Review Article

# Drug Repurposing: A Potentially Emerging Discipline

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## ABSTRACT

Drug repurposing is the remodeling of already existing drugs to reduce the time frame, costs, and efforts in developing a new novel drug. This strategy has secured significant momentum in the previous decade. It overcomes the snags and pitfalls in the traditional means of drug discovery. This core research strategy has now become the sole approach to containing many deadly diseases that have no cure in the present. In astound, for pandemics like COVID-19 that is spreading like a wildfire worldwide, large-scale research programs and trials have been carried out to identify and modify existing drugs to counter the novel virus. Thus, this technology of drug repurposing offers a new lease of life, and greatly promotes the progress of the medicine, health, and pharma sectors. The purpose of this study is to understand the current status of drug repurposing in the field of virology, bacteriology, mycology, and oncology for clinical translatability.

**Key words:** Drug repositioning, Drug development, Antibacterial, Antiviral, Anticancer, SARs-Cov-2.

## INTRODUCTION

Drug repurposing is an emerging field in drug discovery that finds various therapeutic opportunities to administer existing medicine. In recent years, repurposed drugs have contributed to nearly 25% of the yearly return for pharmaceutical production.[1] Moreover, many academic publications on drug repurposing mark the increasing interest in this discipline.[2] The ancient practice of drug discovery was a prolonged, effortful, troublesome, and costly method. Drug repurposing has an added benefit over typical drug manufacture because it decreases the production cost of the drug. Further, toxicity testing and clinical trials have already been performed, which offer extra benefit. Drugs that have failed to reach the market despite being effective in late-stage trials can be exploited for effectiveness in a different disease conditions. Since repurposing is focused on prior research, new drug candidates could be easily subjected to clinical trials, speed up the certification procedure by the Food and Drug Administration (FDA), and minimize their entire processing period. The timeline for repurposing medicines is often reduced since most medicines are already established and have undergone clinical trials and analysis. Traditional drug development strategies usually include five stages: target discovery and preclinical stage, hit-to-lead process (to improve potency, selectivity, and physicochemical properties), Lead optimization (to synthesize lead compounds, new analogues with enhanced efficacy, limited off-target activities), candidate selection, clinical development (clinical trials and volunteer studies, registration and marketing (drug approval and marketing). Nevertheless, in drug repurposing, there are only four steps: identification of compounds, acquisition of compounds, development and registration, and marketing (Figure 1).[3] According to a recent study report on 30 pharmaceutical and biotech firms, the value to release a repositioned drug averages $8.4 million, while launching a novel drug cost an

Submission Date: 13-06-2021;
Revision Date: 02-12-2021;
Accepted Date: 02-04-2022.

**DOI: 10.5530/ijper.56.2s.83**

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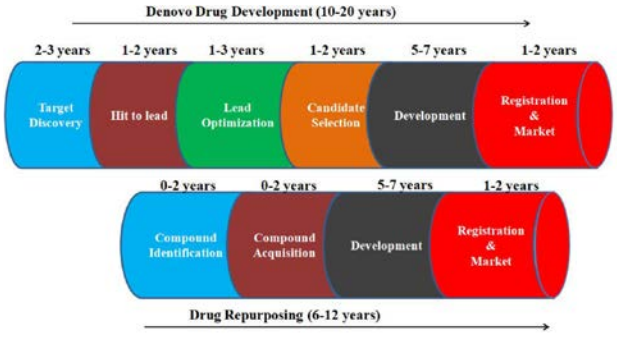



**Figure 1: Conventional drug discovery compared with drug repurposing approach. In drug repurposing (lower panel), the time needed from hit detection to lead optimization (upper panel) is saved.**

average of $41.3 million.[4] Despite recent advancements in the control of certain pathogenic agents, most diseases often lack precise treatment. Therefore, there is a need for successful therapeutic approaches to fight the old, evolving, and re-emerging pathogens. Therefore, the repurposing of currently used drugs for treating infections becomes highly relevant. In recent years, drug repurposing, together with novel drug validation methods and acceptable animal models, has dramatically led to discovering new drug-like molecules and drug targets. In this review, we will discuss the approaches used for drug repurposing in the field of virology, bacteriology, mycology, and oncology.

## DRUG REPURPOSING IN VIROLOGY

Recently, drug repurposing has been commonly used to treat critically re-emerging pandemic-positive viruses that have triggered alarming outbreaks, which require immediate attention and specific treatment, such as the Zika virus (ZIKV), Ebola virus (EBOV), SARS-CoV-2, Dengue Virus, HIV, and the Middle East coronavirus respiratory syndrome (MERS-CoV). The lists of drugs with potential for repurposing as anti-viral agents are given in Table 1.

