novo* drug discovery. The costing of effective repurposing varies between $40 to $80 million [13], and the time period varies between 3 years and to12 years [14], in comparison with recently developed chemical entities whose estimated cost varies between $2-3 billion and the time period varies between 13-15 years from the time of discovery to sanction [15]. In reality, repurposed drugs are used as a backbone for the medical care of RAIDs such as RA, pSS, SLE, AS, and PsA.

In its previous form, drug repurposing was empirical: mixtures were repurposed based on abnormal clinical results. The following therapeutic improvements from the repurposing of drugs in RAIDs were associated with diseases, generally giving a demonstration of the advantage of repurposing based on the similarity of putative diseases. In fact, there are various agents that constitute the current standard of protection for those RAIDs that are repurposed between one RAID and another, as well as through other diseases, including particular success in treatment, which was first in RA and then in AS and PsA. Drug repurposing has poor success in pSS and SLE due to the increase in disease heterogeneity and multi-organ complexity, as well as the measures that need to be taken in clinical trials to address the problematic consequences. However, repurposing remains a vital procedure for providing more advanced treatment to RAIDs. There are so many recently developed approaches which are undertaken to encourage repurposing which comprises some government-driven schemes like a programme launched by the NIH National centre in the year of 2012 for advancing translational Sciences and also the improvement of novel computational programs is enhancing drug repurposing as a viable option to *de novo* drug discovery [16], making it more effective to transfer compounds to patients more easily and fluently. Therefore, we analyse the results of drug repurposing in RAIDs, including their favourable outcomes and failures, and identify new data that could revolutionise the field of drug repurposing.

HISTORICAL DRUG REPURPOSING IN RAIDS

The classical period was characterised by minor academic repurposing of drug attempts that were based on ideas about the disease origin, randomness, and observations of off-target effects. Several contemporary standard-of-care drugs used to treat RAIDs were repurposed after being used in other diseases, driven by scholars, conceptual advances, or molecular theories. All these endeavours together lead to the discovery of new implications for existing drugs. Some drug classes, often related by their mechanism of action, were investigated for several RAID indications during a timeframe.

One of the first examples of repurposing of drugs is the therapeutic use of gold salt marks. Kitasato and Koch initially investigated gold salts, later followed by Mollgaard, who used it for treating diseases such as tuberculosis [17, 18]. Based on some studies, scientists examined gold compounds for the treatment of RA and other forms of arthritis in the nineteenth century, believing that these were chronic inflammatory diseases of infectious origin [19]. A classic example of academic repurposing of drugs is gold-based therapies. The development of these interventions was driven by a robust conviction in their functionality grounded in existing evidence. This was followed by numerous preliminary trials and extensive implementation across various RAID systems, predating their confirmed effectiveness by several years and regulatory endorsement by decades [20 - 22]. Several cases of drug repurposing adhered to a similar model, which led to the discovery and identification of many drugs that are presently being used in the treatment of RAIDs.

The assumption that some microorganisms may be responsible for certain rheumatoid arthritis-related diseases has generated enthusiastic attempts at repurposing. McPherson Brown proposed using antibiotics to treat RA in the late 1930s after noting mycoplasma-like structures in synovial fluid [23]. Nevertheless, it wasn't until trials controlled for the first time during the nineties that tetracycline derivatives like minocycline were found to be beneficial for RA [24, 25]. Sulfasalazine, a salicylic acid and an antibiotic, was similarly developed for treating ulcerative colitis and rheumatic polyarthritis in the latter years of the 1930s [26]. After its approval for use in RA in 1996 [27], sulfasalazine was thereafter utilised for other RAIDs and has been the subject of comprehensive research in AS. The treatment is effective in treating peripheral arthritis [28, 29] and has demonstrated moderate efficacy in addressing axial symptoms in patients with a short duration of the disease. Some studies have shown limited effectiveness of certain medications in treating Psoriatic Arthritis (PsA) [30, 31]. However, it is important to note that minocycline and sulfasalazine are not recom-

