Chapter

Reprofiling of Octogenarian Antiviral Agent: A New Avenue Venture to Discover Viral Infection

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Abstract

Identification of a new drug molecule to a new target, specifically viral, bacterial, and fungal infection, is the prime focus of time immortal. The tridiagonal practice of drug discovery for emerging viral infection turned out to be a new venture to combat the morbidly and mortality of recent pandemics due to viral, bacterial, fungal, infection and infestation, the emerging number of viral infections day by day, the targeted therapy with the gap in assessment lead to reprofiling or repositioning available FDA-approved formulation give promising drug candidate for various infection specifically the current scenario of antiviral drug-reprofiling through drug designing approach, the emergence of resistance to existing antiviral drugs and re-emerging viral infections are the greatest challenges in antiviral drug discovery. The reprofiling approach is a worthy strategy to get the potent antiviral in brief span of time to overcome the challenges in antiviral therapy. The present chapter will be another representing the most promising results of reprofiling (Repositioning or repurposing) approach in the treatment of various infectious diseases.

Keywords: antiviral, drug-resistance, re-emerging, viral infection, fungal infection, bacterial infection

1. Introduction

Drug Repurposing, repositioning and reprofiling is trending initiative adopted by the researcher to identify the new target with existing drug molecule, the chemotherapeutic intervention of antiviral drugs discovery, frequently unsynchronized with development and licensing of the new drug, diseased caused by the virous is not an exceptional way of treating with antiviral agents. COVID-19 was turnout to be the major pandemic of the 21st century which is highly contagious, with more the 200 million cases and 4.5 million deaths worldwide to date, this pandemic created

wreaked havoc in society with immense human suffering. In a race against time to stop the spread of the disease. Contemporaneous endeavor scientific research community put forth several active molecules which inhibit the SARS-CoV-2 infection within period. Based on the background of literature report viral entry and replication within the host of the cell involves multiple molecular factors associated with the host and virous both, among this important one is a Main protease (M^{pro}), which is also referred to as 3C-like protease (3C-L^{pro}). M^{pro} cleavage of the viral polyprotein PP1ab at 11 discrete sites (polyproteins encoded with Leu-Gly-fl-Ser/Gly/Ala as motif cleavage). After cleavage it released non-structural protein from replicase complex, which is essential for viral replication, the proteolytic cleavage inhibition can prevent SARS-CoV-2 replication inside the host cell, hence in antiviral drug discovery, the M^{pro} is a prime target against SARS-CoV-2. Beginning of the first case of COVID-19, intensive literature reviled that M^{pro} is prime suspect targeted with several drug candidates which include both ab initio designed as well as repositioning of drugs. Notable recent discovery reports on repositioning approach with electrophilic and noncovalent fragment screening against M^{pro} in combination with Mass spectrometry and X-ray crystallography found to be an excellent technique to figure out the active site as well as dimerization interface, several potent small-molecule inhibitors of SARS-CoV-2 M^{pro} were predicted in a recent year since the beginning of this pandemic outbreak with all-inclusive nature of work vindicated by the discovery of both mentioned above in the paragraph.

However, to be noted here, 12 antiviral drugs were approved by FDA in the USA till date, among these 8 are used to treat hepatitis C virus (HCV)-related pathologies and 2 are in the combination of anti-human immunodeficiency virus (HIV) agents. WHO

S.NO	PRECEDENCE	PITFALLS
1	Low cost and less time-consuming (essential for the development of drugs to treat neglected diseases)	Target identification can be circuitous, and identified drugs may show poly-pharmacology
2	Possibility to skip preclinical trials (no animal studies) and to directly enter phase 2 clinical trials	Due to the high doses employed ill the screenings, toxic drugs can be initially misidentified as active
3	Potential for combination strategies with the possibility to delay or reduce resistance associated with monotherapy	Effective concentrations are often higher than the plasma levels achievable in humans
4	Often analogy (together with pharmacological information) are already available for testing	Medicinal chemistry to design more potent analogy is not applicable without losing repurposing potential
5	Academic/small laboratories can be determinant in the drug-discovery process	Identified drugs are often under intellectual property and/or programs that make them unavailable or unattractive for other pharmaceutical companies that could take over the further development and costs of clinical trials
6	Formulations and manufacturing chains are already established for the large-scale production (launching costs are avoided)	

Table 1.
Precedence and pitfalls of a drug repurposing approach for antiviral drug discovery.

