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Drug Repurposing: Innovative Approaches and Clinical Impact

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Abstract: Drug repositioning, or drug repurposing, is a purposeful mission that involves coming up with new therapeutic applications for existing drugs. This is the case since the method utilizes existing safety data and pharmacokinetic attributes in a more cost effective and less time-consuming manner. In this paper, we look at the principles, approaches, achievements and obstacles of medication repurposing with the aim of arguing in favor of its use as a means of fostering therapeutic innovation and improving the efficiency of drug development processes. Drug repositioning is also referred to as drug repurposing and is defined as finding new therapeutic indications for a drug which was developed or approved for other indications. Clinical data, which has been verified for use, is used in this method to accelerate the finding of breakthrough treatments.

Key words: In Silico Drug Discovery,High-Throughput Screening,Clinical Trials,Drug Repositioning,Computational Medicine.

Introduction:

The discovery of drugs is a long, expensive, and time-consuming process. While the traditional drug development process involves numerous phases of clinical trials, including much preclinical research, the entire process is over a decade old and costs billions of dollars. Drug repurposing, therefore, is an attractive alternative: using drugs already approved for one indication to explore their new therapeutic uses. This strategy can speed up the development process by using existing data, thus reducing the risk and cost of bringing a new treatment to market. The process of bringing a new drug to market is notoriously lengthy and expensive, usually taking over a decade and billions of dollars. Drug repurposing offers a promising alternative by identifying new applications for already-approved drugs. This approach reduces the time and costs involved in the discovery of new therapeutic drugs while simultaneously reducing the issues associated with drug safety and toxicity. The process of drug repurposing, sometimes called drug repositioning, can be envisioned as the reframing of already known drugs for new uses not originally intended by their original design. Lately, a heightened interest towards this strategy is observed because it is regarded as an extreme shift in the trajectory of pharmaceutical research and development and is perceived to suit medicine's requirements much better compared to traditional methodologies in drug discovery. The benefits of drug repurposing are multifold and, many of them are even related to one another. First, drugs that are already in the market have already been tested and therefore have built a safety net which in turn reduces the battle that is involved with regulatory processes. In addition, there is an enormous database of clinical studies that have been performed and marketed drugs that can assist in the development of new models for the mechanisms of action. Advantages of big data analytics also added up to the light, in which researchers have developed many computational methods promoting drug advancement from a clinical viewpoint. Big data analytics may serve as an effective means to implement drug repurposing in response to urgent public health threats such as emerging infectious diseases, chronic diseases, and rare diseases. This approach was recently tested by scientists when the world was combating COVID-19: within just a short time, scientists were able to discover already known viral treatments that could be applied against the virus and thus, demonstrated the importance of and feasibility of this approach. This paper aims to critically evaluate some of the latest strategies in drug

repurposing, look for illustrative examples, and discuss the challenges and opportunities associated with one of the most revolutionary approaches of medicine today. Since the best avenues for clinical advancement are derived from the repositioning of already approved drugs, the ecological consequences of future medical treatments can be mitigated simultaneously.

Principles of Drug Repurposing:

1. Mechanism of Action: Drugs often modulate many biological networks. Elucidation of drug's major and minor modes of action helps define new therapeutic potential. Monoxides, the antihypertensive agent, was redeployed topically in treating alopecia by virtue of this effect on hair growth. Drugs often target numerous biological pathways. The knowledge about the mechanism of action of the drug provides one with a foundation to make plausible predictions about a new therapeutic area. Sildenafil, a medication initially designed to treat angina, was later repurposed for the treatment of erectile dysfunction through its effects on blood circulation.

2. Bioinformatics and Data Mining: The combination of bioinformatics and computational biology has improved medication repurposing. Data mining by using electronic health records, omics information, and clinical trial databases may show previously unknown drug-disease relationships. These may suggest new uses for existing medications. Improvements in bioinformatics allow researchers to mine existing data for new therapeutic targets. Scientists can find new uses for current medications by integrating data from genomic, proteomic, and pharmacological studies.

