IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
**Review Article**
January 2022 Vol.:23, Issue:2


# Pharmacological Elements of Drug Repurposing Against COVID-19 Pandemic

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

**Abdolrab Malekraeisi*[1], Fazel Farmahinifarahani[2], Prerana Mahesh Bhalerao[3], Sobhan Setoodeh[4], Faezeh Farmahinifarahani[5]**

[1,2,3] *Research Scholar, Department of Pharmacy, Indira College of Pharmacy ( Affiliated to Savirtibai Phule Pune University), Tathwade, Pune- 411033, India*

[4] *Department of Pharmacy, Poona College of Pharmacy, Bharati Vidyapeeth, Pune, India*

[5] *Department of Pharmacy, Ramsar International Campus Faculty (Affiliated to Mazandaran University of Medical Science, Ramsar, Iran*

**Submitted:** 24 December 2021
**Accepted:** 31 December 2021
**Published:** 30 January 2022

**Keywords:** Drug Repurposing, COVID-19

**ABSTRACT**

The purpose of this study is to outline the regulatory and pharmacological elements of medication repurposing, as well as to identify drugs recommended for repurposing in COVID-19 based on clinical studies, and to examine their use in the treatment. In COVID-19, the issues of correctly interpreting existing clinical data and the new evidence for medication repurposing are explored.

HUMAN JOURNALS
www.ijppr.humanjournals.com

## INTRODUCTION

'Drug repurposing' means the process of discovering new medicinal potential for existing drugs. The method, also known as 'repositioning' or' re-profiling,' is typically viewed as both cost-effective and efficient. Drug repurposing is the method of identifying a new function for an old drug. It provides economical, low-cost, and expedited therapy. Strategies such as in-silico modelling, data mining, artificial intelligence, and so on assist to expedite progress. Collaboration across many sectors, as well as awareness and encouragement, may boost the development of drug repurposing, which has a bright future in the contemporary medical sector. Drug repurposing is analogous to recycling. It is the usage of well-known drugs for purposes other than their intended use. Drug repurposing makes drugs more affordable, quicker, and accessible to patients[1]. The drugs being explored for repurposing are those that have been shelved because they have failed the clinical trials testing. Because the effectiveness, safety, and toxicity of the drug are already established, the earliest stages of clinical trials may be omitted. A new drug takes around Fifteen years to reach the customer base, but a repurposed drug reduces both the length and the expenses. "COVID-19" is the acronym for the coronavirus disease of 2019. It has now been proclaimed a pandemic by the World Health Organization (WHO). Because there is an urgent need for an authorised, safe, and effective therapy during this public health emergency, it is fair to look into the effectiveness of previously licenced drugs. The drug development process costs time and resources, and the safety of new drugs is critical. Drug repurposing focuses on identifying new uses for patented drugs and may assist to alleviate the problems involved with drug development. Repurposing may be a speedy and effective therapeutic strategy in which drugs with proven human safety are recycled for the treatment of new diseases. Existing drugs may be studied and developed for effectiveness against ailments other than those for which they were originally authorised. Off-target drug binding, for example, may be exploited as a vital point in drug repurposing studies due to its high promiscuity[2].

## MATERIALS AND METHODS

Preclinical studies demonstrated the efficacy of lopinavir ($C_{37}H_{48}N_4O_5$) /ritonavir ($C_{37}H_{48}N_6O_5S_2$) combination treatment against COVID-19. Lopinavir is a human immunodeficiency virus (HIV-1) protease inhibitor that, when combined with ritonavir, is a powerful cytochrome CYP3A4 inhibitor that increases lopinavir concentrations, blocks the primary protease of SARS-CoV-1, and slows viral replication[3]. This combination is being

evaluated as a treatment for COVID-19, although more study has yet to corroborate the findings[4]. Immunological and pharmacological research is still underway in terms of therapy. Numerous previously approved drugs are being tried on COVID-19 by efficient strategy to drug discovery known as drug repurposing. The type and complimentary impact of interventional drugs in clinical trials may be categorised. Antivirals, nutritional drugs and combination therapy, are being studied. The identical mechanism of action may be seen within and outside each group. However, many drugs are developed for one condition and then repurposed for another.

Several studies from on-going clinical trials that have not yet been peer-reviewed suggest that convalescent plasma from recovered patients has neutralising activity that might be given to recipients by plasma infusion[5]. A group of researchers claimed that human recombinant soluble ACE2 (hrsACE2) may prevent SARS-CoV-2 infections in their early stages[6]. Angiotensin-converting enzyme (ACE2) seems to be an important and common receptor for multiple coronaviruses, since it was previously shown to be essential for Severe acute respiratory syndrome (SARS-CoV-1) and non-critical for Middle East respiratory syndrome (MERS-CoV), and it is now reported[7] to be critical for SARSCoV-2. As a result, limiting the interaction of SARS-CoV-2 and ACE2 is recommended as a therapy for COVID-19 patients; however, it is unclear if hrsACE2 can inhibit SARS-CoV-2 growth. Remdesivir, like its promising effects on SARS-CoV-1 has shown significant in vitro action[8] against SARS-CoV-2. Tocilizumab, a humanised monoclonal antibody, blocks all interleukin-6 (IL-6) receptors (membrane bound or soluble). Tocilizumab is known to reduce the impact of cytokine storming, notably IL-6, which has been linked to poor results in COVID-19 patients[9]. Dornase alfa (biosynthetic deoxyribunuclease I enzyme) is now being tested in individuals[10] with severe COVID-19. Dornase alfa is just a mucolytic enzyme that degrades neutrophil extracellular traps by separating chromosomal DNA.