CHAPTER 6

Exploring Drug Repurposing: Approaches for Mitigating Parkinson's Disease

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Abstract: Among the various kinds of neurodegenerative diseases that affect individuals worldwide, Parkinson's disease (PD) is one of the most common that affects an estimated 1-2 percent of individuals over the age of 65 all across the globe. The gradual degeneration of dopaminergic neurons within the substantia nigra pars compacta is a signature characteristic of PD, resulting in a deficiency of dopamine, a neurotransmitter vital for regulating motor functions and coordinating movements. While scientists are yet to have a complete picture of the cause of the deterioration of the neurons due to PD, it has been hypothesized that genetic mutation, amyloid deposition, environmental toxins, and inflammation are among the factors responsible, making the disease complex and multifaceted. Despite PD being such a common neurodegenerative disease, there is currently no available cure for it. A drug that functions as a one-size-fits-all is a challenging task, given the multifaceted nature of the disease, as well as the cost and risks associated with the discovery of a novel drug, which makes pharmaceutical companies hesitant to invest. This makes repurposing already existing and approved drugs for mitigating symptoms and slowing down the progression of PD for individuals suffering from the disease all the more important, with a handful of repurposed drugs already in the market and others currently being in the pipeline. We take a look at the pathogenesis of the disease and discuss drugs that are either approved or currently in clinical trials, alongside future prospects for repurposing drugs against PD.

Keywords: Alpha-synuclein, Clinical trial, Dopaminergic neurons, Motor symptoms, Oxidative stress.

INTRODUCTION

In order to meet the UN Sustainable Development Goal targets by 2030, efforts to lessen the impact of non-communicable diseases, such as neurological disorders,

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have not been sufficiently robust, according to a report released by the UN General Assembly in December 2017. In the world today, neurological disorders rank as the second most significant cause of death and the primary cause of disability. Thus, reducing the burden of these disorders through the implementation of efficient policies and initiatives may be crucial to achieving the Sustainable Development Goals [1]. One such neurological disease is Parkinson's Disease. PD has been one of the most concerning neurodegenerative diseases around the world for decades, as it affects a vast number of individuals. In 2016, about 6.1 million individuals were affected with PD worldwide, and further, the count is estimated to be around 10 million. It is well known that PD is a progressive disorder and becomes more common as people get older [2]. PD is characterized by its progressive symptoms, ranging from motor to non-motor symptoms in terms of their nature. Among the motor symptoms, resting tremors are the trademark clinical feature, followed by bradykinesia (slowness of movement) and muscular rigidity. Approximately 80% of individuals with PD experience limb tremors, most commonly presenting as a resting, pill-rolling tremor of the hands. Prior to the onset of motor symptoms, patients may experience pre-motor or non-motor symptoms that precede motor symptoms by several years. Daytime sleepiness, apathy, and anhedonia are among the non-motor symptoms [3]. PD primarily occurs due to the selective degeneration of dopaminergic neurons. It takes place in the critical brain region called the substantia nigra, which helps control movements. The consequent decline in dopamine levels in the striatum results in the aforementioned symptoms.

Rationale

Exploring drug repurposing for Parkinson's disease (PD) offers several significant advantages. The creation of novel drugs is both an expensive and time-consuming endeavor [6], since identifying and validating biological targets and hits for new drugs requires large investments in specialized research tools, equipment, and clinical trials. At the same time, failures are always a part of experimental research, which lead to wasted time and money. Besides all that, patients who are suffering from a disease cannot be left without treatment. This is where repurposed drugs come in. Repurposing existing drugs can be considerably less expensive compared to developing new drugs from scratch. This is due to the fact that existing drugs for diseases unrelated to those researchers are trying to mitigate have already gone through rigorous trials, and their pharmacokinetics and safety profiles are well established, making the development timeline for repurposing substantially shorter. The accelerated development of repurposed drugs for Parkinson's disease, in particular, can lead to increased accessibility and availability for patients to relieve their symptoms since there is currently no available cure for it.

Pathogenesis

Movement-related difficulties in PD include rigidity, balance issues, resting tremors, and bradykinesia (slow mobility) as primary symptoms. Bradykinesia, a key feature of PD, is characterized by significant delays in beginning and completing actions. Rigidity is characterized by increased muscle tension, resulting in stiffness and difficulty moving in both flexor and extensor muscles. Involuntary shakes, known as resting tremors, are commonly seen in the hands or fingers when the muscles are not in use. Postural instability leads to diminished equilibrium and coordination, elevating the likelihood of falling. The main reason behind these motor symptoms is the gradual decrease in dopamine-producing neurons located in the substantia nigra pars compacta (SNc) of the brain. A shortage of dopamine, a key neurotransmitter that regulates movement, results in disturbances of the motor pathways, causing the typical motor problems seen in individuals with Parkinson's disease [7].