3. Pharmacovigilance and Clinical Observations: The clinical practice and post-marketing surveillance observations usually reveal some un-expected benefits of drugs previously approved. Clinical observations and epidemiological studies found potential in using the antidiabetic drug, metformin, for the treatment of cancer. Clinical observations usually reveal un-expected effects of treatment. The most common examples are the use of metformin for the treatment of cancer, which was discovered in diabetic patients who were on the drug to control their glucose levels.

4. Regulatory and market considerations: Repurposing medicinal products frequently entails managing intellectual property and regulatory barriers. Understanding market dynamics and exclusivity extensions can help determine the sustainability of a repurposing project.

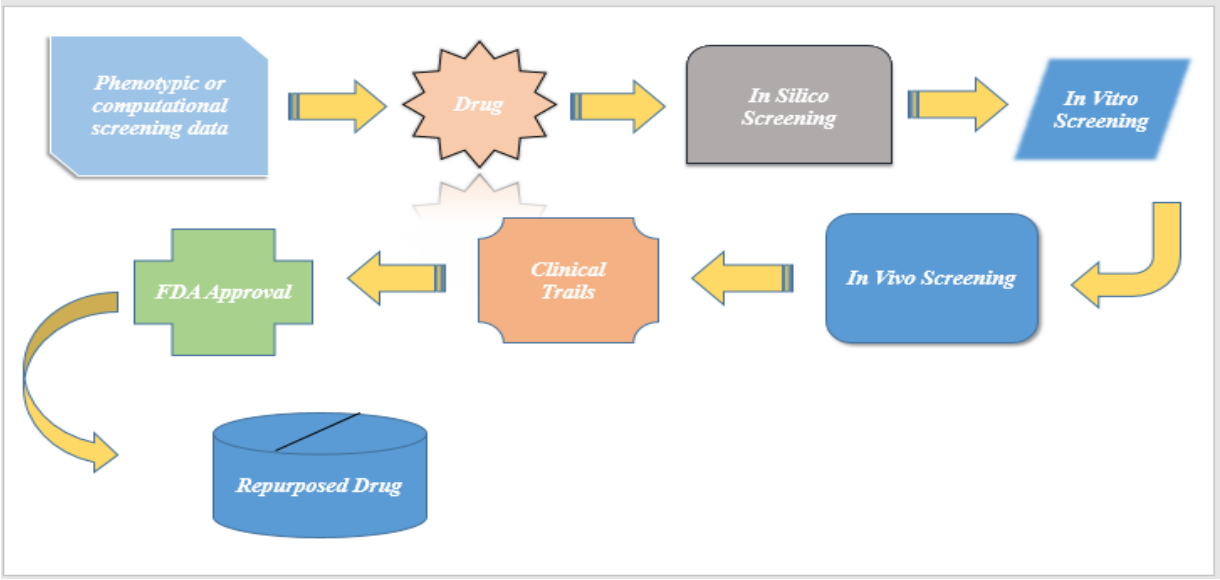
For example, a patent strategy for making a generic drug for a particular use is needed to make it profitable.

Methodologies in Drug Repurposing:

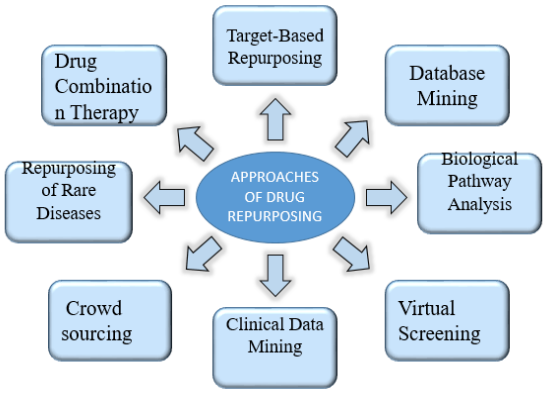
1. **High - Throughput Screening (HTS)*:*** HTS testing includes the use of various target compounds against varying parental strain libraries in the search of new or better applications. This is a useful method in the rapid identification of drugs with new specificities. For instance, existing drugs have been screened against numerous vectors by virus hunting has quite been interesting. HTS involves testing large libraries of drugs against a variety of biological targets to identify new interactions. This approach can rapidly identify potential new uses for existing drugs.

