International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Drug Repurposing and Its Various Approaches

Gaurav Thakur[1], Anish[2], Shivani Chaudhary[3], Dr. Kapil Kumar Verma[4]

[1,2,3,4]Minerva College of Pharmacy (HP)

Abstract

Drug repurposing has the possibility of providing drugs with established safety profiles to different groups of patients. A large number of examples exist showing new uses found for already existing molecules, commonly discovered by chance or targeted research efforts related to a drug's specific mechanism of action. The development of systematic methods for drug repurposing has been sparked by the necessity for new approaches in drug research, as well as the advancement of big data repositories and their corresponding analytical techniques. Numerous novel computational techniques have emerged to facilitate systematic repurposing screens, both in experimental settings and through computer simulations. Effective drug repurposing pipelines need strong understanding, skills, and a solid experimental framework for integrating molecular data and clinical development expertise. This review outlines various systematic repurposing approaches and explores key players in the field. Strategic collaborations are essential for enhancing the success of repurposing existing molecules for new indications. The review also examines the pros, cons, and challenges of repurposing as a drug development strategy adopted by pharmaceutical firms.

INTRODUCTION

Repurposing an existing drug or drug candidate for a novel treatment or medical condition for which it was not previously indicated is known as drug repurposing.

It was first created to address a different kind of illness.

Some have referred to it as an unforeseen, serendipitous process. Typically, medications with proven hu man safety records are also tested and produced for a specific condition other than the one for which the y were intended.(1) By bypassing the medication development process and going straight to preclinical and clinical trials, this approach lowers risk and costs. Repurposing drugs is a significant aspect of the pharmaceutical industry and has gained a lot of traction in recent years among researchers and industry players. Finding novel applications and indications for both successful and unsuccessful medications is essentially what it means. Comparatively speaking, this is more dependable and less expensive than experimental drug discovery.(2)There are few targets for experimental drug discovery, and the process is costly, time-consuming, and hazardous. As a result, numerous computer techniques that may evaluate hundreds of thousands of medications for repositioning using readily available high-throughput data have been developed. However, the literature currently in publication lacks a comprehensive and up-to-date examination of contemporary computational drug repurposing techniques.(3) Without specifically identifying the mechanism of action, repurposing can help discover novel drugs based on their phenotypic advantages. Preclinical animal models can be used to evaluate this directly, and research and clinical applications can benefit more from these findings. It might move right forward to Phase II clinical trials. Repurposed medications carry a little risk of failure. Compared to normal discovery, repurposing pharmaceuticals offers a substantial benefit in terms of lower development costs and faster time to market.

Safety, toxicological, and pharmacokinetic data from the conventional discovery process.[5] Synthetic intelligence the biological and health sciences have demonstrated the promise of artificial intelligence (AI) and machine learning. Previous studies have shown that AI is capable of absorbing new data and turning it into insightful knowledge. Pharmacology's objective is to use this technique to create innovative, cost-effective vaccinations that are more effective. One of those fundamental truths that increases the likelihood of developing new drugs is the ability to forecast the molecular mechanism and structure. Clinical, electronic, and high-resolution imaging datasets can be used as inputs to support the drug development speciality. Furthermore, by expanding the target profiles of medications to include off-targets with therapeutic potential, comprehensive target activity has been carried out for the purpose of repurposing a pharmacological molecule.[5]

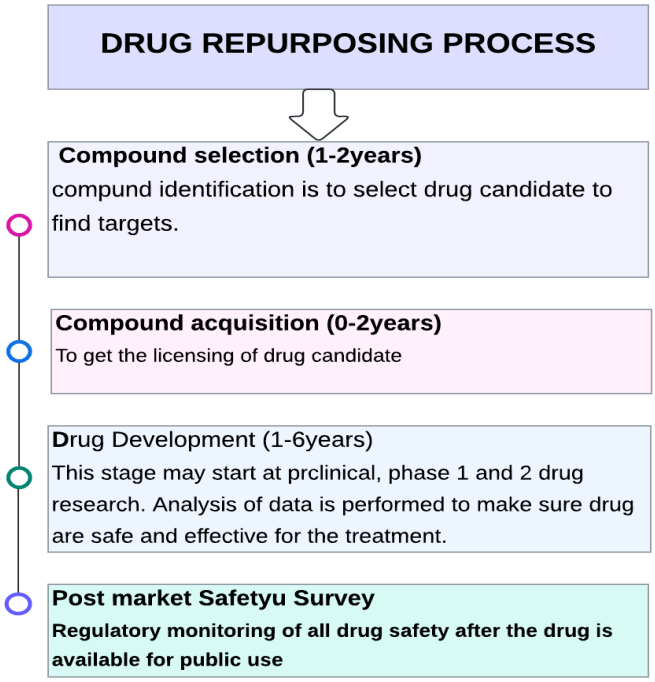

Fig.1: Drug Repurposing Process

Difference Between Traditional Drug Discovery and Drug Repurposing

The history of drug repositioning has largely been serendipitous. One of the most successful examples of repurposing drugs is sildenafil, which was initially designed as an antihypertensive drug, but was later repurposed to treat pulmonary arterial hypertension and erectile dysfunction, and marketed as Viagra.[6] Thalidomide is another well-known example that was withdrawn from the market due to its association with severe defects in fetuses. However, later research has proven its effectiveness in treating leprosy and multiple myeloma. These success stories have inspired the global pharmaceutical industry to explore the potential of existing drugs further. In the last decade, governments, researchers, academics, and pharmaceutical companies have supported activities related to drug repositioning.[7]