S.No	Library (Vendor)	Description
1	SCREEN-WELL FDA-Approved drugs Library (Enzo Life Sciences)	774 approved drugs
2	Library Of Pharmacologically Active Compounds (LOPAC, Sigma-Aldrich)	1280 bioactive compounds including FDA-approved drugs
3	Bioactive Compound Library (Selleck Chemicals)	>2000 bioactive compounds including FDA-approved drugs
4	Prestwick Library	1280 bioactive compounds including FDA-approved drugs and candidate drugs
5	Spectrum Collection (Micro-source)	2320–2560 bioactive compounds including FDA-approved drugs
6	UCSF Small Molecule Discovery Centre Library	2177 bioactive compounds including FDA-approved drugs
7	National Institute of Health (NIH) Clinical Collection Library and Chemical Genomics Centre (NCCGC)	>7600 bioactive compounds including FDA-approved drugs and candidate drugs

Table 2.
Small-molecule libraries used in antiviral drug repurposing.

dealing with the re-emerging viruses responsible for pandemic potential and alarming outbreak in recent years, which was still lacking specific treatment, such as Zika virus (ZIKV), Ebola Virus (EBOV), Middle East respiratory syndrome coronavirus (MERS-CoV), COVID-19, delta virus and nowadays the popular one OMICRON. The recent advancement in controlling this viral pathogen, drug discovery in the drug repurposing approach emerged as giving the old drug to new symptoms which unlock the unidentified molecular pathway with the target of intervention. Basically, this strategy was adopted to combat viral infectious disease, by integrating with combination with computational methods (in silico screening, mining of database with transcriptomic profile, etc. (**Tables 1** and **2**), and collective screening of small bioactive molecules.

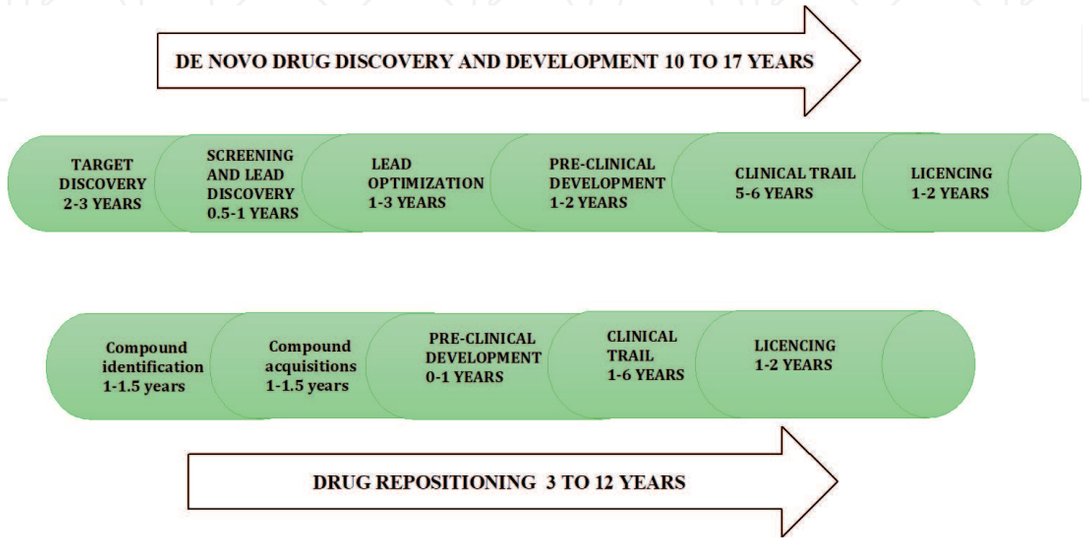

Figure 1.
DD and DR pathway.

Unquestionably a new drug development, in order to search for the lead molecule or pathway with biological screening that could be recycled against the viral pathogen, will be a competitive economic advantage, on the level of fundamental needs, indeed repurposed drugs quickly enter the clinical trial especially in case of viral disease lacking specified treatment (**Figure 1**) [1].

DR represents the constant source, to update and upgrade, cognition, in viral biology with available antiviral molecules hidden potentiality, which comes out as a tool to unlock the molecular mechanisms of virous replication and pathogenesis. No doubt, DR explore unidentified cellular pathway, turning them into target for the unexplored therapeutic strategy to available molecules which were not even under clinical trial. This book chapter is a unique and only compact reference to the researcher who are involved in reprofiling existing drugs, with promising drugs, meaningful results, and conclusions on the repurposing of antiviral drugs discovery [2].

