Short review

Drug repurposing: An alternative drug discovery approach

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Abstract

There are 7000 identified rare diseases in which only 400 have a licensed treatment. As the drug discovery process is very lengthy and probability of failures are quite prominent, that's why scientists prefer drug repurposing approach to bypass the hectic, lengthy, unsure and much costly process of drug discovery. Thus, it shows a promising approach in drug discovery by identifying new therapeutic prospects for same old drugs. In spite of the stones to be turned, this approach is catching the eye of the scientists since last twenty years. Eventually in the present scenario where the whole world is being a prey to the unwanted guest of a contagious viral disease namely COVID-19, repurposed drugs brought a hope which are now showing very good efficiency in the covid-19 pandemic as well and they are playing the major role now in the treatment therapy. This review is focused on the basics of drug repurposing, the strategies involved, the downsides of it, and actually what makes it an alternative way from the drug discovery process.

Keywords: Drug repurposing, strategy, drug discovery.

Introduction:

Why restricting the usage of a drug into only one disease, when it can cure others too? Yes, the fundamental of Drug Repurposing is putting a drug into trial to check whether it is effective against other disease or condition for which it was not approved or not yet indicated. Discovering a new drug and introducing that to the market takes 10-15 years, with the expenses of 1-2 billion dollars; that too, with a 5% success rate. We know that the journey of a new drug discovery is very time consuming, too expensive and have prominent chances of failure. Whereas, the drug repurposing approach can put this whole process of drug discovery in fast track. This is possible because of the available in-vivo and in-vitro screening data, toxicity studies data, bulk manufacturing, formulation development and all pharmacodynamics and pharmacokinetics profiles of that FDA approved drug. A repurposed drug can be marketed within 3-5 years with a success rate of 3 in every 10 drugs discovered. A good amount of successes had been achieved; the most common includes slidenafil citrate (Viagra) which metamorphosed from a common antihypertensive drug to a treatment therapy for erectile dysfunction. Other examples include Thalidomide for leprosy and multiple myeloma, retinoic acid for leukemia [1], cycloserine, and ivermectin for tuberculosis, astemizole for malaria etc. [2]. Recently reported, various clinically approved drugs screened for covid-19, and scientists found that Teicoplanin being used for prophylaxis of serious infections showed better efficiency in inhibiting protease activity than other drugs in use, such as lopinavir, hydroxychloroquine, chloroquine, azithromycin, atazanavir etc. Thus this review discusses about drug repurposing, its strategies in brief and the challenges to be conquered. It also aims to get a clear idea about drug repurposing so that the actual facts and mere fictions can be differentiated.

Drug repurposing approaches:

As so far it is clear to us that, drug repositioning is completely dependable to the existing data available from existing drugs and diseases and the advanced computational abilities have given a wing to think out of the box and has help us to go deep in the versatility to develop computational drug repositioning approaches.

There are various approaches via which drug repurposing can be executed, i.e., binding assays, phenotypic screening, pathway based or network mapping, drug centric, target based, knowledge based, signature based (Table 2) [3]. Selection of suitable approach is a crucial step. Recently many drugs are getting repurposed for Covid19 treatment as they have showed anti-covid efficacy in in-vitro, preclinical and clinical trials.

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Received on 07 October 2020
Revised on 05 November 2020
Accepted on 07 November 2020
PHARMAWAVE 2020; 13:25-27.

Drug	Inhibition of viral incorporation into host cells	Inhibition of viral replication in the host cells	Modulation of immune response to viral infection	Effectiveness against virus
Hydroxycholoroquine	Yes	No	Yes	Probably effective in initial stage
Azithromycin	Yes	Yes	Yes	Probably effective in all stages
Doxycycline	Yes	Yes	Yes	Probably effective in all stages
Ivermectin	No	Yes	No	Probably effective in all stages
Remdesivir	No	Yes	No	Probably effective in all stages

Table 1: MOA of some anti-covid drugs [4]

Repurposing approach	Description
Binding assay	Docking and the molecular activity exploration of the ligands with assay components, receptors by the help of computational methods [3]
Phenotypic screening	Screening and evaluation of a large no of evolving drugs in various in-vivo and in-vitro models [5]
Pathway based / network mapping	Discovering drug-target or drug-disease relationships based on gene expression patterns, disease pathology and protein interaction [6]
Drug centric	Connecting known drug to a new target and predicting the new use. It involves molecular docking, pharmacophore modelling algorithm and detailed analysis of protein-ligand interaction profiles [7]
Target based	Identifying the new treatment based on the drugs' protein targets. It requires a deep analysis of the molecular interaction between the target and the disease [7]
Knowledge based	Connecting the dots of known information to predict the unexplored new indications with new biomarkers [5]
Signature based	Comparing the distinct characteristics or 'signature' of a drug against that of another drug or disease [8]

Table 2: Drug- Repurposing Approaches

Examples of such drugs include – Hydroxycholoroquine, Azithromycin, doxycycline Ivermectin, Lopinavir, Remdesivir, Favipinavir (considered the best candidate in covid treatment), Dexamethasone etc (Table 1) [3].

Challenges:

Some downsides to drug repurposing are also there as well, few of these are discussed below:

1. The dosage needed for the treatment of novel disease often differs from its 'repurposed' target disease. So the scientists have to start from Phase I of clinical trials which makes the process somewhat lengthy.

2. Successful repurposing is not only the end. For proper utilization of the repurposed drug, suitable drug delivery and efficient route of administration is crucial too. So, along with clinical criterias, formulation development and the route of administration must be kept in mind. Reformulation with right drug delivery device is especially necessary for local infections, so that drug intimacy to nearer tissues is less.

3. Repurposed drugs and their safety, efficacy, quality etc. parameters need establishment from previous data.

4. Patent right issues makes the process very much complicated as the drug repurposing area lacks legal experts in this field.

Conclusion:

Traditional drug discovery process is too expensive, too time consuming and have more failure rates. The coronavirus pandemic has taught us how important it is to be prepared for any biological mishap. Drug repurposing provides identification of new uses of old approved drugs thus making it time efficient. With increasing no of sudden emerging epidemics, viral and bacterial infections fast track discovery is always an added advantage. However, with the modern and target specific research we can hope that the limitations of drug repurposing can be overcome and we shall bring modern and efficient repurposed delivery systems and optimal strategies that must help us to achieve some more pebbles amongst the seashore of science.

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