The ability of any drug to act on multiple targets, the possibility that two different diseases may have cellular and molecular similarities, and the fact that a target can have multiple effects are all important aspects of drug repositioning. With the rapid development of current high-throughput technologies, the amount of data they generate has significantly increased. These technologies support the use of computational methodologies to find associations between drugs, diseases, and targets, thus improving

the drug repurposing process.[8] New information technologies, including cloud computing, social media, and the Internet of Things, generate a large amount of data that continues to grow across various fields of study. However, these technologies are complex due to the vast variety, rapid production, and large volume of data. Advances in genomics sequencing and biomedical data acquisition technologies have led to lower costs and enabled researchers to produce a tremendous amount of experimental data. This includes data generated by powerful analytical technologies such as DNA or RNA sequencing, mass spectrometry, and various applications like transcriptomics, proteomics, metabolomics, and epigenomics. The complexity is further increased by the inclusion of large volumes of clinical data from electronic health records (EHRs), clinical trials, and biobanks. The data is often stored in diverse, unstructured formats, making data integration extremely complex and challenging. While some databases offer direct access to structured data, much of the genomic data is only accessible in raw, unstructured formats, such as in the Sequence Read Archive.[9]

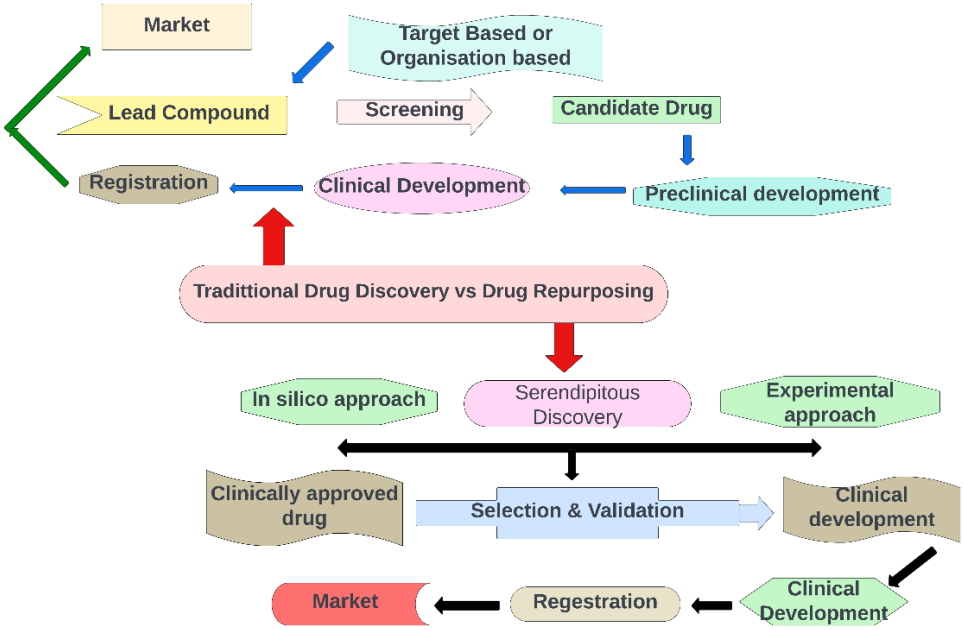

Fig.2: Traditional Drug Discovery vs Drug Repurposing

CLASSICAL DRUG DETECTION DRUG REPURPOSING

Having 5 main phases: -

- FDA post-market safety monitoring
- clinical research
- safety review
- FDA review
- discovery and preclinical

FDA Post marketing safety monitoring

Drug repurposing is significantly aided by Food and Drug Administration (FDA) post marketing safety monitoring. FDA post-marketing safety monitoring, also known as Phase IV studies, is required due to the possibility that certain medications may have side effects that don't show up until after they are launched. This is a crucial step in the process of repurposing drugs, which allows a medication

created for one illness to be used to treat another indication. This is a detailed overview of the FDA's post-marketing safety monitoring strategy from the standpoint of drug repurposing.[10]

Clinical Research

A number of processes are included in the clinical research workflow for drug repurposing in order to evaluate the safety and efficacy of an existing pharmaceutical used in novel therapeutic indications.[11]

Safety Review

Drug repurposing, sometimes referred to as therapeutic switching or drug repositioning, is the act of giving an established pharmaceutical that has been licensed to treat one condition a new usage. Numerous advantages might result from this, including a reduction in expenses and time when compared to creating new medications from scratch. It does, however, also come with certain safety risks.[12]

FDA REVIEW

The FDA is undoubtedly in charge of drug repurposing, which gives already-approved medications new uses outside of their prescribed indications.

