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Review Article

Drug repositioning: current scenario and future prospective for rewriting saga of drug development

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ABSTRACT

Drug development is a process that demands huge investment of resources and time with only 1 drug candidate successful in reaching market among 10,000 screened taking time duration of 10-15 years and millions of dollars. This high attrition rates discourage investors and researchers. The pharmaceutical industry is shifting its attention away from *de novo* drug research and towards discovering novel targets and indications for already-approved drugs. In order to accelerate the drug development process with reduced risk of failure and relatively lower costs, pharmaceutical companies have adopted drug repositioning as an alternative. Therefore, a good strategy for drug development would be drug repositioning or drug repurposing, which is to identify, investigate, and exploit new therapeutic uses of already-available, on-market drugs, as well as those that have been withdrawn due to toxicities or that remain on shelves in various stages of development. The outbreak of SARS-COV-19 shows that humanity is constantly vulnerable to epidemics and new microbial attacks and that there is no time to create disease-specific therapies. Consequently, it would seem advantageous to use what is already accessible. Novel therapeutic indications that have previously been approved by the market can reduce investment costs significantly in terms of money, resources, and most importantly, time, as long as they meet PKPD and toxicity standards. Sponsors and pharmaceutical corporations get enthusiastic about additional investments and initiatives related to drug development as a consequence. The upcoming therapeutic revolution, especially with the aid of artificial intelligence, is indicated by the successful applications of several already-available drugs against COVID-19 and the various phases of repurposed drugs against TB, colorectal cancer, Alzheimer's disease, cervical cancer, and Parkinsonism.

Keywords: Drug development, Drug repurposing, Drug repositioning

INTRODUCTION

The amount of input (investment) made and the amount of output (new pharmaceuticals and financial profits) obtained are the key indicators of pharmaceutical productivity and growth.

The last ten years have seen a sharp decline in productivity and results, despite a sharp rise in pharmaceutical investments.

This issue of declining productivity has been compounded by several causes, including rising competition from generic drugs, global pressure related to increased costs in the development process, extremely conservative regulatory regimes, and a lack of innovative breakthroughs. Consequently, the pharmaceutical industry is shifting its attention away from de novo drug research and toward discovering novel targets and indications for already-approved drugs.[1]

The drug development and discovery process is divided into three main stages: the preclinical stage, where compounds are tested in vitro and in animal models to obtain pharmacokinetic, pharmacodynamic, and toxicity data; the clinical development stage, where drug candidates are tested in human subjects as clinical trials to check their safety, efficacy, and adverse effects; and finally, the drug discovery phase, where new candidate compounds are screened based on their pharmacological properties.[2] In order to accelerate the drug development process with reduced risk of failure and relatively lower costs, pharmaceutical companies have adopted drug repositioning as an alternative. National Centre for Advancing Translational Services defines it as studying drug that are already approved for treating one disease or condition to see if they are safe and effective for treating another disease.

This approach involves exploring drugs that have been approved for use in treating other diseases, whose targets have already been identified, failed or idle drugs, i.e., finding new uses for old or failed drugs, since the lead compound in drug repositioning tends to be pharmacologically well understood as compared to the novel compound discovered by de novo method; this approach offers a significant reduction in the risks associated with drug development, such as better chances of getting drug to market at much reduced time and research and development cost, which is a win-win situation for manufacturers and consumers.[3,4]

Although the concept of drug repurposing is not new the way of implementing it is new. Repurposing has come a long way from a serendipitous eureka moment to a refined and rational approach, this explains the shift in attitude from Henri Laborit being termed a medical heretic for Laborit cocktail to one in three of all new drugs introduced in 2009 being repurposed. This approach to drug discovery is also known as redirecting, reprofiling, repurposing, rescuing, or therapeutic switching of drugs.[5,6]

WHY THIS PARADIGM SHIFT?