The crucial protein for controlling synaptic vesicles, alpha-synuclein, is produced by the SNCA gene. Changes or duplications in SNCA cause alpha-synuclein to build up and clump together in Lewy bodies, harming neurons. LRRK2 mutations are the primary genetic factor in PD, leading to increased kinase activity that is linked to the death of neurons. Autosomal recessive types of PD are associated with PARK2, PINK1, and DJ-1 genes. The PARK2 gene is known for working as an E3 ubiquitin ligase, but changes in the gene result in the buildup of faulty proteins and issues surrounding the proper functioning of mitochondria. Similarly, mutations in the PINK1 lead to the generation of oxidative stress as a direct result of mitochondrial dysfunction. Mutations in DJ-1 decrease the protein's ability to protect neurons against oxidative damage, increasing the susceptibility of neurons. The glucocerebrosidase (GCase) gene is associated with lysosomal function; mutations in the gene result in lysosomal dysfunction and the aggregation of alpha-synuclein [8].

One of the signature characteristics of Parkinson's disease pathology is the accumulation of alpha-synuclein in the form of Lewy bodies. Alpha-synuclein is a protein found in the presynaptic neurons that play a role in synaptic vesicle trafficking and neurotransmitter release, which, when misfolded, aggregates and combines to form Lewy bodies and Lewy neurites, impacting synaptic vesicle transportation and neurotransmitter release. These aggregates create poisonous clusters and fibers that disturb the balance within cells. When synaptic function is disrupted, it hinders the proteasome and autophagic degradation pathways, leading to the promotion of mitochondrial dysfunction by the aggregates. Additionally, they prevent the cell from adequately cleaning itself, which can harm the mitochondria, the cell's powerhouses, and result in cell death.

CHAPTER 7

Drug Repurposing of Aspirin and Metformin with Special Reference to Colorectal Cancer Mitigation

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Abstract: With an escalating increase in ailments and drug treatment failures, there has arisen a pressing need for the pharmaceutical industry to come up with effective drugs faster than ever before. Traditional drug development entails extensive research, augmentation, screening, and rigorous clinical trials, all of which are resource-intensive. An alternative approach has therefore been adopted in recent times, known as drug repurposing. Repurposing drugs involves finding new uses for an existing medication and demonstrating its effectiveness in treating diseases different from its prior indications. As recently as 2020, drug repurposing has found its place in the scientific community in light of the COVID-19 pandemic. Salient features of drug repurposing include reutilization of current and even household drugs, thereby expediting clinical trials and research time. The aegis of drug repurposing has stretched its branches to two ubiquitous drugs: Aspirin and Metformin. Customarily consumed aspirin, an over-the-counter drug, is conventionally used to treat a range of bodily pains and as an antiplatelet. Nevertheless, it has been found that aspirin can be repurposed to prevent cancer metastasis and revitalize the immune response. On the other hand, metformin, known for its hypoglycaemic activity, is a go-to choice for patients with Type II Diabetes. Over time, it has been observed that, when used as an adjuvant or administered directly, metformin can arrest cancer progression. Furthermore, its utility extends to age-related concerns, inflammation, and even COVID-19. This review presents the current scenario of repurposing these two drugs, taking into consideration both the long-term benefits and challenges.

Keywords: Aspirin, Antiplatelet, Adjuvant, COVID-19, Drug repurposing, Metastasis, Metformin.

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INTRODUCTION

Drug repurposing, also known as drug reconfiguration, is a deliberate tactic to identify new therapeutic uses for pharmaceuticals that have already received approval, as well as those that have been withdrawn from the market or shelved because of initial indications where they did not work as intended. Recently, there has been significant interest in this method, as it can accelerate drug development, reduce costs, and improve the efficacy of drug discovery [1].