Here is a general rundown of the steps involved and how the FDA fits in:

Regulatory Pathways

NDA

A Supplemental New Drug Application (sNDA) Orphan and Fast Track Drug Designation

Labelling and Marketing.

After-Market Monitoring Even after receiving approval for a novel use, a medication is subjected to post-market surveillance (PMS) in order to ensure its efficacy and safety.[13]

Repurposing medications is a technique to more skill fully open the door to the market for novel therapeutic treatments because much of what we currently know about their pharmacokinetics and toxicity will still apply, saving time and money on development. Therefore, the FDA is ensuring that patients may benefit from these novel uses in a safe and effective manner.[14]

Discovery and Preclinical

Finding new applications for already-approved drugs is known as drug repurposing (DR), sometimes known as drug repositioning. Compared to creating a whole new medication, this may be a quicker and less expensive solution. A succinct overview of drug repurposing's preclinical and discovery stages.[15]

Phase of Discovery

1. Recognizing Potential Candidates
2. Formulation of Hypotheses
3. Screening in advance

Preclinical Phase

1. Action Studies' Mechanism:
2. Models of Animals
3. Formulation Development.

Methods Used in Drug Repurposing

Three primary methods for repurposing drugs As part of a systematic strategy, pharmaceutical companies usually employ one of three approaches:

According to a drug's therapeutic effect, targets are seen differently in disease- and target-centric approaches, which both examine the connections between medications, diseases, and targets.

1. **Drug Centric/ Medication Centric**
2. **Disease Centric**

3.Target Centric

1. Drug centric /Medication centric

A drug-centric strategy broadens the use of an already-approved medication to a new indication. Drug-focused repurposing could start with finding an authorized drug being used off-label for a new patient population or medical condition that is not covered by the drug's current license or patent examining experimental or discontinued medications that, at first, proved to be ineffective for a certain use or failed to receive regulatory approval. Finding new applications for medications that have been taken out of circulation for safety or post-market concerns but are still effective for other medical purposes Prescription medications for new ailments that have generic competition and have passed the patent exclusivity term.[17]

2. Disease Centric

A disease-centric strategy links licensed or unapproved drugs with therapeutic effects with diseases that have no treatment or a medication that is only partially successful. It is especially helpful in attempts to repurpose drugs for uncommon illnesses. Finding illnesses with underlying biological pathways similar to the indication that the original medication cures is part of the process. For instance, a medication intended to treat cancer may also be used to treat psoriasis or other conditions characterized by unchecked cell development.[18]

3. Target centric

A target-centric strategy pairs an established medicine and its known target with a newly identified indication that does not yet have a treatment; these indications usually differ dramatically. It entails identifying the precise molecular targets linked to a disease's pathogenesis and applying the current medication that has been shown to modify those targets. This method is also very helpful when trying to repurpose medications to treat uncommon illnesses.[19]

VARIOUS APPROACHES USED IN THE DRUG REPURPOSING

This approach usually utilizes public databases for drugs. Data from primary and translational research, clinical trials, anecdotal reports regarding off-label uses, and other published human data information available are included. Using artificial intelligence algorithms and other bioinformatics tools, investigators systematically try to identify the interaction between drugs and protein targets. In silico drug repositioning is a powerful technology with significant advantages, including speed and reduced costs.[20]

There are usually three kinds of approaches:

- Computational approach
- Biological experimental approach
- Mixed approach.

Computational Approaches

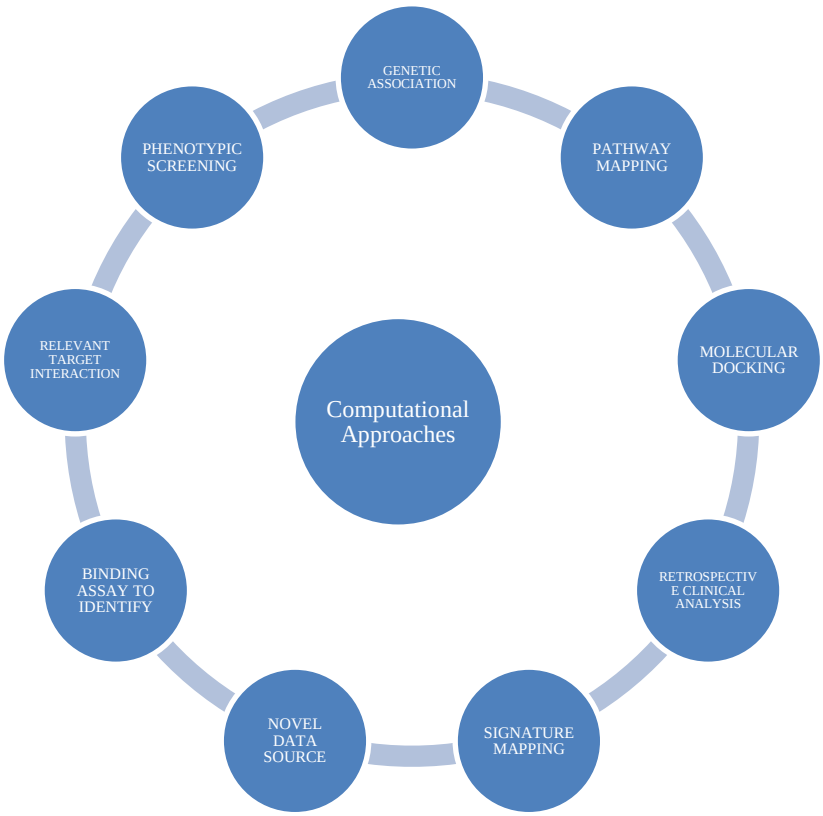

Fig.3 Computational Approaches

GENETIC ASSOCIATION

By utilizing insights from genetic data, genetic association studies in drug repurposing can be a potent method to find new uses for already-approved medications.