The life cycle of new drug development is a lengthy process that includes three broad steps, namely drug discovery, preclinical step, and clinical step. Even promising compound has a amount of uncertainty regarding its usefulness in human beings, as preclinical studies cannot always account for the physiological differences between human beings and animals. Consequently, the development of serious adverse events and decreased efficacy in human beings during clinical trials are two common reasons for a compound failing to reach the market. The average cost of introducing one new drug to the market in developed countries, including the cost of failures, has been estimated to be USD 1.24 billion.[7]

In addition, the time required to develop a new drug *de novo* varies between 10 to 17 years due to regulatory requirement.[8] A Tufts Centre for the study of drug development study has shown that for candidate drugs which entered the clinical development phase during 1999-2004, the likelihood of a compound eventually reaching the marketplace is only 16%.[9] The current pharmaceutical research and development (R&D) productivity is insufficient, with the regulatory authorities in developed markets approving 18 to 20 new drugs annually, despite current pharmaceutical industry research outlays of more than USD 50 billion per year. It has been estimated that only 3 in 10 new products generate revenues equal to or greater than average industry R&D costs.[10] In order to recover R&D costs as early as possible, sponsors are increasingly focusing on drugs to treat chronic and complex indications, such as cardiovascular, endocrine, psychiatric, and neurological disorders and cancers, while several other diseases that are economically small lags behind.[11] This productivity problem, along with worldwide pressure on prices, competition from generics, and ever-increasing regulatory challenges, has driven many drug companies to find new uses for existing drugs.

SOURCES OF REPURPOSED DRUGS

Based on given below listed sources the candidate drug can be chosen, but with options running in thousands it can be a tough task to choose a candidate, and running a hit-and-trial method for all the options for all the possible clinical scenarios will be a futile approach as it will beat the very purpose for what it was initiated i.e., to cut time and cost for drug development, but at the same time if drug candidates are not selected then the whole concept of drug repurposing would hit a dead end. Normally, drug repositioning identifies new indications for drugs that fall into the following categories.

Drugs whose mechanism of action is relevant to more than one disease entity, clinical development for the new indication and the original indication can be carried out simultaneously (development of duloxetine, a nonselective serotonin-reuptake inhibitor was simultaneously carried out for depression and stress urinary incontinence).[12]

Drugs that failed to demonstrate efficacy for a particular indication during phase II or III clinical trials but have no major safety concerns (more than 2000 compounds are lying idle at major pharmaceutical companies after failing phase II or III trials, and the industry shelves a further 150 to 200 compounds every year due to efficacy issue).[13]

Drugs that have been discontinued for commercial reasons.

Drugs that have been discovered, developed, and marketed in emerging markets but not launched in large Developmental drugs abandoned by academic institutions and public sector laboratories (lack of resources, expertise, and collaboration).[14]

To solve the selection criteria for repurposing two concepts are utilized to recognize the potential of a drug to become a candidate.[15] The first concept is the identification of a drug to interact with multiple targets relatable to multiple diseases. These additional targets, i.e., off-targets, can arise serendipitously through screening or observed side effects. In some cases, these secondary targets cause the drug to be labeled as 'dirty' for the specified indication due to the undesired side effects produced. However, a certain target can prove beneficial for a new indication. Where a drug is found to have beneficial off-targets, it can be known as being 'desirably promiscuous'. The second concept is identifying multiple diseases, where one target is relevant to the progression of them all. The discovery of these new indications often occurs from a known target-based screen of a library of established and/or shelved compounds such as the Johns Hopkins library.

METHODS OF REPURPOSING

There are several methods through which the repurposing of drugs is done.

Blinded search or screening methods

This type of method is based on blinded research without considering any known pharmacology or biological data and often results from serendipitous observations.[8] Blinded searches and screens have the advantage of flexibility associated with the application to a diverse number of target diseases. Between 1999 and 2009, around 34% of FDA-approved small molecules and biologics were identified via this method. Drugs repurposed beyond their labeled indications approved by the FDA using this method include sildenafil citrate for erectile dysfunction, rituximab for breast cancer, and etoposide for bladder cancer.[16]

Target-based methods

Target-based methods of drug repurposing involve high throughput screening (HTS) both, *in vivo* and *in vitro*, of drugs. The screening aims to identify a drug with a particular biomarker or protein of interest from a complex library of compounds. The likelihood of a successful discovery of a potential drug is much higher than with the blinded screening method as most of the targets will link directly to the mechanisms of disease. Target-based repurposing allows for large libraries of drugs or compounds to be screened efficiently within a few days. This method is particularly popular with research groups when attempting to develop new treatments.[17]