The conventional drug development process is expensive and time-consuming, often taking over 10 years and costing billions of dollars to introduce a new medication to the market. This procedure is made more difficult by the substantial rate of attrition in clinical trials, where many attractive prospects fail because of unanticipated safety issues or inadequate effectiveness in subsequent phases of development. By utilizing already-existing pharmacokinetics and safety data, drug repurposing provides a solution to these problems and may shorten the time and cost needed to introduce a medication to the market.

The growing interest in medication repurposing is caused by a number of factors. First, a wide range of "off-target" effects linked to several medications raises the possibility of novel therapeutic uses. Second, a more complex investigation of drug-target interactions has been made possible by developments in computational biology and bioinformatics, which have made it easier to find novel uses for already-approved medications [2]. Furthermore, the screening procedure for medication repurposing has been completely transformed by the availability of extensive databases with genomic, proteomic, and phenotypic data.

The usage of sildenafil, which was first created to treat angina, to address erectile dysfunction, and then authorized for the use of the medication Revatio to treat pulmonary arterial hypertension, is a noteworthy example of effective pharmacological repurposing. The medication thalidomide, which was formerly known for causing birth deformities, is now used to treat leprosy and multiple myeloma. These encouraging tales demonstrate how repurposing drugs can lead to the discovery of cutting-edge treatments for a range of illnesses.

Drug repurposing has benefits but also drawbacks. Intellectual property concerns can be a major obstacle, as they make it less likely that pharmaceutical corporations will participate in repurposing initiatives, since the patents for certain medications' original uses may have expired. Furthermore, repurposed medications may be subject to complex regulatory processes, requiring extensive evidence to support novel therapeutic claims [3].

To sum up, drug repurposing is an exciting trend in contemporary drug discovery that provides a workable solution to reduce the considerable expenses and hazards involved in traditional drug research while also accelerating the creation of novel medicines. To fully exploit the promise of medication repurposing, technological advances and collaboration between the pharma and academic sectors are needed.

ASPIRIN

Classification and Functions

ASA, the molecular name for aspirin, is a commonly used medication with a lengthy history and a wide range of medical uses. Based on its medicinal applications and pharmacological activities, it is divided into many groups:

Analgesic

The main purpose of aspirin is as an analgesic, which reduces minor to moderate pain. It functions by blocking the cyclooxygenase enzymes, particularly COX-1 and COX-2, which are necessary for the synthesis of prostaglandins, chemicals that act as mediators of pain and inflammation. Aspirin significantly reduces pain and inflammation by inhibiting the generation of these prostaglandins [4].

Anti-Inflammatory

As an NSAID, aspirin is also categorized. Because it inhibits COX enzymes, fewer pro-inflammatory mediators are produced, which has anti-inflammatory benefits. Because of this characteristic, aspirin can be beneficial in the management of inflammatory diseases, including osteoarthritis and rheumatoid arthritis.

Antipyretic

Aspirin is used as an antipyretic to lower fever. Once more, the medication's ability to lower body temperature is linked to its inhibition of prostaglandin synthesis [5]. This inhibition affects the hypothalamic thermal-regulating centre, which, in turn, promotes heat dissipation and lowers fever.

Antiplatelet

Because of its well-known antiplatelet (or antithrombotic) properties, aspirin is used extensively in the management and prevention of cardiovascular illnesses. Aspirin decreases the synthesis of thromboxane A2, a powerful inducer of coagulation and vasoconstriction, by permanently inhibiting COX-1 in platelets. As a result, platelet aggregation is prolongedly reduced, which makes aspirin a

APPENDICES

Chapter 1: The Triumphant Journey of Drug Repurposing: *In Vitro, In Vivo* and *In Silico* Approaches