Here is a quick rundown of how this operates:

1. Knowing How to Repurpose Drugs Finding new therapeutic applications for medications that were initially created to treat different conditions is known as drug repurposing. By using this method instead of creating new medications from scratch, time and resources can be saved.(22)
2. Research on Genetic Associations These investigations look at the connection between illness characteristics and genetic changes, such as single nucleotide polymorphisms, or SNPs. Through the identification of genetic markers linked to various diseases, researchers can identify possible targets for medication intervention.(23)
3. Linking Genetics to Drug Action Research on genetic associations can reveal: Disease Mechanisms: By identifying a disease's genetic foundation, one might potentially target ther apeutic targets and uncover underlying biological mechanisms.
4. Drug Targets: Prexisting medications that impact a disease pathway may be repurposed if genetic var iations are discovered to affect it.
   Patient Subgroups: More individualized treatment plans may be guided by the identification of peopl e whose genetic profiles indicate will benefit from a certain medication.(24)
5. How It Operates Determine Genes Associated with Diseases: Genetic data is used by researchers to determine the genes linked to a certain condition. Match Genes with Drug Targets: Find out whether these disease-associated genes or their pathways are impacted by the medications already on the

market.

Preclinical and Clinical Testing: To assess the drug's efficacy for the new indication, test the repurposed medication in appropriate models or clinical trials.[25]

6. Illustrations and Uses Cardiovascular Disease: Drugs that alter cholesterol levels have been repurposed due to genetic variations linked to lipid metabolism.
7. Cancer: By identifying genetic abnormalities in cancer pathways, current medications may more effectively target those pathways.
8. Difficulties: Complexity of Genetic Data: It's not always easy to understand how genetics and medication responses combine, and it can be difficult to interpret genetic correlations. Validation: To ensure that medications repurposed for new applications are effective, findings from genetic investigations must undergo thorough validation in preclinical and clinical settings. In general, the incorporation of genetic association data into drug repurposing procedures exhibits potential to expedite the creation of novel medicines and enhance patient outcomes.[26]

1. PATHWAY MAPPING

Using genetic disease data, known metabolic or signaling pathways, and protein interaction networks, this technique reconstructs disease-specific pathways and pinpoints the critical target for medication repurposing. They assist in reducing the size of broad signaling networks from many proteins to a small number of proteins (or targets) in a particular network. In order to identify new targets for repositioning medications, these techniques leverage network biology or pathway analysis techniques to identify critical pathways from disease-related genetic, genomic, proteomic, and metabolic data. For instance, the signaling pathways of metastatic subtypes of breast cancer are difficult to decipher from the gene signatures or the current pathways for breast cancer.[27]

2. MOLECULAR DOCKING

Molecular docking is a versatile tool used to predict the geometry and to score the interaction of a protein in a complex with a small-molecule ligand. Docking can be performed by docking a known drug into a large set of different target structures or a database of approved medications into one intended target. Molecular docking is a convenient and fast method to screen large libraries of ligands and targets, with a full range of sampling options.[28] 3D structures of the target shall be available through crystallography, nuclear magnetic resonance (NMR), or comparative models to carry out docking. Drawbacks and limitations include approximate scoring function and imperfect binding mode placement algorithms. However, these problems can be overcome by post processing docking results with more accurate scoring functions and other criteria.[29]

3. RETROSPECTIVE CLINICAL ANALYSIS

The origin of using sildenafil for erectile dysfunction is widely recognized to have come from the side effects noted during a Phase I human volunteer trial, originally intended for angina treatment. This is a case of drug rescue, where a developmental drug that did not work for its original purpose is now being used for a different purpose, in contrast to drug repurposing, which involves finding a new use for a drug that is already on the market.(30) Unintended outcomes may occur with any scientific pursuit, and we must remain vigilant about their potential. Previously, unsuccessful clinical trials usually resulted in discontinued drug development projects and significantly influenced the total expenses of new

pharmaceutical products. Therefore, it is important to regularly conduct comprehensive analysis of data from clinical trials to uncover any unforeseen discoveries that may facilitate the advancement of the experimental drug for a specific group of patients or for a new purpose. We offer instances of repurposing drugs through analyzing past clinical trials and propose that this approach offers a hopeful method for salvaging unsuccessful drug candidates in development. We argue that the obstacles for successful drug rescue are not as severe as those for drug repurposing. We suggest practical methods to extract data from previous clinical trials, for either new uses or for particular groups of patients.[31]