2. **Computational Models:** computer-aided molecular modelling, molecular docking techniques, network pharmacology, and systems biology seems to be in tandem with the efforts of providing new targets for the drugs and drug interactions. These models give a pictorial expression of what a drug specific molecule would do in a living biological context that allows to probe for abandoned opportunities for repurposing the drug.

3. **Clinical Trials:** Originally commenced on the patients for whom these drugs were designed, payer-provided or repurposed medicines are often quite ready to enter phase clinical trials for their new conditions. Owing to the prior safety data, they do not need to complete the new drug application process and instead go fast tracked. For instance, the antimalarial over-the-counter medicine has a brand name of hydroxychloroquine and has undergone trials for application in the infection of Coved 19.



Steps involved in drug repurposing.



Approaches of drug repurposing.

1. Drug repositioning utilizing computer technologies

We employ computer algorithms for drug repurposing, along with bioinformatics, to structure data in the existing medicines database which cover their chemical, biological, genomic, and clinical facets. The aim of the research is to identify existing medicines that could potentially be used for treating new diseases.

2. Assessing the image of functional genes

This strategy looks at the effect of certain drugs in changing the gene expression of particular cell type. It will change the expression so that it will enable treatment for the disease ascribed to it and so this drug needs to be investigated further.

3. Database Mining and Virtual Screening

It is possible to search large chemical and biological files for therapies that were not specifically designed for particular conditions. This can include virtual screening, which is performed by 'imposing' the molecular model of the drug on the structure of the new disease.

4. Target-Based Repurposing

This concerns determining novel targets (proteins, enzymes, receptors, etc.) within the scope of the disease and finding out whether there are existing drugs which act on these targets. The attempt is to evaluate if a known drug can bind to the same target in the newly defined illness.

5. Drug Combinations

In lieu of a monotherapy approach, therapy categorization utilizes different therapeutic drugs meant for other medical conditions. Repurposing works by merging strategies so that the efficacy of the drug increases while the adverse effects decrease.

6. Clinical Data Mining

This approach reframes analysis from already conducted clinical trials and patient files to find evidence of activities or behavioural consequences that may point to a drug being useful for another ailment. This can also encompass investigation of secondary indications of a drug, that is the use of a medication for a condition other than that for which it was approved by the health authorities.

7. Biological Pathway Analysis

Drugs exert their actions through target biological pathways, for instance, the signalling pathways for growth, immune signalling, etc. Looking at the pathways for the condition of interest can enable the scientists to find other drugs that could potentially be used in novel ways to treat the condition.

8. Dilapidated or Neglected Disease Reassignment

Studies concentrate on poorly marketed diseases like neglected tropical diseases and uncommon inherited disorders. In a number of instances, already existing medications may have some action on these diseases, and so repurposing drugs can help paraphrase treatment approaches.

9. Open Data Portals and Crowdsourcing

The use of crowdsourcing platform is highly deemed as significant when it comes to assisting open data initiatives. Various institutions like educational agencies, government bodies, and NGOs seek the help of volunteers via social media to examine the information and records gathered. In the end, these organizations not only foster trust by promoting transparency but also enhance productivity and acquire new means of information to analyse. As referenced by Tan and El Azab, it is possible to design open data platforms aimed at harnessing public passion where citizens act as micro monitoring agents for governmental and other institutions.

Drug Repurposing vs. Traditional Drug Discovery

The traditional approach to drug discovery involves de novo identification and of new molecular entities (NME), which include five stages: discovery and preclinical, safety review, clinical research, FDA review, and FDA post-market safety monitoring. On the other hand, there are only four stages in drug repositioning, which include compound identification, compound acquisition, development, and FDA post-market safety monitoring. In recent years, the use of *in silico* techniques along with the application of structure-based drug design (SBDD) and artificial intelligence (AI) technology has further accelerated the drug purposing process. Drug repositioning has several advantages in comparison with traditional approaches to drug discovery. When comparing with traditional drug discovery program, a significant reduction of the time spent in R&D can be observed. In traditional approach, it is estimated that 10–16 years are spent for the development of a new drug, while in the drug repositioning estimated time is between 3 and 12 years. A repositioned drug does not require the initial 6–9 years typically required for the development of new drugs by traditional process, but instead enters directly to preclinical testing and clinical trials, thus reducing the overall risk, time and cost of development.