- **Therapeutic** – a treatment of disease by remedial agents.
- **Sedative –** a drug having a sleep-inducing effect.
- **Anaesthetic –** a drug inducing insensitivity to pain.
- **Ephedra –** a genus of gymnosperm shrubs that has been used in Traditional Chinese Medicine for 5000 years to treat asthma, bronchitis, and hay fever.
- **Willow bark –** willow bark contains a chemical named salicin, which has fever-reducing and pain-relieving effects in the body similar to aspirin.
- ***De novo* identification** – a computational approach that harnesses molecular design to generate novel chemical entities to create drug-like molecules that fulfil pharmaceutical requirements.
- **New molecular entity** – new drug containing a specific substance which has not been approved by the FDA previously.
- **Pharmacophore** – a description of the chemical characteristics of a molecule that are required for it to adhere to a biological receptor.
- **Toxicological –** study of chemical substances harming living organisms and treatment of exposure to toxins.
- **High-throughput screening –** high-throughput screening uses automated technology to swiftly examine hundreds to millions of specimens for biological activity at the model organism, cellular, pathway, or molecular levels.
- **Genomic –** study of the complete set of genomes of a specific organism.
- **Proteomic –** study of the complete set of proteins present in a cell, organ, or an organism.

Chapter 2: Evolution in the Method of Drug Repurposing Past, Present, and Future, A Chronological Doctrine Journey

- **Phenotypic screening** – the methods used for testing current drugs in a disease model to observe the impact of the drug on the model.
- **Molecular docking** – a process used for the prediction of interaction between biological targets and drugs.
- **High-throughput screening (HTS)** – the method for speedy testing of drug libraries against the disease's targets.
- **Omics technologies** – the process of integrating metabolomics, genomics, and proteomics together for target identification.
- **DrugBank** – the process used for virtual screening from the database of drugs and their molecular targets.
- **PubChem** – used for bioinformatics analysis for the repository of chemical compounds.
- **SwissTargetPrediction** – a computational modelling tool for the prediction of

drug–protein interactions.
- **RepurposeDB** – a drug discovery method for the collection of repurposed drugs.

Chapter 3: Methodologies in Drug Repurposing: From Phenotypic Screening to Molecular Docking

- **Binding assays** – experimental methodologies used to analyze drug–protein target interaction. A very popular and broadly employed experimental methodology is the Cellular Thermal Shift Assay (CETSA), which determines ligand-mediated stabilization of a protein.
- **Phenotypic screening** – a screening strategy that examines a compound's effect on biology within a disease model before its actual specific molecular target has been discovered.
- **Genome-wide association studies (GWAS)** – a research approach that scans the genetic differences among individuals for associations with a particular trait or disease, based mainly on single-nucleotide polymorphisms (SNPs).
- **Molecular docking** – a computer method applied to predict how a drug (ligand) will bind to a target protein (receptor).
- **Retrospective clinical analysis** – a process which examines available clinical information, like electronic health records and post-approval drug research, to discover possible new uses for approved drugs.

Chapter 4: Biological Insights into Neurodegenerative Disorders and the Use of Drug Repurposing for Their Treatment

- **Frontotemporal dementia (FTD)** – a condition of the brain affecting the frontal and temporal lobes of the brain, leading to the alteration of personality, behaviour, and speech.
- **Frontotemporal degeneration** – a pathological process that causes the gradual degeneration of the nerve cells of the frontal and temporal lobes of the brain.
- **Grey matter disintegration** – defined as the breaking down of the neuron-rich outer layer of the brain.
- **Neurodegeneration** – the loss of structure and function of neurons, causing neurological disorders.
- **Protein aggregation** – the gathering of misfolded proteins, making the cells toxic and implicated in neurodegenerative disorders.
- **Neuroinflammation** – a type of inflammation occurring in the brain or spinal cord that can cause neuronal damage.
- **Synaptic dysfunction** – the malfunctioning of communication occurring between neurons at the synapses, affecting brain function.
- **Antipsychotics** – drugs used in the treatment of psychosis such as delusions and hallucinations.
- **Antidepressants** – drugs used in the treatment of depression and other mood disorders.
- **Neuropsychiatric disorder** – disorders that affect the nervous system and cause changes in mood, behaviour, and cognition.

- **Metabolic diseases** – diseases that affect or cause changes in the body's metabolism and can also affect the brain.
- **Kinase inhibitors** – a class of drugs used for blocking the action of kinases, a type of enzyme involved in cell signalling.
- **TDP-43 pathology** – defined as the abnormal buildup of the TDP-43 protein associated with FTD and other neurodegenerative diseases.
- **Off-label medications** – the application of medications for a purpose not approved by regulatory agencies.
- **Behavioral interventions** – techniques used to change behaviours for the improvement of health.