Knowledge-based methods

A bio- or chemo-informatics analysis is applied in a knowledge-based method of drug repurposing. The utilization of information is already available from clinical trial information, drug-target networks, identified chemical structures of drugs and their target, and pathways involved in the drug activity used in this method. Researchers using the knowledge-based method avail the published information to predict similarities in drugs and recognize potential new targets. This enables the identification of new targets for the drug, which would not be possible in the previous two methods. Drug repositioning has improved using this method as it is associated with a reduced failure rate especially if the drug has already been successful in gaining FDA approval.[18]

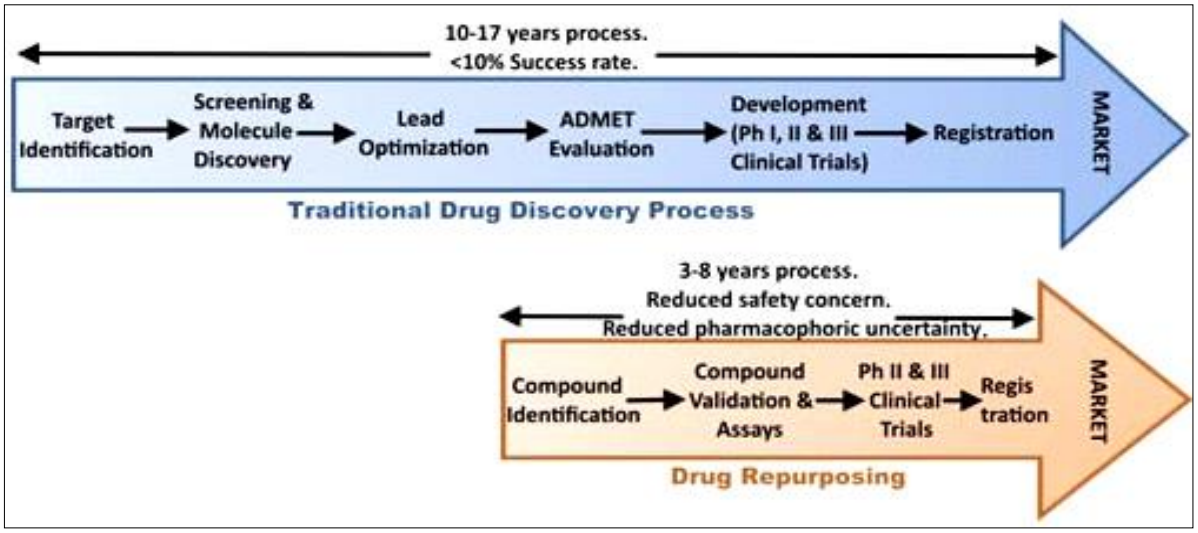

Figure 1: Depiction of traditional and repurposing process.[8]

Signature-based methods

Gene signatures derived from disease 'omics' data with or without treatments are applied in signature-based methods to find unknown off-targets or unknown disease mechanisms. The volumes of genomics data available are increasing exponentially with advances in microarrays and next-generation sequencing techniques. These advances are significant for the repurposing of drugs as genomic databases are continuously built upon. Unknown mechanisms of drugs can be revealed via this method. Computational approaches are particularly important in signature-based methods. Sirolimus was repurposed with this method for patients with acute lymphoblastic leukemia with dexamethasone resistance by linking diseases treated by drugs by using gene signatures.[19]

Pathway- or network-based methods

Similarly to signature-based methods, pathway- or network-based methods of drug repurposing utilize disease 'omics' data. In addition, this method uses available signaling or metabolic pathways and protein interaction networks to recreate disease-specific pathways that provide the key targets for repositioned drugs.[20] The main advantage of this method is the use of large amounts of diverse information to narrow general signaling networks to a specific network with few proteins/targets.

