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A REVIEW ON DRUG REPURPOSING

J.Suma, B. Swapna, M. Gurava Reddy, Prof. Dr. K. Venugopal
Krishna Teja Pharmacy College, Chadalawada Nagar, Renigunta Road
Tirupati -517506

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Abstract:
Drug repurposing is a promising approach to identify new therapeutic uses for existing drugs, potentially speeding up the process of drug development by bypassing early stages of preclinical testing. Drug repurposing holds the potential to bring medications with known safety profiles and pharmacological properties of existing compounds, reducing the time and cost required to bring treatments to market. Recent advances in bioinformatics, computational biology, and machine learning have expanded the potential of drug repurposing, allowing researchers to mine vast datasets for drug-disease relationships and molecular targets. Methodologies behind drug repurposing, including in silico methods, high-throughput screening, and network pharmacology, as well as successful case studies where repurposed drugs have been approved for new indications. Drug repurposing represents a vital avenue in drug discovery, offering innovative solutions to unmet medical needs and facilitating more efficient therapeutic development. For example, mifepristone, an anti-progesterone medication initially prescribed for abortion, showed promise in treating psychotic depression in experiments.

Keywords: *Drug Repurposing, Drug Screening, Target-Based repurposing, Artificial intelligence, Drug developments, Therapeutic innovative, Safety monitor, Clinical studies.*

Corresponding author:
J.Suma,
Krishna Teja Pharmacy College,
Chadalawada Nagar, Renigunta Road
Tirupati -517506

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INTRODUCTION:

Drug repurposing is also known as rediscovering, repositioning, reprofiling, or redirecting [1]. The process of using a current medication or medication candidate for a new medical illness or treatment for which it originally was not recommended is known as drug repurposing [2]. When compared to de novo drug discovery, drug repurposing gives advantages such as reduced early drug development requires, reduced costs and time, and a greater success rate in approval by regulators [3]. By reducing the high financial cost, prolonged development time, and increased failure risk, innovative medication repositioning techniques may be used instead of standard drug discovery programs. It offers a lower chance of failure, as typical drug discovery programs have a failure rate of about 45% because of safety or toxicity problems [4]. Drug repurposing studies are utilized for delivery, combination, dosage, old/banned/withdrawn formulations, approved/failed drugs, and current candidates. any medication that has been approved by the Food and Drug Administration for reuse [5].

Drug repositioning has also made use of a variety of computational techniques, which have increased the effectiveness and success rates of this strategy. Since natural products have been used for thousands of years for a variety of medical purposes, they hold great promise for drug repositioning. For instance, the dosage needed for new medical indications is often different from the original disease for which it was intended [6]. Drug repurposing techniques discover medicines' hidden therapeutic potential through a variety of methodologies, such as computational tools, clinical trials, and other *in vitro* techniques. For examples Thalidomide and Metformin [7].

Different types of drug repurposing:

Drug repurposing/repositioning becomes different from drug reformulation, repositioning, and combination [8].

Drug Repositioning

It discovers new uses for a drug that has previously been used for other purposes. For example, mifepristone, an anti-progesterone medication initially prescribed for abortion, showed promise in treating psychotic depression in experiments [9].

Drug Reformulation

It has to do with taking a drug in a different way. The new formulation might be administered through a different route or through the same old route. Making ketamine for nasal and sublingual administration to treat MDD is an example of medication modification [10].

Drug Combination

It describes the combination of two or more drugs to increase safety and effectiveness. For instance, seniors with MDD and cerebrovascular loss benefit more from antidepressant drugs when the medication and antidepressants are used together. Furthermore, antidepressant responses are improved when anti-inflammatory medications are taken with antidepressants. For examples Lisinopril + Hydrochlorothiazide (Zestoretic) [11].

Drug repurposing steps:

They are four steps in drug repurposing

- Compound selection
- Compound acquisition
- Drug development
- Post market safety survey

Compound selection(1.2years):

When selecting a potential medication for a specific medication target in the human body, compound identification is performed.