4. SIGNATURE MAPPING

Methods for repurposing drugs based on signatures use gene signatures obtained from disease omics data, either with or without treatment, to identify new off-target or disease mechanisms. Publicly accessible databases, such as CMAP Connectivity Map and CCLE Cancer Cell Line Encyclopedia, provide access to genomics data for analysis. Signature-based techniques aid in the discovery of previously unknown functions of molecules and medications. Utilizing computational methods involves mechanisms at the molecular level, such as genes that undergo significant changes.[32]

5. NOVEL DATA SOURCES

This study utilized data obtained and cleaned from common databases like PubChem, InterPro, UniProt, and DincRNA, which was originally sourced from Liang et al. This dataset contains three different types of drug feature matrices, along with an integrated similarity matrix and a drug-disease association matrix, each with the following characteristics: Chemical compositions of medications were acquired from the PubChem database. Information on gene characteristics related to the target proteins was gathered from the InterPro database. 3D and spherical shapes of target proteins were obtained from UniProt database. Genes associated with each disease were retrieved from the DincRNA database.[33] Analyzing web articles related to each disease helped extract semantic characteristics of diseases. The drug-disease association matrix was acquired from research done by Liang et al. Datasets utilized in this research and defined as previously mentioned can be examined in the reference, displaying the quantity of each data within the corresponding category. In order to enhance the efficacy of the proposed approach, a different drug attribute related to the side effects of the drug has been computed as well. Additionally, adverse reactions of every medication in the SIDER repository were obtained and changed into a format that can be utilized. It is important to mention that the disease-related matrices mentioned earlier were not readily accessible. Thus, the combined matrix referred to in Liang et al, has been utilized.[34]

6. Binding Assay To Identify drug repurposing

Identifying both intended and unintended targets of chemical probes across the system helps enhance knowledge about their therapeutic promise and potential risks, speeding up and reducing the uncertainty in the drug discovery journey. Due to the expensive nature of experimental profiling of all potential drug-like compounds, computational models provide a methodical approach to direct mapping endeavors. These models indicate the most powerful interactions for additional experimental or pre-clinical assessment in both cell line models and patient-derived material.[35] Regions included Here, the authors emphasize the importance of network-based machine learning models in predicting new compound–target interactions for both target-based and phenotype-based drug discovery. Although they are currently utilized primarily to enhance experimentally mapped compound-target networks for drug

repurposing, such as expanding the target range of already approved drugs, network pharmacology methods could also propose completely unforeseen and innovative investigative tools for drug development.

Expert opinion: Despite the evidence from previous studies showing the capability of network-centric modeling methods in pinpointing potential compounds and targets in disease networks, there are still several obstacles to overcome. Specifically, these obstacles involve integrating the cellular environment and genetic makeup into disease networks for better targeted predictions, and ensuring prediction models are realistic for drug discovery and therapy.(36)

7. Relevant Target Interaction

Discovering medications that can interact with a particular target to produce a desired medical result is a crucial achievement in the field of targeted therapy drug development. Hence, it is crucial to not only discover new connections between drugs and targets, but also to determine the nature of the drug interaction in drug repurposing research. An approach for drug repurposing was suggested for predicting new drug-target interactions (DTIs) and the type of interaction they cause. The approach relies on exploring a diverse graph that combines drug-drug and protein-protein similarity networks, along with confirmed drug-disease and protein-disease connections. To obtain suitable features, the three-tier mixed graph was transformed into low-dimensional vectors through node embedding techniques. The issue of predicting DTI was defined as a task of classifying multiple labels and classes to identify drug actions.(37) DTIs were identified by combining drug and target vectors from graph embedding in pairs, which were then fed into gradient boosted trees for classification, training a model to anticipate the interaction type. After confirming the predictive capabilities of DT2Vec+, a thorough analysis of all unidentified DTIs was carried out to anticipate the level and nature of interaction. In the end, the model was utilized to suggest potential approved medications for targeting cancer-specific biomarkers.(38)

8. Phenotypic Screening drug repositioning:

The key to a successful beginning the lack of success in target-based drug discovery, which relies on biased hypotheses limited by our current knowledge, gives a strong reason for considering a different method. Although the industry is currently focused on target-based and hypothesis-based drug discovery, it is worth mentioning that several new drugs have been discovered outside of this paradigm in recent years.

An approach to phenotypic screening that is not driven by a hypothesis would appear to ignore proper scientific methodology. However, the majority of cases where new uses for current compounds are discovered actually involve 'on-target' effects. The surprising discovery in biology was due to the compound's modulation of a specific molecular target it was expected to affect, rather than interacting with a different target.(39) Contrast between conventional drug discovery process and drug repurposing Drug discovery in the traditional sense is a process that is intricate, time-consuming, risky, and expensive. Typically, it takes 10 to 15 years and costs billions of dollars to bring a new drug to the market. Drug repurposing is a different method from the conventional drug development process, which aims to lower expenses, minimize failure rates, and accelerate time to market by identifying new uses for current medications. Repurposing drugs involves using existing drugs for different purposes, which has several benefits compared to creating new drugs from scratch, as these already-established drugs have been shown to be safe for human use.(40)

Significance of DRUG REPURPOSING

Utilizing existing drugs offers a major benefit in reducing both the cost and time needed to bring a product to market compared to traditional drug discovery methods. Information such as pharmacokinetics, toxicology, and safety data obtained through the conventional discovery method. This method offers numerous important advantages: The man was walking his dog in the park. Paraphrased: The man strolled with his dog in the park. Development time and costs are decreased by repurposing existing drugs, which have already been extensively

tested for safety and effectiveness, compared to creating new drugs from the beginning.(41)

CNN reported that the new technology will revolutionize the way we communicate. Established Safety Record: Medications with a history in the market have been thoroughly researched, leading to a clear understanding of their safety profiles. This decreases the chances of negative consequences while repurposing.