2. Identification of antiviral drug repurposing

The drug repurposing approach is the process of finding new indications for existing FDA-approved drugs, is promising alternative to accelerate the process of drug development for infectious diseases and many other disorders and diseases, DR can be pursued by three possible strategies which are as follows.

Pre-clinical studies: This study was conducted in-vitro or in-vivo animal models before proceeding towards the clinical studies in the patient, whether healthy or sick. This also includes in silico in-vitro such as receptor-binding sassy to identify drug ligands and studies using cell line or tissue excised from animal or human representative of the specific disease, to examine how biological milieus of varying complexity response to the drug. In-vivo is also conduct in animals to test the biological parameters by sacrificing an animal for histological behaviors in rats or mice, here the available preclinical model can be used for repurposing to generate a hypothesis, this study is a preliminary study which is the base for setting up the clinical studies.

Clinical studies: Ranging from single-arm open-label **trial** to randomized controlled trial (RCTs) provides information on drug tolerance and efficacy, the notable interplay between regulatory and government bodies and research conducting clinical trial, as such entity have role in regulating clinical trial.

Observational studies: This study provides evidence to the findings it relays on data that is existing or data collected quickly in a prospective manner using previously established data system and conducted rapidly. The main aim of observational study evidence generation concerned drugs which use off-label for COVID-19 for example retrospective observational studies during the pandemic in Italy hospital. The limitation of observational studies is often based on secondary data. Refer **Figure 2**.

- **Same target-new virus:** These kinds of antiviral agents are having target-specific cellular function/pathway found to possess activity against other viruses (relies on homology and common enzymatic features of viral replication process).

1. Example-RNA-polymerize inhibitors such Favipiravir and sofosuvir. (Approved drug to treat influenza and HCV infection) this shows repurposing potential against EBOV and ZIKA

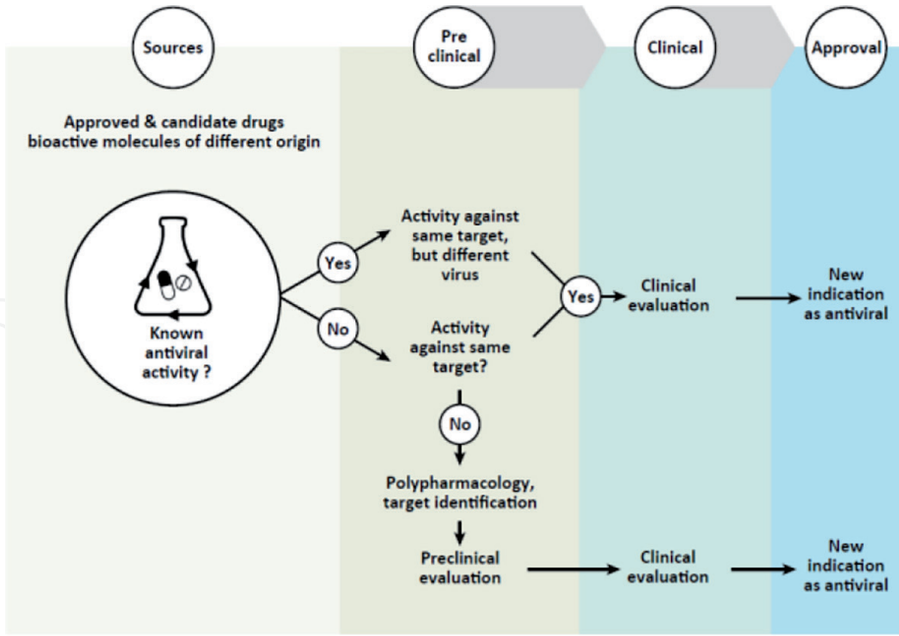

Figure 2.
FDA-approved formulation proceeds through 3- strategy steps, identified molecule-based target similarity hypothesis on viral pathway, absence of activity shows poly-pharmacology interference with different function (cellular or viral).

2. Example- Cellular endocytic pathway to enter the host cell (Chloroquine), interferes with the late-stage entry process of viruses (Filoviruses & coronaviruses)

- **Same target-new indication**: Pharmacological target essential in the pathogenesis of viral infection is modulated by approved drugs.

Example-1: Here approved drugs were exploited as an antiviral therapeutic agent (new indication).