Targeted mechanism-based methods

Targeted mechanism-based methods identify unknown mechanisms of drug action by combining information based on protein interaction networks, signaling pathways, and treatment 'omics' data. This method proves particularly important in studies where patients can develop resistance to a drug after initial success indicating that successful drug treatment must also include studies of the mechanism of drug action allowing better drug targets to be identified.[21] The significant advantage of this method is the potential to identify the mechanisms related to the treatment of drugs in their specific diseases.

ADVANTAGES OF REPURPOSING DRUGS

It is attractive as an alternative to the current methods due to the huge reduction in time needed to achieve accreditation and introduce the drug into the market. There is great detail of pharmacokinetic and pharmacodynamic data already available with preclinical (failed or idle drug), multiple years of post-marketing data (approved drug) available, thus increasing safety at reduced cost.

Reduction in the time frame for drug development (3 year as compared to 12 years on average). This opens up new ray of hope for patients suffering from terminal cancer, orphan disease.

Reduces the number of animal sacrifices making it a more humane as well as economical approach.

Opens new avenues for rapidly emerging, re-emerging, neglected tropical diseases which are considered economically less significant by the pharmaceutical industry but are of great public health importance, especially in developing and underdeveloped countries.

The targets that are nodal points in general mechanisms such as cell division, autophagy, apoptosis, and metabolism can be subjected to therapeutic manipulation for various, sometimes clinically different endpoints.

This enables both pharmaceutical companies, non-commercial agencies (academic centers, public sector laboratories in developed and developing countries), and regulators to quickly and efficiently address medical needs that have continued to be unmet despite *de novo* drug discovery efforts.

Success rate is around 3 for every 10 drugs as compared to 1 for every 10000.[22]

Limitations of drug repurposing

Drug may show good efficacy for a new indication but at a much higher dosage than previously approved thus further needing phase-I trials and also high risk of failure over toxicity concerns.

One of the major challenges in drug repositioning is choosing the therapeutic target to prospectively test a drug of interest. Evidence suggests that a large number of drugs interact promiscuously with biological elements outside of their targets (off-target effects).

The focus is on certain disease areas that are economically lucrative, so, potential indications for drugs for other indications can go untested. Patent (pharmaceuticals) and intellectual property-related issues (academia) can play a major role in limiting the potential of repurposing a drug.

Repurposing relies heavily on systems-wide host response datasets, publicly available datasets of known drugs or small molecules, and computational approaches that are used to predict potentially effective disease-drug combinations, and as most of the publically available drug profiles have been obtained using cell lines as model systems, meaning that information related to intercellular mechanisms is not captured.

BARRIERS IN DRUG REPURPOSING

Lack of financial incentives

Repurposing offers a better starting point for new therapeutic potential but the financial gain is nowhere near what is offered by *de novo* drug discovery process as

they offer patent and exclusive market rights overcoming obstacles to repurposing for neurodegenerative disease.[23] Because many of the potential repurposing uses are already known in the scientific literature or clinical practice. Even though they have not been proven to work through clinical testing, they can no longer be patented, since there has already been public disclosure.

Undermines existing markets

Industry often avoids supporting the repurposing of generic drugs, even with the promise of novel and patentable new uses. If the repurposed drug works in the new disease indication using its available formulation and doses, there is no current method for the company to charge a higher price for the new disease indication, while patients continue to pay a lower price for the old disease indication. The low cost and wide availability of the repurposed drug can reduce a company's chance to profit from the repurposing, so they avoid getting started, even though it will help patients.

If the researchers get a patent for a repurposed indication of the generic drug; as it is widely available from many manufacturers, and the patient could be prescribed another manufacturer's drug, there is no extra profit to be made, even after holding the patent.

HISTORICAL BACKGROUND

Typhoid fever affected large numbers of French citizens in 1942 during the Second World War. Marcell Johnson was the physician who administered the sulfonamide antibiotics to these patients. What surprised him was that some of the patients had a drop in blood sugar, and a few of them even died away from hypoglycemic coma.[24] As a result, in 1946, sulfonamides were first commercially available as an anti-diabetic drug after several complementary studies about this phenomenon. Chlorpropamide and acetohexamide, the first-ever anti-diabetic drugs from this class, were released into the market four years later, in 1950.[25]

Although some historical examples exist, drug repositioning (also referred to as drug repurposing, reprofiling, redirecting, or switching, is a relatively recent concept that seems to have emerged in 2004 with an article by Ashburn et al who established an initial definition.[26] They defined drug repositioning as the process of finding new uses for existing drugs, sometimes but not necessarily when they fall into the public domain and become generic drugs.