TRADITIONAL DRUG DISCOVERY	DRUG REPURPOSING
● Drug Discovery start from scratch, finding completely new drugs.	• In Drug Repurposing a drug that's already been used for something else is taken and try it for a new disease.
● It takes many years (usually 10-15 years or more).	• It's much faster (usually 2-5 years).
● High risk because you're starting from zero and don't know if it will work.	• Lower risk because the drug has already been tested for safety.
● Very expensive, costing billions of dollars.	• Cheaper, since the drug already exists and has been tested.
● Traditional Drug Discovery we have to go through the whole approval process (safety, effectiveness, etc.).	• The process can be quicker since the drug is already approved for something else.
● It can create totally new treatments or ideas.	• It's more about rethinking how an existing drug could be used in a different way.

Success Stories:

Relaying Some Real-World Cases of Drug Repurposing for The Target.

1. Thalidomide: This was a drug manufactured and marketed for use as a sleeping potion; it was removed from the market as research showed it caused severe abnormalities during pregnancy. Thalidomide was eventually used to treat multiple myeloma and leprosy where it showed the effects of reducing inflammation and power on the immune system. These new phenomena and effects transformed understandings in drug repurposing.

2. Sildenafil: Originally, sildenafil was intended for treatment of angina, but then its vasodilator effects were used for management of erectile dysfunctions. This was owing to the drug's ability to increase blood supply through the inhibition of phosphodiesterase type 5.

3. Ruxolitinib: As a Janus kinase (JAK) inhibitor, ruxolitinib was designed for the treatment of myelofibrosis but has since found new use in the treatment of COVID-19. This repurposing took advantage of its activity to modulate the immune response in severe forms of the disease.

4. Doxycycline: Due to antibiotic activities, doxycycline has been studied for repurposing in the treatment of diseases like cancer and cardiovascular disorders evidenced by anti-inflammatory properties. It has been established that doxycycline may have an anti-tumor effect and limit the vasculature hardening process.

Some examples include:

Drug	Primary Indication	New Indication	Date of Approval
Zidovudine	Cancer	HIV/AIDS	1987
Sildenafil	Angina	Erectile dysfunction	1998
Thalidomide	Morning sickness	Erythema nodosum leprosum	1998
Minoxidil	Hypertension	Hair loss	1988
Celecoxib	Pain and inflammation	Familial adenomatous polyp	2000
Atomoxetine	Parkinson disease	Attention deficit hyperactivity disorder	2002
Duloxetine	Depression	Stress urinary incontinence	2004
Rituximab	Various cancers	Rheumatoid arthritis	2006
Raloxifene	Osteoporosis	Breast cancer	2007
Fingolimod	Transplant rejection	Multiple sclerosis	2010
Duloxetine	Analgesia and depression	Premature ejaculation	2012
Topiramate	Epilepsy	Obesity	2012
Ketoconazole	Fungal infections	Cushing syndrome	2014
Aspirin	Analgesia	Colorectal cancer	2015
Raltegravir	HIV	Metnase; adjuvant therapy in cancer	2007
Cyclobenzaprine	Skeletal muscle relaxant	Serotonin syndrome	1977
Benzbromarone	Gout	Antibacterial	1970S
Mometasone furoate	Seasonal allergy	Adjuvant therapy in cancer	2005
Ivermectin	Antiparasitic agent	Treatment for COVID-19, scabies	1981
Metformin	Type 2 diabetes treatment	Cancer treatment, anti-aging	1957
Prednisolone	Anti-inflammatory, immunosuppressant	Treatment for various autoimmune diseases	1955
Clofazimine	Antimicrobial	Treatment for COVID-19	1969
Propranolol	Beta-blocker for hypertension	Anxiety, migraine prevention	1964
Hydroxychloroquine	Antimalarial	COVID-19, autoimmune diseases	1955
Dexamethasone	Inflammation, allergies	COVID-19	2020
Colchicine	GOUT	Cardiovascular disease	2020
Baclofen	Muscle relaxant	Alcohol dependence	1977
Topiramate	Epilepsy	Migraine prevention	2004
Atorvastatin	Hyperlipidemia	Cancer, Alzheimer's prevention	ONGOING
Tamoxifen	Breast cancer	Infertility (off-label)	Not approved formally
Naltrexone	Opioid addiction	Alcohol dependence, weight loss	1994