## RESULTS AND DISCUSSION

Ebola, Dengue, Zika, and coronaviruses have all become public health concerns in recent years, generating a continual need for quick and viable therapeutic treatments based on antiviral medication repurposing methodologies[11]. When an epidemic strikes, immediate response by recognised drugs may assist to mitigate the harm until virus-specific antiviral drugs or vaccinations become available. Chloroquine has been extensively studied[12] for their potential use in the treatment of COVID-19. Due to the scarcity of targeted therapies for

certain emerging viruses, the antiviral capabilities of repurposed drugs have received a lot of interest during the past decade[13]. Numerous technological and logistical hurdles in de novo antiviral medication development have resulted in a relatively low therapeutic molecule approval rate, leaving viral illnesses like hepatitis C and HIV without a vaccine. Most regularly used antiviral drugs come with significant drawbacks such as inadequate selectivity, resistance, latency promotion, toxicity, or experimental challenges[14]. Medication repurposing techniques for infectious illnesses combine a wide range of applications by combining essential bioinformatics and cheminformatics technologies to identify a drug target that may be repurposed in the fight against a viral infection. In certain cases, drug repurposing finds previously unknown biomolecular networks, changing them into fresh pharmacological targets, even if the identified compounds may not be used in clinical trials [15]. In addition to undeniable cost-effective advantages in the process of drug development, recycled drugs are immediately accepted into clinical trials or are taken up with compassionate use programmes, especially in the context of incurable viral illnesses or pandemics. Furthermore, medication repurposing offers an additional source of data for a unique knowledge of metabolic reprogramming in viral infections, as well as organic compounds with previously unknown antiviral characteristics that have the potential to grow in exposing virus biology features[16].

There are several chances to find target human proteins for repurposing established drugs by thoroughly examining the dynamic interactions between host and SARS-CoV-2. Targeting host-virus interactions, have a lower likelihood of mutational resistance, may be beneficial in establishing strong therapy options for viral infections[17]. The function of drugs targeting the Sigma receptors is not well characterised many licenced medicines have been repurposed[18]. Characterization of viral evolution and changes in host cell metabolism using single-cell viral metagenomic research might offer insight on viral infection processes, including the identification of molecular markers linked with virus-induced diseases[19]. Drug repurposing approaches are primarily based on the examination of biological data, which allows for the generation of hypotheses for the rediscovery of accessible medications for innovative clinical solutions, and has been widely discussed elsewhere[20]. Computational drug repurposing techniques are roughly classified into four types: (1) signature-based, (2) molecular docking, (3) network-based, and (4) genome-wide association analyses (GWAS). Finally, GWAS strive to identify changes in genetic material associated with prevalent illnesses and lead to a better knowledge of disease physiology[21].

## CONCLUSION

The repurposing technique has resulted in unanticipated discoveries in novel diseases with a great potential for commercial success, hence substantially adding to modern biology knowledge innovation. Repurposing is the most effective method for drug development against COVID-19, whether employing wet laboratory techniques or system biology approaches, owing to the fundamental need. To understand the repurposed drugs better , further data analysis is constantly essential. The general success rate of repurposing drugs for new medical illnesses is low, and despite their modest manufacturing costs in contrast to the massive investment of inventing a new treatment, another restriction to consider in repurposing is the likelihood of unexpected ramifications. The COVID-19 pandemic demands a range of safe and effective therapeutic medicines as soon as possible, although no medication, vaccine, or therapy modality has been licenced or demonstrated entirely comforting outcomes thus far. Repurposing will undoubtedly offer a big scientific contribution to innovation in medication creation and pharmacological practises for the treatment of new or existing diseases.