Since then, the term drug repositioning has been expanded to cover drugs that were withdrawn from the market due to safety concerns as well as active substances that were toxic or inefficacious during the clinical phase of their development. However, drugs that haven't been subjected to clinical trials should not be included.[27]

The principle of drug repositioning excludes structural modification of the drug. Rather, it uses a new indication of the biological properties for which the drug has already received approval (perhaps by a different formulation, at a new dose, or via a new route of administration), or the property of a drug responsible for any adverse effects.[28]

Some of the significant historical events with respect to drug repositioning

Aspirin

Bleeding was a well-known aspirin adverse effect in 1891 then research was carried out until 1953, when it was hypothesized that aspirin would be an effective drug to prevent thrombosis. Complementary studies on aspirin's mechanism of action on arachidonic acid were conducted between 1973 and 1975, establishing aspirin as one of the most widely used and safest drugs for the treatment or prevention of thrombosis.[29]

Sildenafil

Sildenafil has been known as an inhibitor of phosphodiesterase (PDE) for the treatment of angina and coronary artery disease since PDE was discovered; however, the drug failed to complete the second stage of its clinical trial. Studies on the drug demonstrated the beneficial effects on erections in 1980, subsequently in 1988 the FDA approved sildenafil for the treatment for male erectile dysfunction.[30]

Thalidomide

Thalidomide was first marketed as a sedative and tranquilizer in 1975, however, it was recalled from the market shortly after due to a teratogenic incident that resulted in phocomelia in over 10,000 children across 46 countries. Subsequently, studies began to look into the teratogenic side effects; and it was accidentally found that the drug had some anti-cancer properties because of anti-angiogenic action. Thus, thalidomide is currently used to treat multiple myeloma and prostate cancer.[31]

Cyclosporine

A long-used antifungal drug, cyclosporine was isolated from a fungus in 1957. However, in 1976, Borel and colleagues identified its immunosuppressive action, which fundamentally transformed cyclosporine into a lymphocyte-specific immune-regulatory drug.[32]

Lithium

While working on the petalite, Weston made the first discovery of lithium. Other research conducted later in 1895 showed that it could dissolve urate stones in cases of gout. William Homond also noticed that when lithium was used to treat gout, mental patients' behaviors

improved. He initially believed it was the result of treating the gout encephalopathy. Later Australian psychologist John Kidd established the anti-maniac action of lithium in 1950.[33]

Drug repositioning during COVID era

WHO declared the coronavirus disease (COVID-19) outbreak as pandemic on 12 March 2020. With no vaccine or antiviral therapeutic agent available for COVID-19 treatment, there was an urgent need to identify novel measures for its treatment and prevention. Since vaccine development could take well over a year, and novel treatment even longer, researchers explored drug repurposing as an alternative. COVID disaster provided the opportunity and extensive work took place to repurpose the available drugs since there was immediate need and time constraint. This line of scientific research pursued to development safe and effective COVID-19 treatment.[34,35]

Several drugs were being investigated as COVID-19 treatments during the pandemic, including antiviral medications that had been developed or used as treatments for HIV/AIDS, malaria, severe acute respiratory syndrome (SARS), and Middle East respiratory disease (MERS). Some of these drugs have even moved into clinical trials.[36-38]

Overall, the methods of drug repurposing share a common sequential process consisting of analysis, hypothesis generation, and validation. No drug was proven to be safe and effective for treating COVID-19 with no FDA-approval for specifically treating patients with COVID-19.

Although reports have appeared in the medical literature and the lay press claiming successful treatment of patients with COVID-19 with a variety of agents. In the time of disaster, the following drugs were repurposed against COVID-19.