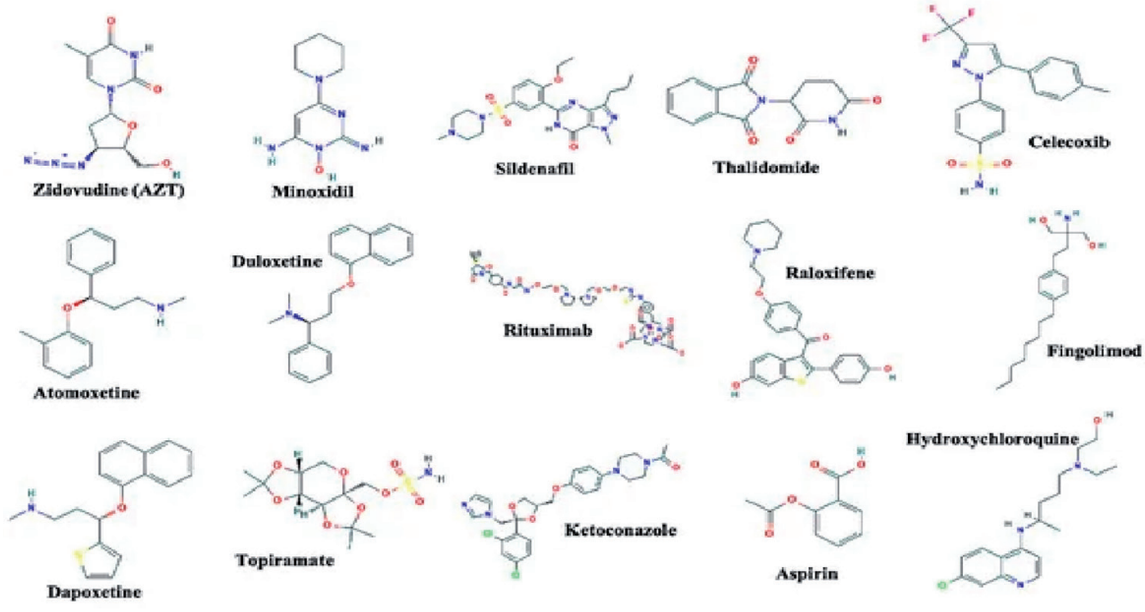

Figure 3.
FDA-approved multiply-acting drugs.

Example-2: Anticancer agents such as imatinib were found to be active against coronaviruses by inhibiting cellular Abelson (ABL) kinase

- **New target- new indication:** Here approved drugs were established with bioactivity in specific pathway/mechanism with new molecular target [Poly-Pharmacology (ability of approved drugs or pharmaceutical molecule to act on multiple targets might be toxicity or side effect) represent important opportunity to repurposing] molecule essential for virus replication.

Example-1: Antimicrobial agent which found to have targeted virus-infected cells as well as inhibition of viral replication (teicoplanin, ivermectin, itraconazole, and niazoxanide).

Example-2: Recently used SARS-CoV-2 and HIV drug to combat morbidity and mortality causes of viruses' outbreak examples of drugs are given (**Figure 3**).

Mentioned chemical structures are promising re-profiled candidates of FDA-approved drugs with its multiple actions, [3].

3. Repurposing in Zikv virus and other Flaviviruses infection

It was a mosquito-borne flavivirus, associated with several birth defects which are associated with infant neurological disorder (Gullain-Barre syndrome and other) and severe congenital defects in Newbern (microcephaly and ophthalmological alteration) such infection occurs during pregnancy. These viruses are capable of spreading both vertical (transplacental) and sexual, this infection is prime concerned for globule and public health, neither specific antiviral treatment nor a vaccine to counteract ZIKV diffusion is available to date. Henceforth FDA-approved drug repurposing camping started by WHO.

The library of 774 FDA-approved immunosuppressant drugs candidates were tested on HuH-7 hepatocytes cell-cultured strains isolated from ZIKV, among which 24 candidates showed potent anti-ZIKV activity which inhibits the ZIKV replication,

Drugs:

- Ivermectin, mycophenolic acid, daptomycin (Cross placenta barrier). FDA-approved Anthelmintics such as Niclosamide, Macrolide Azithromycin (Category B used during pregnancy).

- The structural based in silico screening followed by in-vitro and in-vivo leads to the identification of potent anti-ZIKV antibiotics such as Novobiocin, niclosamide, nanchangmycin, natural alkaloidal compound like hippeastrine hydrobromide (HH) and temoporfin which inhibits NS3/NS2B protease.

- Sofobuvrin Anti-HCV and anti-alzheimer's also reprofiled for Anti-ZIKV infection and to date, none of this are evaluated for the clinical trial [4].