Quick Development: If a medication proves effective for a different illness, it has the potential to be released faster than a new medication, which is important in dealing with immediate health emergencies. Broadening Treatment Choices: Repurposing can offer fresh therapeutic options for diseases with scarce treatments, possibly enhancing patient results. People often say that taking risks is necessary for growth and success in life.(42) Dealing with Unmet Needs: It can assist in discovering remedies for uncommon or intricate illnesses in cases where creating new medications could be economically impractical or excessively time-consuming.

The cat finally caught the mouse after chasing it around the house for hours. Accelerated Progression: Repurposed drugs can advance through clinical trials faster than new drugs due to their prior safety and efficacy testing. In general, repurposing drugs provides a practical method for improving medical treatments and making the most of current resources.(43)

ADVANTAGES

The process of repurposing drugs, also known as drug repositioning, provides numerous benefits. Decreased Development Time: Established medications have already been extensively tested for safety and effectiveness, potentially leading to a shorter timeframe for developing new uses. Reduced Expenses: With the drug already developed, costs for preclinical and early clinical trials are greatly lowered. Proven Safety Record: Extensively documented drug safety can decrease the chances of unforeseen side effects.

Current Manufacturing Processes: The establishment of manufacturing processes and quality control measures enables a more efficient production of repurposed drugs. Quick access to the market can be achieved more rapidly with repurposed drugs, leading to earlier availability of new treatment choices. Possibility of Finding New Applications: Drug repositioning has the potential to reveal new medical uses for current drugs, potentially meeting unmet medical demands.(44)

DISADVANTAGES

Despite its potential benefits, repurposing drugs has various drawbacks. Limited Effectiveness Information: Drugs used for a different purpose may not work as well as they do for their

original use, and their effectiveness for the new purpose may not be well-known. Safety Issues: Medications that work well for treating one illness could cause unexpected reactions or complications when used for another illness. Regulatory hurdles: Obtaining approval for a new indication can be intricate

and may necessitate conducting more clinical trials, resulting in time and cost implications. Challenges related to intellectual property: The patents for the drug's original use may have ended, reducing the attractiveness for companies to invest in repurposing initiatives. Insufficient information regarding dosage and administration: The best dosage or route of administration for the new usage may not be clear, which could result in less than ideal treatment results. Market competition: It may exist if there are already established treatments for the new indication, which could limit the market potential for the repurposed drug. Insufficient knowledge in the field of science: The basic reasons why a medication is effective for a new use may not be completely known, making it challenging to plan and develop treatments.[45]

Conclusion

Drug repositioning or repurposing, a fascinating strategy in pharmaceutical R & D which ensures finding new applications to already well-investigated drugs aside from their actual therapeutic indications. This method has a number of benefits:

1. Time and Money Saved: Repurposed drugs have already been tested for safety (through human or animal trials) this means repurposing a drug rather than inventing one from scratch saves money in bringing the expensive process of pre clinical trial to market. This can speed the availability of new treatments to patients.
2. Lower Risk: Existing drugs have known side effects and safety profiles, so they pose a lower risk for patients than new-to-the-hospital compounds.
3. Treatment development options: Drug repositioning has the possibility of creating treatment solutions for diseases having fewer therapeutic alternatives such as rare and/or complex diseases.
4. Increasing drug use: Through repurposing, the value of existing drugs can be increased by providing new uses that can be introduced into markets with medicinal benefits. But reuse also has several disadvantages: Intellectual property rights: Patents and IP can create financial incentives to implement projects and reuse them.
5. Science and Law: Even if a new drug is very safe to use, it still needs to undergo proper scientific testing for legal approval in a very difficult environment.
6. All reuse research: Funding for reuse research is a serious problem. It becomes more difficult in cases where the patent-off determines the combination to reduce the product.

   In general, drug reform is a powerful and cost-effective strategy to promote treatments that benefit patients and the healthcare system. This is an opportunity to use existing knowledge and structures to develop new medicines that address unmet medical needs by improving treatment programs.