## REFERENCES

1. Alan Talevi (2021) Drug Repurposing, Reference Module in Biomedical Sciences, Elsevier.
2. Badria. A, Farid (2020). Drug Repurposing - Hypothesis, Molecular Aspects and Therapeutic Applications || Drug Repurposing (DR): AnÂ Emerging Approach in Drug Discovery. , 10.5772/intechopen.83082(Chapter 1), –. doi:10.5772/intechopen.93193
3. Rtia, K., Pegan, S., Takayama, J., Sleeman, K., Coughlin, M., Baliji, S., Chaudhuri, R., Fu, W., Prabhakar, B.S., and Johnson, M.E. (2008). A noncovalent class of papain-like protease/ deubiquitinase inhibitors blocks SARS virus replication. Proc. Natl. Acad. Sci. U S A 105, 16119–16124.
4. Cao, B., Wang, Y., Wen, D., Liu, W., Wang, J., Fan, G., Ruan, L., Song, B., Cai, Y., Wei, M., et al. (2020). A trial of lopinavir–ritonavir in adults hospitalized with severe COVID-19. N. Engl. J. Med. 382, 1787–1799.
5. Shen, C., Wang, Z., Zhao, F., Yang, Y., Li, J., Yuan, J., Wang, F., Li, D., Yang, M., and Xing, L. (2020). Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA 323, 1582–1589.
6. Monteil, V., Kwon, H., Prado, P., Hagelkru?ys, A., Wimmer, R.A., Stahl, M., Leopoldi, A., Garreta, E.,Hurtado del Pozo, C., Prosper, F., et al. (2020). Inhibition of SARS-CoV-2 infections in engineered human tissues using clinical-grade soluble human ACE2. Cell 181, 905–913.e7.
7. Muller, M.A., Raj, V.S., Muth, D., Meyer, B., Kallies, S., Smits, S.L., Wollny, R., Bestebroer, T.M., Specht, S., and Suliman, T. (2012). Human coronavirus EMC does not require the SARScoronavirus receptor and maintains broad replicative capability in mammalian cell lines. MBio 3, e00515–e00512.
8. Wang, M., Cao, R., Zhang, L., Yang, X., Liu, J., Xu, M., Shi, Z., Hu, Z., Zhong, W., and Xiao, G. (2020a). Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res. 30, 269–271.
9. Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., Xiang, J., Wang, Y., Song, B., and Gu, X. (2020a). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 395, 1054–1062.
10. Pottecher, J., Noll, E., Borel, M., Audibert, G., Gette, S., Meyer, C., Gaertner, E., Legros, V., Carapito, R., and Uring-Lambert, B. (2020). Protocol for TRAUMADORNASE: a prospective, randomized, multicentre,

double-blinded, placebo-controlled clinical trial of aerosolized dornase alfa to reduce the incidence of moderate-to-severe hypoxaemia in ventilated trauma patients. Trials 21, 1–13.
11. Boldescu, V., Behnam, M.A.M., Vasilakis, N., and Klein, C.D. (2017). Broad-spectrum agents for flaviviral infections: dengue, Zika and beyond. Nat. Rev. Drug Discov. 16, 565–586.
12. Cortegiani, A., Ingoglia, G., Ippolito, M., Giarratano, A., and Einav, S. (2020). A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. J. Crit. Care 57, 279–283.
13. Law, G.L., Tisoncik-Go, J., Korth, M.J., and Katze, M.G. (2013). Drug repurposing: a better approach for infectious disease drug discovery? Curr. Opin. Immunol. 25, 588–592.
14. De Clercq, E., and Li, G. (2016). Approved antiviral drugs over the past 50 years. Clin. Microbiol. Rev. 29, 695–747.
15. Turanli, B., Zhang, C., Kim, W., Benfeitas, R., Uhlen, M., Arga, K.Y., and Mardinoglu, A. (2019). Discovery of therapeutic agents for prostate cancer using genome-scale metabolic modelling and drug repositioning. EBioMedicine 42, 386–396.
16. Pizzorno, A., Padey, B., Terrier, O., and RosaCalatrava, M. (2019). Drug repurposing approaches for the treatment of influenza viral infection: reviving old drugs to fight against a long-lived enemy. Front. Immunol. 10, 531.
17. Kaufmann, S.H.E., Dorhoi, A., Hotchkiss, R.S., and Bartenschlager, R. (2018). Host-directed therapies for bacterial and viral infections. Nat. Rev. Drug Discov. 17, 35–56.
18. Gordon, D.E., Jang, G.M., Bouhaddou, M., Xu, J., Obernier, K., White, K.M., O'Meara, M.J., Rezelj, V.V., Guo, J.Z., Swaney, D.L., et al. (2020). A SARSCoV-2 protein interaction map reveals targets for drug repurposing. Nature. https://doi.org/10. 1038/s41586-020-2286-9.
19. Xu, Y., and Zhao, F. (2018). Single-cell metagenomics: challenges and applications. Protein Cell 9, 501–510.
20. Pushpakom, S., Iorio, F., Eyers, P.A., Escott, K.J., Hopper, S., Wells, A., Doig, A., Guilliams, T., Latimer, J., McNamee, C., et al. (2019). Drug repurposing: progress, challenges and recommendations. Nat. Rev. Drug Discov. 18, 41–58.
21. Sanseau, P., Agarwal, P., Barnes, M.R., Pastinen, T., Richards, J.B., Cardon, L.R., and Mooser, V. (2012). Use of genome-wide association studies for drug repositioning. Nat. Biotechnol. 30, 317–320.