3.1 Repurposing in Ebola virus infection

EBOV was discovered in the late 1970s but the outbreak was in 2014-2016 was an alarming period due to its size and spread, the cases were reported internationally in

S.NO	COMPOUND	STATUS/INDICATION	VIRUS	EXPERIMENTAL MODEL	TARGET
	FDA-Approved Synthetic drug candidates with repurposing potentials				
1.	Mycophenolic acid	Approved/immunomodulator	ZIKV	Infected cells in vitro	Undetermined
2.	Daptomycin	Approved/antibacterial	ZIKV	Infected cells in vitro	Undetermined
3.	Niclosamide	Approved/antiparasitic	ZIKV	Infected cells in vitro	ND and NS2B/NS3 protease
4.	Azithromycin	Approved/antibacterial	ZIKV	Infected cells in vitro	Undetermined
5.	Novobiocin	Approved/antibacterial	ZIKV	Infected cells in vitro mouse model	NS2B/NS3 protease
6.	Nanchangmycin	Investigational	ZIKV	Infected cells in vitro, mouse neuron–glia ex vivo cultures	Virus entry
7.	Hippeastrine hydrobromide	Investigational	ZIKV	Infected cells in vitro, organoids, mouse model	Undetermined
8.	Sofosbuvir	Approved/antiviral	ZIKV	Infected cells in vitro, mouse model	NS5 RNA polymerase
9.	Ribavirin	Approved/antiviral	ZIKV	Infected cells in vitro, mouse model	NS5 RNA polymerase
10.	Chloroquine	Approved/antimalarial	ZIKV, –	Infected cells in vitro, mouse model of vertical transmission	Undetermined
			MERS-CoV SARS- CoV	Infected cells in vitro	Undetermined
11.	Memantine	Approved/treatment of Alzheimer's disease	ZIKV	Primary neurons in vitro, mouse model	Undetermined
12.	Prochlorperazine	Approved/antiemetic	DENV	Infected cells in vitro, mouse model	Entry?
13.	Chlorcyclizine	Approved/antihistamine	HCV	Chimeric mouse model	Entry?

S.NO	COMPOUND	STATUS/INDICATION	VIRUS	EXPERIMENTAL MODEL	TARGET
	FDA-Approved Synthetic drug candidates with repurposing potentials				
14.	Manidipine	Approved/antihypertensive	JEV, ZIKV	Infected cells in vitro, mouse model	NS4B
			HCMV,	Infected cells in vitro	IE2
15.	Favipiravir	Approved/antiviral	EBOV	Phase 2 clinical trial	RNA polymerase
16.	GS-5734	Investigational/antiviral	MERS- and SARS-CoV	Nonhuman primates	RNA polymerase
17.	Imatinib	Approved/anticancer	MERS- and SARS-CoV	Infected cells in vitro	Viral fusion
18.	Chlorpromazine	Approved/antipsychotic	MERS- and SARS-CoV	Infected cells in vitro	Undetermined
19.	Chlarithromycin/Naproxen + Oseltamivir	Approved/antibacterial, anti-inflammatory (+antiviral	Influenza	Phase 2b/3 clinical trials	Undetermined
20.	Nitazoxanide	Approved/antiparasitic	Influenza	Influenza	Maturation of hemagglutinin
			Rotavirus	Rotavirus	Viral morphogenesis
			Norovirus	Norovirus	Undetermined
21.	Raltegravir	Approved/antiviral	Herpesvirus	Infected cells in vitro	Terminase
22.	Lopinavir/ ritonavir + interferon b-1b	Approved/antiviral	MERS-CoV	Nonhuman primates, phase 2/3 clinical trial	Protease
23.	Lopinavir/ritonavir		HPV	Proof-of-concept clinical trial	Overexpression RNAse L and?
24.	Zidovudine	Cancer	AIDS	T-cell culture	Undetermined
25.	Minoxidi	Hypertension	Hair loss	Animal study	Undetermined
26.	Sildenafil	Angina	Erectile dysfunction	Animal study	Undetermined
27.	Thalidomid	Morning sickness	Erythema nodosum leprosum and multiple myeloma	Infected cells in vitro	Undetermined