Chloroquine/hydroxychloroquine

Chloroquine is an anti-malarial medication that is also used against some auto-immune diseases. On 18 March, the WHO announced that chloroquine and the related hydroxychloroquine would be among the four drugs studied as part of the solidarity clinical trial. FDA authorized the use of hydroxychloroquine sulfate and chloroquine phosphate under an Emergency Use Authorization (EUA).

The treatment has not been approved by the FDA's clinical trials process. The CDC said that the use, dosing, or duration of hydroxychloroquine for prophylaxis or treatment of SARS-CoV-2 infection are not yet established. If chloroquine or hydroxychloroquine is used, clinicians should monitor the patient for adverse effects, especially prolonged QTc interval.[39,40]

Remdesivir

It was created and developed as a treatment for Ebola virus disease. No specific antiviral drug has been proven effective for the treatment of patients with severe coronavirus disease 2019 (COVID-19). Remdesivir (GS-5734), a nucleoside analog prodrug, has inhibitory effects on pathogenic animal and human coronaviruses, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in vitro, and inhibits Middle East respiratory syndrome coronavirus, SARS-CoV-1, and SARS-CoV-2 replication in animal models.[41]

Lopinavir/ritonavir or other HIV protease inhibitors

Lopinavir/ritonavir, a USFDA approved oral combination agent for treating HIV, demonstrated in vitro activity against other novel corona viruses. Early reports of lopinavir/ritonavir for the treatment of COVID-19 are mostly case reports and small retrospective, nonrandomized COHORT studies, making it difficult to ascertain the direct treatment effect of lopinavir/ritonavir.[42]

Ribavirin

Ribavirin, a guanine analog, inhibits viral RNA-dependent RNA polymerase used along with other combinations to treat chronic hepatitis C. Its activity against other nCoVs makes it a candidate for COVID-19 treatment. However, its *in vitro* activity against SARS CoV was limited and required high concentrations to inhibit viral replication, necessitating high-dose (e.g., 1.2 g to 2.4 g orally every 8 hours) and combination therapy.[43]

Azithromycin

It is an antibiotic used for the treatment of a number of bacterial infections. This includes middle ear infections, strep throat, pneumonia, traveler's diarrhea, and certain other intestinal infections. When azithromycin was added to hydroxychloroquine, the efficiency of SARS-CoV-2 elimination was significantly improved leading to a significantly more rapid virologic cure as evidenced by a negative nasopharyngeal PCR, and healing in COVID-19 patients.[44]

Ivermectin

Ivermectin is an FDA-approved broad-spectrum anti-parasitic agent that in recent years we, along with other groups, have shown to have anti-viral activity against a broad range of viruses *in vitro*.[45]

Favipiravir

Favipiravir, an RNA-dependent RNA polymerase inhibitor is also FDA approved drug originally indicated for influenza and is repurposed for COVID-19. A 14-day

regimen of FPV (dosage 1600 mg BID followed by 600 mg) combined aerosol inhalation of 5 million units of interferon-alfa cleared SARS-CoV-2 infection more rapidly than treatment with lopinavir–ritonavir (400 mg/100 mg) plus interferon-alfa combination therapy, according to an open-label RCT conducted by Cai et al.[46] This was demonstrated by notable improvements in chest imaging.[46-48]

Baricitinib

On May 10, 2022, FDA approved Olumiant (baricitinib) for the treatment of COVID-19 in hospitalized adults requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). An orally bioavailable inhibitor of Janus kinases 1 and 2 (JAK1/2), with potential anti-inflammatory, immunomodulating and antineoplastic activities. Typically used to treat autoimmune disorders such as rheumatoid arthritis.[32] Cytokines implicated in causing the cytokine storm like the IFN-γ, IL-6, have a JAK-mediated mechanism of action. IL6 is associated with JAK1, JAK2, and TYK2, whereas IFN-γ activity is mediated by JAK1/JAK2.[49]

Molnupiravir

Broad spectrum antiviral that induces RNA mutagenesis during viral replication. On 23 December 2021, FDA issued an EUA for emergency use of molnupiravir as treatment of mild-to-moderate COVID-19 in adults with positive results of direct SARS-CoV-2 viral testing, who are at high risk for progression to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate.[50]

Promising avenues towards novel therapeutic approach and effective strategy to accelerate drug discovery-future potentials

Drug repositioning is being continuously explored in the present scenario, and some of the results seem very encouraging. Quest for novel treatment modalities, and new drug development as well as patent protection and cost and time-saving factors makes it more favorable to the sponsor besides the investigator. Some notable developments are listed below.