Compound acquisition(0-2years):

(0–2 years) collecting licenses for an original treatment proposal

Drug development (1-5years):

Preclinical, phase 1 or phase 2 drug research may be the foundation for this step. Analysis of the available data is required to ensure that pharmaceuticals are both safe and effective.

FDA Post market safety survey:

The FDA maintains vigilant tabs on the safety of all medications and devices after they are made affordable to the general population [12].

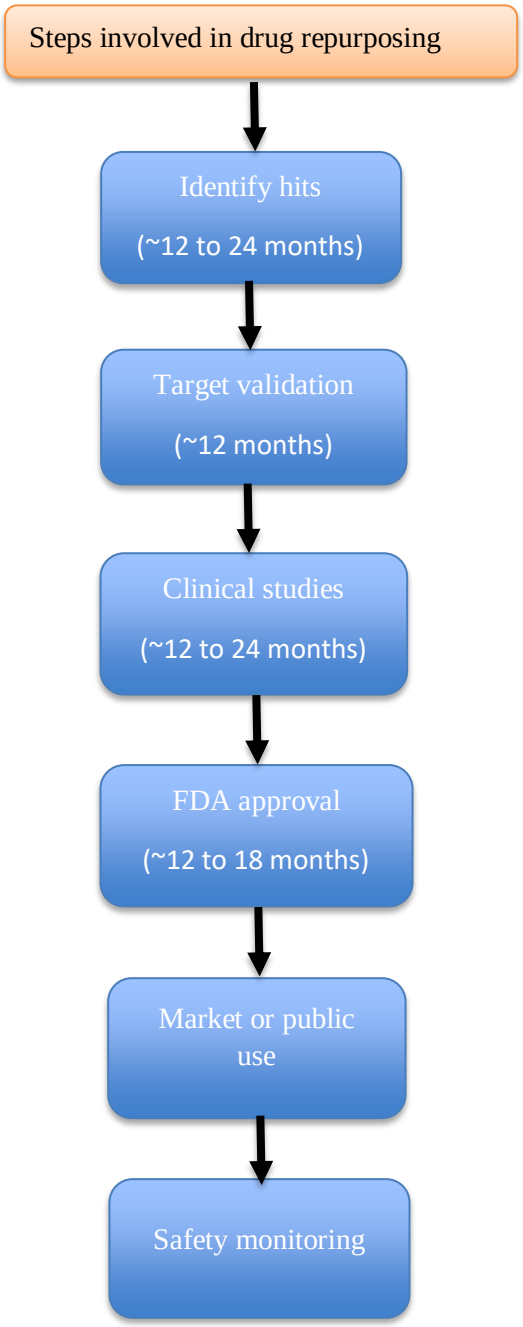

Fig. (1): Steps involved in drug repurposing

Stages and procedures involved in repurposing drugs. Repurposing old medications to treat new ailments is the concept behind drug repurposing. There are only five steps in the drug repurposing technique as opposed to the six in the traditional method: find hits, target validation, clinical research, FDA submission, and public usage. It omits the traditional methods of discovery and development and expedites the release of the potential medication into the market. It shortens the medication development process from around 15 years to about 4–5 years [13].

Strategies for drug repurposing:

This method typically makes use of open-source drug databases. Included are data from clinical experiments, primary and translational research,

anecdotal stories about off-label uses, and other published human data material. Researchers methodically attempt to determine when medications interact with protein targets using bioinformatics tools and artificial intelligence systems. A potent technology with several benefits, such as speed and lower expenses, is *in silico* medication repositioning **[**14**].**

Knowledge-Based Methods:
These techniques use cheminformatics or bioinformatics techniques for incorporating into drug-repositioning studies the available data on drugs, drug-target networks, chemical structures of drugs and targets, clinical trial data, FDA approval labels, indicating or metabolic pathways, and so forth [15]. Knowledge-based approaches have information that is sufficiently detailed compared to blindfolded or target-based approaches. Since the existing information may be used to anticipate, it can be used to predict new and unknown mechanisms, such as new disease biomarkers, unknown drug targets, and unknown drug-drug similarities. Knowledge-based approaches increase prediction accuracy by incorporating well-known information into the medication repositioning procedure [16].