S.NO	COMPOUND	STATUS/INDICATION	VIRUS	EXPERIMENTAL MODEL	TARGET
	FDA-Approved Synthetic drug candidates with repurposing potentials				
44.	Danoprevir + ritonavir + interferon inhalation or lopinavir + ritonavir or TCM plus interferon inhalation	Protease inhibitors with cytokine as aerosol	COVID-19	Infected cells in vitro	Undetermined
45.	Xiyanping or lopinavir-ritonavirinterferon inhalation	Anti-inflammatory (Xiyanping) or Protease inhibitors with cytokine	COVID-19	Infected cells in vitro	Undetermined
46.	Xiyanping combined with lopinavir + ritonavir	Anti-inflammatory (Xiyanping) in combination with Protease inhibitors	COVID-19	Infected cells in vitro	Undetermined
47.	Combinations of oseltamivir, favipiravir, and chloroquine	Neuraminidase (Oseltamivir) in combination with antimalarial/amebicide	COVID-19	Infected cells in vitro	Undetermined
48.	Vitamin C	Vitamin (Ascorbic acis)	COVID-19	Infected cells in vitro	Undetermined

Table 3.
Approved and candidate drugs with Re purposing potential as antiviral agents.

nonendemic geographical areas such as the USA and Europe. EBOV causes lethal sign and symptoms such as acute hemorrhage, fever, and 90% high fatality rate, it needs high-level biocontainment (BSL-4) which hamper the development of drugs and vaccines to act against EBOV hence no specific therapeutic agents are available yet. In this context, DR prompted the EBOV infection in the last outbreak which shows promising results to lethal the EBOV infection.

Drugs:

- This includes viral RNA polymerase inhibitors Favipiravir (Influenza A virus Japanese approved drug).
- GS-5734 adenosine analogs, amodiaquine, chloremiphene, toremifene, bepridil.
- In combination, DR treatment shows antiviral activity against EBOV but not approved regimen
- Targeted drug-combination approach results in the identification of toremifene–mefloquine–posaconazole and toremifene–clarithromycin–posaconazole, all previously identified by DR) that act synergistically in an EBOV (**Table 3**) entry-inhibition assay and at concentrations achievable in humans [5].

4. Drug repurposing in coronavirus

CoVs are RNA-viruses responsible for GIT respiratory and neurological disease in animals and zoonotic infection in humans, it has the potential to cross-species to species transmission in the domesticated animal which will become the source of spread in human. The major concern of outbreak is the morbidity and mortality of infection in human, and animal adaptability according to the physiological system and ability to upgrade itself to suppress the immune system which make life decline.

SARS-CoV is highly pathogenic it emerged in China in 2002/2003 with 8098 infections and 10% mortality, on the other hand in 2012 MERS-CoV outbreak spread to 27 countries so far by 35% mortality rate, to manage the threat of both the outbreaks by adopting three independent studies reporting an approach by DR for anti-CoV drug discovery were published, this methodology tested against MERS- and SARS-CoV, came up with the screening of dopamine receptor antagonist and antimalarials [6].

Drugs:

- FDA-approved drugs were tested against MERS- and SARS-CoV are dopamine receptor antagonist chlorpromazine and antimalarials chloroquine by DR-approach.
- The DR approach worked on ABL tyrosine kinase oncogene pathway which is essential for the entry of CoVS, whereas imatinib inhibits the replication of both MERS-and SARS-CoV, other host-targeting anti-CoV are Cyclophylin A, cyclosporin A, alispovir and cyclophilin A need further investigation.
- Other drug is in combination currently under clinical evaluation against MERS-CoV syndromes and now vaccines are available to control the SARS-CoV.

4.1 Drug repurposing in influenza and dengue

Influenza is an air-borne disease, belong to the family Orthomyxoviride and it causes a major pandemic outbreak. DR camping identified FDA-approved drugs which are under clinical evaluation with anti-influenza activity [7].

Drugs:

- The kinase inhibitors namely Dinaciclib, Flavopiridol, and PIK-75 reported to be highly effective H7N9, pdm H1N1, and H3N2.
- DR-approached inhibitors are Dapivirine, Naproxen, and antibiotic Clarithromycin.
- The three-drug combination therapy for the treatment of influenzas by targeting mutant viral neuraminidase Clarithromycin+ naproxen along with Oseltamivir was found to be very effective.
- Currently available repurposed drug for influenza treatment is anti-parasitic are nitazoxanide.

whereas Dengue virus (DENV) is a mosquito-borne disease, currently it is rapidly spreading important arthropod-born viral disease in the world. It requires the new drug to target the host cells, whereas the repurposing approach was found to be effective for therapeutic intervention.