Artificial intelligence in drug repositioning

The challenges and limitations of using a computational approach for drug repositioning have significantly decreased with the advancement of computational artificial intelligence. Artificial intelligence (AI) can be simply defined as the mimicking of human intelligence demonstrated by machines which entails reasoning, planning, learning, and perception to maximize the chances of achieving different goals under extreme load and urgencies like pandemics or diseases of unknown etiology.[51]

Although AI is a component of computer-aided drug design (CADD), drug discovery and repositioning have long benefited from this computational method. The prime machine learning (ML) theories have relied on AI integration for the intended interpretation of drug repositioning opportunities. These theories include logistic regression (LR), naive Bayesian classifier (NB), k-nearest neighbours (KNN) algorithm, multiple linear regression (MLR), Gaussian process, and many more. AI development and machine learning (ML) theory have led to the development of deep learning (DL) techniques, which support more robust data processing and reliable results in the shortest possible period of time with cost efficiency.[52]

New hope for orphan disease drug development

Orphan drugs development for orphan diseases has been made possible by drug repositioning. Research and pharmaceutical industries have overlooked orphan diseases since it may not be profitable to devote time and money to them. Drug repositioning may play a very crucial role so far therapeutic approach towards orphan diseases are concerned as it pulls the closer between the availability of drug treatment to diseases within a population. Repositioning of mifepristone for Cushing syndrome is worth mentioning in this regard.[53]

TB drug repurposing

TB continues to pose challenge in many developing nations like India claiming mortality and morbidity. The emergence of resistance has further worsened the management; therefore, the role of drug repositioning for TB seems promising. Metformin, celecoxib, and verapamil showing synergistic effects with existing TB drugs and statins (enhance autophagy and phagosome maturation) has been demonstrated. These findings are encouraging.[54]

Drug repositioning in oncology

Azithromycin, captopril, indomethacin, and propanolol have been demonstrated to be useful for colorectal cancer in various in vitro and in vivo studies.[55] Nelfinavir a protease inhibitor used against HIV found to be a potential candidate in preclinical studies against cervical cancer.[56]

CONCLUSION

Drug development is a process that demands huge budgets, extensive research, manpower and large scale of time. Despite rigorous efforts and resources, only a handful of eligible drug candidates reach phase III and eventually phase IV. Despite costs ranging from $150 million to several billions, consuming 10-15 years and

power, only 1 drug molecule reaches the market among 10,000 compounds screened. So, from an economical point of view, pharmaceutical companies and sponsors are reluctant because of high attrition rates. So, drug repositioning or drug repurposing that is to find explore and exploit the new therapeutic use of already available drug that is in market, or those withdrawal because of toxicities as well as those lying in shelves of different phases can be a suitable approach for drug development. Mankind is always at risk of epidemics and novel microbial attacks as evident with an outburst of SARS-CoV-19 with no time to develop disease specific interventions. Therefore, using what is already available seems to be beneficial. Since novel indications of drug that are already available in the market have clear toxicity and PKPD standards, investment in terms of economics, resources, and most important, time can be cut short to a great extent. This makes sponsors and pharmaceutical companies enthusiastic for further investment and initiatives towards drug development. Successful uses of many already available drugs against COVID-19 and, the success of different phases of repurposed drugs against TB, colorectal cancer, Alzheimer's disease, Cervical cancer, and parkinsonism indicate the impending therapeutic revolution, especially with the help of artificial intelligence. High-cost drugs against rare diseases may also be managed to mitigate adverse pharmacoeconomic impact by extensive drug repurposing research. Therefore, use of drug repurposing for novel therapeutic indications is an area of high potential that requires systematic and further attention.

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