REFERENCES

1. Goel G. Drug Repurposing: A strategic approach to addressing unmet medical needs. International Journal of Pharma Professional's Research (IJPPR). 2024;15(2):136-53.
2. Ng YL, Salim CK, Chu JJ. Drug repurposing for COVID-19: Approaches, challenges and promising candidates. Pharmacology & therapeutics. 2021 Dec 1;228:107930.
3. Somolinos FJ, León C, Guerrero-Aspizua S. Drug repurposing using biological networks. Processes. 2021 Jun 17;9(6):1057.
4. Otero-Carrasco B, Ugarte Carro E, Prieto-Santamaría L, Diaz Uzquiano M, Caraça-Valente Hernández JP, Rodríguez-González A. Identifying patterns to uncover the importance of biological pathways on

known drug repurposing scenarios. BMC genomics. 2024 Jan 9;25(1):43.
5. Pan X, Lin X, Cao D, Zeng X, Yu PS, He L, Nussinov R, Cheng F. Deep learning for drug repurposing: Methods, databases, and applications. Wiley interdisciplinary reviews: Computational molecular science. 2022 Jul;12(4):e1597.
6. He H, Duo H, Hao Y, Zhang X, Zhou X, Zeng Y, Li Y, Li B. Computational drug repurposing by exploiting large-scale gene expression data: Strategy, methods and applications. Computers in biology and medicine. 2023 Mar 1;155:106671.
7. Sadeghi SS, Keyvanpour MR. An analytical review of computational drug repurposing. IEEE/ACM transactions on computational biology and bioinformatics. 2019 Aug 12;18(2):472-88.
8. Saha S, Chatterjee P, Nasipuri M, Basu S, Chakraborti T. Computational drug repurposing for viral infectious diseases: a case study on monkeypox. Briefings in Functional Genomics. 2024 Jan 5:elad058.
9. Park K. A review of computational drug repurposing. Translational and clinical pharmacology. 2019 Jun 1;27(2):59-63.
10. Pinzi L, Bisi N, Rastelli G. How drug repurposing can advance drug discovery: challenges and opportunities. Frontiers in Drug Discovery. 2024 Aug 20;4:1460100.
11. Katukam LP, Padakanti AP, Chella N. Drug Repurposing: History, Significance, Benefits, Approaches, and Challenges. Drug Repurposing: Innovative Approaches to Drug Discovery and Development. 2024 Aug 29:1-1.
12. Goel G. Drug Repurposing: A strategic approach to addressing unmet medical needs. International Journal of Pharma Professional's Research (IJPPR). 2024;15(2):136-53.
13. Kulkarni VS, Alagarsamy V, Solomon VR, Jose PA, Murugesan S. Drug repurposing: an effective tool in modern drug discovery. Russian Journal of Bioorganic Chemistry. 2023 Apr;49(2):157-66.
14. Selvaraj G, Kaliamurthi S, Peslherbe GH, Wei DQ. Application of artificial intelligence in drug repurposing: A mini-review. Current Chinese Science. 2021 Mar 1;1(3):333-45.
15. Chowdhury N, Nanjappan SK. Role of Artificial Intelligence (AI) and Machine Learning (ML) in Drug Purposing. InDrug Repurposing: Innovative Approaches to Drug Discovery and Development 2024 Aug 29 (pp. 43-56). Singapore: Springer Nature Singapore.
16. Xia Y, Sun M, Huang H, Jin WL. Drug repurposing for cancer therapy. Signal Transduction and Targeted Therapy. 2024 Apr 19;9(1):92.
17. Kumbhar NM, Aparna MA, Nimal SK, Shewale P, Barale S, Gacche R. New targets for old drugs: drug repurposing approach for accelerating the drug discovery engine with minimum financial inputs. InNew Horizons in Natural Compound Research 2023 Jan 1 (pp. 315-349). Academic Press.
18. Senanayake SL. Drug repurposing strategies for COVID-19. Future Drug Discovery. 2020 Mar 25;2(2).
19. Pushpakom S, Iorio F, Eyers PA, Escott KJ, Hopper S, Wells A, Doig A, Guilliams T, Latimer J, McNamee C, Norris A. Drug repurposing: progress, challenges and recommendations. Nature reviews Drug discovery. 2019 Jan;18(1):41-58.
20. Kang H, Pan S, Lin S, Wang YY, Yuan N, Jia P. PharmGWAS: a GWAS-based knowledgebase for drug repurposing. Nucleic Acids Research. 2024 Jan 5;52(D1):D972-9.
21. Johnston KJ, Cote AC, Hicks E, Johnson J, Huckins LM. Genetically regulated gene expression in the brain associated with chronic pain: Relationships with clinical traits and potential for drug repurposing. Biological psychiatry. 2024 Apr 15;95(8):745-61.