Drugs:

- The viral protective inhibitors are Nelfinavir, Lopinavir, and Ritonavir are repurposed by *in silico* Drug design for DENV.
- Chloroquine has also proven the inhibition of type-2 replication in vero cells at a dose of 5 μg/ml by plaque assay qRT-PCR.
- Naturally effective alkaloids for the treatments are Castanospermine, cytomegalovirus against HIV-I, DENV-1, and in-vivo against herpes simplex & Raucher Murine Leukemia virus.
- Some chemotherapeutic agents like Dasatinib, Bortezomib, Prochlorperazin (Antipsychotic), Ivermectin, Suramin, Nitrazoxanide A (anti-parasitic) dexamethasone, Prednisolone (Steroids), Genteticin, Narasin and Minocycline (Antibiotic) [8].

5. Drug repurposing in DNA viruses (HIV, CMV, HSV, and HCV)

According to WHO, 26 million people have died due to HIV/AIDS in year 1981, and from 2018 till more than 1.10 million people were affected, this was the worst outbreak managed by hydroxy-chloroquine [9]. HCMV was the best example of host adaptation and the ability of virous to subvert, completely, cellular physiological processes in infected cells (**Table 3**).

Drugs:

- Anti-HCMV drugs are statin, cardiac glycosides & emetine (Anti-parasite).

- Kinase inhibitors Manidipine (anti-hypertensive) this drug modifies the host protein function and takes away from the viruses [10].

- Topical drugs such as Ciclopirox, olamine reduce replication of HSV-1 and HCV replication can be inhibited by Suberoylanilide, erlotinib, Dasatinib, and hydroxamic acid (anticancer drugs).

- Miscellaneous repurposed drugs are Ezetimibe (Cholesterol drug), Ferroquine (anti-malarial), Cyclizine, and phenothiazine (H1-antihistamine) [11].

6. Concluding remarks and future perspectives

Viral infectious diseases remain a major challenge due to the lack of specific medical regimen, to counteract the viral replication and pathogenesis required knowledge to understand the virus-host interaction and mutagenesis, which is now a days remain a puzzle for several known viral pathogens emerging as time and eternity. The development of a drug molecule which is able to target the exact replication is still remain challenging, to encounter the emerging new viral pathogenesis, in this context, DR or positioning approach on FDA-approved drug evaluation, reduce the risk for pipeline new drug discovery, with economic advantages and remarkable generation up to $25 billion annual sales.

The potentiality of the DR approach will target the host function as time and cost-effective route to develop the broad-spectrum antiviral, which already gave a positive outcome successfully by opening-up new pathways for viral infection. The drug repurposing approach feasibly worked on anticancer, antiviral, and antibacterial FDA-approved medicines, to counteract EBOV, MERS-CoV, SARS-CoV, COVID-19, and now a day to control newly emerging OMICRON. Moreover, the successful repurposing is based upon the concentrating required for antiviral activity, which is often higher than approved regimens. Reconsideration on regimen the combined dosage form will be more effective and feasible to reach the new target mentioned in (**Table 3**) [11]. The synergistic therapy will be the milestone formulation to combat EBOVA influenza and could also be the regimen to target other viral infections [12].

On the other hand, the combined formulation will be less toxic and the dose of the drug can also be minimized as compared to the approved formulation with less chances of drug resistance due to synergistic effect, [7, 13].

There is still to be vigilant: synergistic effect at low dose, medication required to interfere with each other to have different mechanism of action. The viral replication pathway or host needs to be targeted early, to inhibit the mutation with antiviral combination, finding the new approach might be the only possible way to encounter such kind of viral outbreak with different therapeutic intervention, it remains mandatory and can be addressed by DR (Drug Repurposing) or reprofiling camping. To overcome the drug discovery bottleneck for emerging and re-emerging viral infectious disease, even the more concerned one is death associated with COVID-19 and HIV, DR will be the major interest due to reduced failure rate and decreased time as well as resource consumptions, to be put forward the first HIV medicine innovated by DR which was initially used to treat cancer patient, this will be the millstone to turn the entire scenario tempted the researcher, during the global pandemic outbreak to design novel molecules by the re-tasking look on FDA-approved drugs.

Before reprofiling, it requires to be vigilant towards the challenges associated with the copyrights. This chapter represents the importance of research that need to be conducted by closing the leftover loops on FDA-approved drugs. The author was overwhelmed to represent the glimpse associated with reprofiling by putting it down, and look forward to work practically at YPCRC for fruitful future.

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Conflict of interest

The authors declare no conflict of interest.