Target-Based Methods:
Target-based drug repurposing involves high-throughput and/or high-content screening (HTS/HCS) of therapeutic compounds given certain proteins or biomarkers of interest and then in silico screening of drug compounds from drug libraries using techniques like docking or ligand-based screening. Target-based repurposing directly connects targets with disease mechanisms, increasing the chance of drug discovery significantly in comparison to blinded search or screening, which does not employ biological or pharmacological knowledge during screening. The ability of the target-based strategy to screen almost all therapeutic compounds with known chemical structures is its main advantage [17].

Pathway- Based Methods:
Pathway-based drug repurposing identifies the similarity or relationship between illness and medicine by using information from protein-interaction networks, metabolic pathways, and signalling pathways. Examples of disease-specific pathways are recreated utilizing omics data extracted from human or animal patients to provide fresh targets for repositioned drugs [18].

Target mechanism-Based Methods
Target mechanism-based drug-repurposing combines data on protein interactions, treatment omics, and signalling networks to find alternative therapeutic mechanisms of action**.** These techniques have the benefit of being able to uncover mechanisms that are directly relevant to the treatment of a particular disease in addition to discovering processes connected to disease or drugs [19].

Signature-Based Method
Leveraging gene signature information gleaned from illness omics data, signature-based repurposing aims to identify novel disease processes or off-targets. By comparing gene expression profiles between drugs and diseases, this method looks for inverse drug-disease connections [20]. These techniques offer a rare chance to customize treatments for highly stratified patient groups by matching these large, fingerprints of disease to substances that have similar effects [21].

Phenotype-based Methods
The phenotypic data is now available as a new medication repositioning source. In the past several years, systems techniques have been using this kind of data more and more to identify genetic characteristics linked to human illnesses. By using natural language processing techniques on electronic health records (EHRs), more adverse drug events that were missed during medication development can be discovered. For instance, it was discovered that metformin may be used to treat cancer because to EHR mining [22]. In addition, growing conditions, viral multiplicity of infection (MOI), and the quantity of infections supplied per cell during infection can all affect the phenotypic result [23].

TABLE 1: Examples of Drug Repurposing

Drug	Original indication	New indication
Amphotericin B	Fungal infection	Leishmaniasis
Aspirin	Pain	Parkinsons disease
Sildenafil	Hypertension	Erectile dysfunction
Thalidomide	Morning sickness	Leprosy
Orlistat	Obesity	Cancers
Metformin	Anti diabetics	Pancreatic cancer stem cell
Tamoxifen	Breast cancer	Anti-bacterial activity

Opportunities in drug repurposing:

- Accelerated Development Timeline
- Existing safety Data
- Cost Efficiency
- Rare and Neglected Diseases
- Combination Therapies

Accelerated Development Timeline:
Repurposing drugs can significantly cut down on the time needed to produce them as opposed to beginning from begin with novel compounds [24]**.**

Existing safety Data:
Repurposed medications reduce the need for comprehensive safety testing because of the wealth of safety data obtained during previous use [25].

Cost Efficiency:
Since drug repurposing reduces many of the costs related to preclinical testing and early-stage research, it may be less expensive than creating new medications [26].

Rare and Neglected Diseases:
Repurposing facilitates the use of current medications that could not otherwise be developed, which could lead to possible treatments for uncommon and neglected diseases [27].

Combination Therapies:
Repurposed medications can be used in combination with current treatments to improve the range of medical disorders that can be treated [28].

CONCLUSION:

Drug repurposing, the strategy of finding new therapeutic uses for existing drugs, offers a promising pathway to accelerate drug discovery, reduce costs, and minimize the risks associated with traditional drug development. By leveraging the established safety profiles, pharmacokinetics, and manufacturing processes of known drugs, repurposing allows researchers to bypass some of the early, high-risk phases of drug development. The success of drug repurposing is evident in multiple therapeutic areas, including oncology, infectious diseases, and neurology, where new applications for existing drugs have significantly impacted patient care. Additionally, advances in data science, bioinformatics, and systems biology have enhanced the ability to identify potential candidates for repurposing through methods such as computational modelling, artificial intelligence, and high-throughput screening.

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