22. Xie C, Zhang Y, Zhu B, Yang L, Ren J, Lang N. Exploring the pathways of drug repurposing and Panax ginseng treatment mechanisms in chronic heart failure: a disease module analysis perspective. Scientific Reports. 2024 May 27;14(1):12109.
23. Kumar S, Kumar S. Molecular docking: a structure-based approach for drug repurposing. InIn Silico Drug Design 2019 Jan 1 (pp. 161-189). Academic Press.
24. Kar A, Paramasivam B, Jayakumar D, Swaroop AK, Selvaraj J. Drug Repurposing for Thioredoxin Interacting Protein Through Molecular Networking, Pharmacophore Modelling, and Molecular Docking Approaches. Letters in Drug Design & Discovery. 2024 Sep 1;21(11):2111-34.
25. Mishra AS, Vasanthan M, Malliappan SP. Drug Repurposing: A Leading Strategy for New Threats and Targets. ACS Pharmacology & Translational Science. 2024 Apr 1;7(4):915-32.
26. Tan GS, Sloan EK, Lambert P, Kirkpatrick CM, Ilomäki J. Drug repurposing using real-world data. Drug discovery today. 2023 Jan 1;28(1):103422.
27. Shukla R, Henkel ND, Alganem K, Hamoud AR, Reigle J, Alnafisah RS, Eby HM, Imami AS, Creeden JF, Miruzzi SA, Meller J. Signature-based approaches for informed drug repurposing: targeting CNS disorders. Neuropsychopharmacology. 2021 Jan;46(1):116-30.
28. Pinzi L, Bisi N, Rastelli G. How drug repurposing can advance drug discovery: challenges and opportunities. Frontiers in Drug Discovery. 2024 Aug 20;4:1460100.
29. Park K. The use of real-world data in drug repurposing. Translational and Clinical Pharmacology. 2021 Sep;29(3):117.
30. Mujwar S, Kumar V. Computational drug repurposing approach to identify potential fatty acid-binding protein-4 inhibitors to develop novel antiobesity therapy. Assay and Drug Development Technologies. 2020 Oct 1;18(7):318-27.
31. Singh J, Quadir N, Vashishtha S, Chakraborty A, Alam A, Kundu B, Ahmad U, Sundar D, Ehtesham NZ, Hasnain SE. Polypharmacological repurposing approach identifies approved drugs as potential inhibitors of Mycobacterium tuberculosis. Biochemical Journal. 2023 Jul 17;480(14):1079-96.
32. Loscalzo J. Molecular interaction networks and drug development: Novel approach to drug target identification and drug repositioning. The FASEB Journal. 2023 Jan;37(1).
33. Parisi D, Adasme MF, Sveshnikova A, Bolz SN, Moreau Y, Schroeder M. Drug repositioning or target repositioning: A structural perspective of drug-target-indication relationship for available repurposed drugs. Computational and Structural Biotechnology Journal. 2020 Jan 1;18:1043-55.
34. Lu Y, Hu Y, Li C. Drugclip: Contrastive drug-disease interaction for drug repurposing. arXiv preprint arXiv:2407.02265. 2024 Jul 2.
35. Schuler J, Falls Z, Mangione W, Hudson ML, Bruggemann L, Samudrala R. Evaluating the performance of drug-repurposing technologies. Drug discovery today. 2022 Jan 1;27(1):49-64.
36. Schcolnik-Cabrera A, Juárez-López D, Duenas-Gonzalez A. Perspectives on drug repurposing. Current Medicinal Chemistry. 2021 Apr 1;28(11):2085-99.
37. Hechtelt Jonker A, Day S, Gabaldo M, Stone H, de Kort M, O'Connor DJ, Pasmooij AM. IRDiRC drug repurposing guidebook: making better use of existing drugs to tackle rare diseases. Nature Reviews Drug Discovery. 2023 Dec;22(12):937-8.
38. Preiss J. Using word evolution to predict drug repurposing. BMC Medical Informatics and Decision Making. 2024 Dec;24(Suppl 2):114.
39. Dixit A, Mishra AK, Singh CV, Gupta VK, Pandey D. Drug repositioning: current scenario and future prospective for rewriting saga of drug development. International Journal of Research in Medical

Sciences. 2024 Apr;12(4):1334.
40. Kasetti K, Kondabathula SK, Koneti SS, Korlepara S. An Overview of Drug Repurposing. Journal of Pharma Insights and Research. 2024 Feb 28;2(1):169-75.
41. Barinda AJ, Hardi H, Louisa M, Khatimah NG, Marliau RM, Felix I, Fadhillah MR, Jamal AK. Repurposing effect of cardiovascular-metabolic drug to increase lifespan: A systematic review of animal studies and current clinical trial progress. Frontiers in Pharmacology. 2024 Jun 20;15:1373458.
42. Lopes RM, Souza AC, Otręba M, Rzepecka-Stojko A, Tersariol IL, Rodrigues T. Targeting autophagy by antipsychotic phenothiazines: potential drug repurposing for cancer therapy. Biochemical Pharmacology. 2024 Feb 21:116075.
43. Natsheh IY, Alsaleh MM, Alkhawaldeh AK, Albadawi DK, Maisa'M D, Shammout MJ. The dark side of drug repurposing. From clinical trial challenges to antimicrobial resistance: analysis based on three major fields. Drug Target Insights. 2024 Jan;18:8.
44. Miera-Maluenda M, Pérez-Torres M, Mañas A, Rubio-San-Simón A, Butjosa-Espín M, Ruiz-Duran P, Seoane JA, Moreno L, Segura MF. Advances in the approaches used to repurpose drugs for neuroblastoma. Expert Opinion on Drug Discovery. 2024 Sep 13:1-1.
45. Barjasteh AH, Al-Asady AM, Latifi H, Al Okla S, Al-Nazwani N, Avan A, Khazaei M, Ryzhikov M, Nadi-Yazdi H, Hassanian SM. Maximizing Treatment Options for IBD through Drug Repurposing. Current Pharmaceutical Design. 2024.