Acronyms and abbreviations

DR	Drug Repurposing
CMV	Cytomegalovirus
HCMV	Human Cytomegalovirus
HCV	Hepatitis C Virus
EVD	Ebola Virous Disease
qRT-PCR	Quantitative Real-Time Polymerase Chain Reaction
RVFV	Rift Valley fever virus
MERS-CoV	Middle East Respiratory Syndrome Coronavirus
SARS-CoV	Severe Acute Respiratory Syndrome Coronavirus
EBOV	Ebola Virus
FDA	Food and Drug Administration
HIV	Human immunodeficiency Virus
AIDS	Acquired Immune Deficiency Syndrome
HSV	Herpes simplex Virus
DENV	Dengue Virus
H1N1, H3N2 & H7N9	Swine Flu Influenza
WHO	World Health Organization
M^{pro}	Main protease
Gly-fl-Ser/Gly/	Ala as motif cleavage
ABL tyrosine	Abelson murine Leukemia Viral gene

Reference tables

- Precedence and pitfalls of reprofiling candidates [13]
- Represents available library of vendors to be referred while designing and figuring out the Reprofiled candidate [14]
- Literature of successful repurposed candidates [15, 16].

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References

[1] Mani D, Wadhwani A, Krishnamurthy PT. Drug repurposing in antiviral research : A current scenario. Journal of Young Pharmacists. 2019;**11**(2):117-121

[2] Pizzorno A, Padey B, Terrier O, Rosa-calatrava M. Drug repurposing approaches for the treatment of influenza viral infection : Reviving old drugs to fight against a long-lived enemy. Journal of Young Pharmacists. 2019;**11**(2):117-121

[3] Mercorelli B, Palù G, Loregian A. Drug repurposing for viral infectious diseases : How far are we ? Trends in Microbiology. 2018;**26**(10):865-876. DOI: 10.1016/j.tim.2018.04.004

[4] Altay O, Mohammadi E, Lam S, Turkez H, Boren J, Nielsen J, et al. iScience ll current Status of COVID-19 therapies and drug repositioning applications. ISCIENCE. 2020;**23**(7): 101303. DOI: 10.1016/j.isci.2020.101303

[5] Sarkar A, Mandal K. Repurposing an antiviral drug against SARS-CoV-2 Main protease. Angew Chem Int Ed Engl. 2021 Oct 25;**60**(44):23492-23494

[6] Pushpakom S, Iorio F, Eyers PA, Escott KJ, Hopper S, Wells A, et al. Drug repurposing: Progress, challenges and recommendations. Nature Reviews Drug Discovery. 2018;7:234-238. DOI: 10.1038/nrd.2018.168

[7] Sultana J, Crisafulli S, Gabbay F, Lynn E, Shakir S. Challenges for drug repurposing in the COVID-19 pandemic era. Front. Pharmacol. 2020;**11**(November):1-13

[8] Yang C, Peng T, Hsu H, Lee Y, Wu S, Lin W, et al. ScienceDirect repurposing old drugs as antiviral agents for coronaviruses. Biomedical J. 2020;**3**:3-9

[9] Parnham MJ, Erakovic V, Giamarellos-bourboulis EJ, Perletti G, Verleden GM, Vos R. Pharmacology & Therapeutics Azithromycin : Mechanisms of action and their relevance for clinical applications. Pharmacology & Therapeutics. 2014;**143**(2):225-245. DOI: 10.1016/j.pharmthera.2014.03.003

[10] Rajkumar RP. Lithium as a candidate treatment for COVID-19: Promises and pitfalls. Drug Dev Res. 2020 Nov;**81**(7):782-785

[11] Cusinato J, Cau Y, Calvani AM, Mori M, Cusinato J, Cau Y, et al. Expert opinion on therapeutic patents repurposing drugs for the management of. Expert Opinion on Therapeutic Patents. 2021;**31**(4):295-308. DOI: 10.1080/13543776.2021.1861248

[12] Results ST. New England Journal. 2021;497-511

[13] Bauso LV, Imbesi C, Irene G, Cal G, Bitto A. New approaches and repurposed antiviral drugs for the treatment of the SARS-CoV-2 infection. Pharmaceuticals. 2021;**14**:1-19

[14] Swathi K, Nikitha B, Chandrakala B, Lakshmanadevi K, Malleswari M. Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company ' s public news and information . 2020;(January)

[15] Trivedi J, Mohan M. Drug repurposing approaches to combating viral infections. J Clin Med. 2020 Nov 23;**9**(11):3777

[16] Moleculer structure which have Repurpusing potential. Molecules. 2021;**24**(1):29-31