CLINICAL IMPLICATIONS :

1. The speed with which drugs can be developed and approved

Repurposed drugs do not need to undergo human safety trials so they can skip over initial phase trials which further aids in development time.

Example: Thalidomide use in leprosy and multiple myeloma came about after it was hypothesized that it could also be used during and after chemotherapy.

2. Cost-effective Analysis

As compared to developing a new drug, repurposing existing drugs is significantly more affordable.

Example: Accompanying metformin with cancer therapy has been tried a lot because the drug is inexpensive and safe.

3. Additional treatment for under provisioned complicated and orphan diseases.

Very few, if any, rare illnesses have any FDA approved medications. This is because the potential return from investment in drug development is very low.

Example: Eflornithine, an anti-cancer drug, was adapted to treat shades of eflomithine for sleeping sickness.

4. Responding to Antimicrobial Resistance

Infection which is resistant to antibiotics can be tackled with drugs which are not classified as antibiotics but have some antimicrobial activity.

Illustration: The antipsychotic drug Thioridazine has been studied for its efficacy on multidrug resistant tuberculosis.

5. Repurposing a drug addresses the specific therapeutic requirement on the basis of the molecular and genetic architecture.

Illustration: The use of PARP inhibitors Olaparib for neoplasms of the breast and ovary with BRCA mutations.

6. Adaptation to Modern Outbreaks

Use of non psychotropic medications for treatment of severe infections during epidemics can be done through repurposing.

Illustration: Remdesivir was developed for Ebola but has subsequently been used to treat COVID-19.

Challenges:

Even if drug repurposing seems promising, it is not free of challenges:

1. **Regulatory Hurdles:** The logic of a clinical study to be performed with these medicines will purpose other than clinical care. Such authorities want evidence to be given if the purpose is changed so that new health hazards might not be invited.
2. **Funding and Investment:** Some companies that invest in repurposing projects have an easier time comparing the drug in question when it is off patent. On the other hand, the problems can be dealt with by forming partnerships with universities, industry, and the government where they can pool their resources and expertise.
3. **Clinical Trial Design:** Determining key issues of endpoints and identification of the eligible population for repurposed patients reminds one of constructional characteristics of clinical trials. These trials are trained on how the drug has been promoted for a new indication to guarantee reasonable safety of the patients.

Conclusion:

Drug repurposing represents a valuable strategy in modern drug development, offering a pathway to accelerate therapeutic discovery and reduce costs. Repurposing drugs is a crucial component for modern drug development because it accelerates the discovery of therapies and lowers the costs of the primary scope. By extending processes on already available drugs, researchers are able to extract other functions which the current information does not cover. The other issues aside, the accomplishments of drug repurposing are signifying with great clarity that this approach has the potential to change the ways in which new therapies are developed and allocated. Undoubtedly, more focus on technology and data analysis will help make the drug repurposing processes more focused and efficient. Drug repurposing enables scientists to address a wider range of diseases, including rare and novel diseases, in a much quicker and cheaper way. Researchers save time on the lengthy traditional drug creation process since the drugs are already known to be safe. Thanks to the advancement of AI and other high throughput screening technologies, re-medicating today is possible. These innovations allow the detection of pressing health problems to be addressed far more quickly.

Some of the prominent but problematic realities of drug repurposing, such as regulations and the limited strength of clinical proofs are its enormous opportunities. Solving these issues will depend on the effective collaboration of the researchers with the regulatory bodies, and the pharmaceutical industry.

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