Chapter 5: Drug Repurposing to Improve Treatment of Rheumatic Autoimmune Inflammatory Diseases

- **Drug repurposing –** the progression of discovering new therapeutic uses for existing drugs.
- **Rheumatic autoimmune inflammatory diseases (RAIDs)** – chronic diseases characterized by immune system dysfunction, such as psoriatic arthritis (PsA), systemic lupus erythematosus (SLE), and rheumatoid arthritis (RA).
- **Signature-based drug repurposing** – computational approaches that match drug-induced molecular signs with disease signatures to classify potential new treatments.
- **Disease heterogeneity –** the various effects of RAIDs that make general therapy problematic.
- **Clinical trial complexity –** repurposed drugs must undertake new trials to test efficacy in different diseases.

Chapter 6: Exploring Drug Repurposing: Approaches for Mitigating Parkinson's Disease

- Pre-clinical Studies – Experimental methodologies used to evaluate the safety, efficacy, and biological activity of a drug candidate before it advances to human trials. These studies are conducted *in vitro* (using cell cultures) and *in vivo* (using animal models) to assess pharmacokinetics, toxicity, and therapeutic potential. Pre-clinical studies provide the foundational data required for regulatory approval to proceed to clinical trials.
- Clinical Trials – A structured process that evaluates the safety and efficacy of a drug in human subjects. Clinical trials are divided into phases: Phase I (safety and dosage determination in a small group), Phase II (efficacy and side effects in a larger group), Phase III (confirmation of effectiveness and monitoring of adverse reactions in an even larger population), and Phase IV (post-market surveillance for long-term effects). These trials follow strict regulatory guidelines to ensure patient safety and therapeutic validity.
- Screening – A systematic process used to identify potential drug candidates by testing compounds for specific biological activity. This includes high-throughput screening (HTS), in which thousands of compounds are tested against a target to determine efficacy, and phenotypic screening, which evaluates a compound's effect on biological

systems without prior knowledge of the target. Screening plays a crucial role in drug discovery and repurposing.

Chapter 7: Drug Repurposing of Aspirin and Metformin with Special Reference to Colorectal Cancer Mitigation

- **Analgesic** – any member of the group of drugs that are used for pain relief.
- **Anti-inflammatory** – any drug or substance that reduces inflammation (swelling, pain, and redness).
- **Antipyretic –** a drug that helps reduce fever.
- **Antiplatelet** – medications that prevent platelets from forming clots and sticking together.
- **VTE prophylaxis** – a medical treatment that decreases the chances of blood clotting.
- **Colorectal cancer** – cancer of the colon or rectum, located at the end of the digestive tract.
- **Antineoplastic drugs** – medications that are used to treat cancer.
- **Polycystic ovarian syndrome –** a hormonal disorder that causes enlarged ovaries with small cysts on the outer edges.
- **Neuropathic pain** – a chronic pain condition caused by nerve damage or nervous system malfunction.
- **NSAIDs** – a class of drugs that reduce inflammation, pain, and fever.
- **Gestational diabetes** – a form of high blood sugar that affects pregnant women.

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Dr. Pratik Talukder is an accomplished Indian scientist and Associate Professor in the Department of Biotechnology at the University of Engineering and Management, Kolkata. He specializes in Plant Molecular Biology, Plant Tissue Culture, and Environmental Toxicology. He earned his Ph.D. from the University of Calcutta, focusing on polyphenols in Plantago ovata, and holds an M.Sc. in Biophysics, Molecular Biology, and Bioinformatics, as well as a B.Sc. in Zoology from Presidency College.

Dr. Talukder has over a decade of research experience and has published extensively in high-impact journals and books. His work explores stress mitigation in plants, biotechnology innovations including CRISPR-based gene editing and potential SARS-CoV-2 vaccines, and molecular pathways in crops such as Plantago ovata, Capsicum annuum, and Solanum melongena.

He has submitted 11 sequences to GenBank, filed four patents ranging from herbal additives to MIOT-based brain cancer detection techniques, and secured multiple national and institutional research grants. Dr. Talukder also serves as an Assistant Editor for Applied Biochemistry and Biotechnology. His contributions have been recognized through prestigious awards and fellowships, reflecting his commitment to advancing plant biotechnology and environmental research.