### Zika Virus

ZIKV is an arthropod-borne virus that ignited a major epidemic in Latin American countries in late 2015. ZIKV infection is linked with neurological conditions such as Guillain – Barré syndrome and serious congenital disorders in neonates like microcephaly.[29] Since the virus has the potential of spreading from human to human, ZIKV pandemics are a significant threat to global public health.[30] Intriguingly, no specific treatment or vaccine is available to date to impede ZIKV. The immunosuppressive medication mycophenolic acid and the antibiotic daptomycin were found effective among the known ZIKV replication inhibitors.[14] Subsequently, anti-helminthic drug, niclosamide, and macrolide antibiotic, azithromycin, were identified as efficient ZIKV replication inhibitors in several neural cell lines infected by ZIKV.[5,11] The computational method along with experimental validations, led to the identification of novobiocin (another antibiotic), niclosamide, and ferroportin as potent inhibitors of ZIKV targeting NS3/NS2B serine protease.[9,12] A polyether of bacterial origin, Nanchangmycin, was found to hinder ZIKV infection in various cell lines.[6] Hippeastrine hydrobromide (HH), a natural alkaloid, has recently been discovered as a promising inhibitor of ZIKV replication.[13] The efficacy of Ribavirin and Sofosbuvir (used for the treatment of hepatitis C) as anti-ZIKV drugs is noteworthy, although contrasting reports on the potency of the latter have been published.[10,16] Therefore, before considering it as an anti-ZIKV drug, a proper investigation into the safety of Sofosbuvir is required. To date, many repurposed drugs, including anti-malarial drugs have been identified to be effective in controlling the virulence of ZIKV. Recently, the efficacy of hybrid compounds derived from anti-malarial drugs, chloroquine, and sulfadoxine was evaluated for ZIKV inhibitory effect, resulting in the development of the new highly potent combination of drug-like compounds.[31] The other drugs repurposed against ZIKV include nitazoxanide (antiparasitic drug), chloroquine (anti-malarial drug], emetine (anti-protozoal drug), ribavirin, and favipiravir (anti-viral drugs).[12,31-33] Overall, these studies suggested that drug repurposing strategy can be rapidly deployed for drug discovery against ZIKV.

### Ebola virus

EBOV is a filovirus that was first identified in 1976, causing two concurrent outbursts. The deadly virus gained considerable attention during 2014-2016 due to its rapid alarming outbreak all over West Africa. Despite the lethal conditions caused by EBOV, no specific therapeutics are available for its containment yet. Drug repurposing studies performed resulted in discovering a cluster of approved drugs that offers safety against EBOV. These include the viral RNA polymerase inhibitor, Favipiravir approved against influenza A virus, an adenosine analogue GS-5734 effective against highly pathogenic coronaviruses, and Amodiaquine, an anti-malarial drug, used widely in Africa.[21,29,34-36] The potent anti-EBOV activity was detected for the FDA-approved selective estrogen receptor modulators, Cloremiphene and Toremiphene, anti-depressant Sertraline and heart drug Bepridil, antibiotic Teicoplanin, cationic

**Table 1: Drugs with potential for repurposing as antiviral agents.**

| Drug | Original Indication | Virus | Target | Reference |
|---|---|---|---|---|
| Azithromycin | Antibacterial | ZIKV | ND* | Retallack *et al*. (2016)[5] |
| Nanchangmycin | Insecticidal, antibacterial | ZIKV | Virus entry | Rausch *et al*. (2017)[6] |
| Memantine | Treatment of Alzheimer's disease | ZIKV | ND | Costa *et al*. (2017)[7] |
| | | SARS-CoV-2 | ND | Hasanagic *et al*. (2020)[8] |
| Novobiocin | Antibacterial | ZIKV | NS2B/NS3 | Yuan *et al*. (2017)[9] |
| Ribavirin | Antiviral | ZIKV | NS5 RNA polymerase | Kamiyama *et al*. (2017)[10] |
| Niclosamide | Antiparasitic | ZIKV | NS2B/NS3 | Xu *et al*. (2016),[11] Li *et al*. (2017)[12] |
| Hippeastrine hydrobromide | Antiviral (avian influenza H5N1) | ZIKV | ND | Zhou *et al*. (2017)[13] |
| Daptomycin | Antibacterial | ZIKV | ND | Barrows *et al*. (2016)[14] |
| Mycophenolic acid | Immunomodulator | ZIKV | ND | Barrows *et al*. (2016)[14] |
| Chloroquine | Antimalarial | ZIKV | Inhibiting endosomal disassembly of the internalized virus | Zhang *et al*. (2019)[15] |
| Sofosbuvir | Antiviral | ZIKV | NS5 RNA polymerase | Bullard *et al*. (2017)[16] |
| Prochlorperazine | Antiemetic | DENV | Viral entry | Simanjuntak *et al*. (2015)[17] |
| Chlorcyclizine | Antihistamine | HCV | Viral entry | He *et al*. (2015)[18] |
| Manidipine | Antihypertensive | JEV, ZIKV | NS4B | Wang *et al*. (2017)[19] |
| Chlorpromazine | Antipsychotic | SARS-CoV-2 | ND | Plaze *et al*. (2021)[20] |
| Favipiravir | Antiviral | EBOV | RNA polymerase L | Sissoko *et al*. (2016)[21] |
| Imatinib | Anticancer | SARS-CoV-2 | Viral fusion | Morales-Ortega *et al*. (2020),[22] Emadi *et al*. (2020)[23] |
| Nitazoxanide | Antiparasitic | Influenza | Maturation of hemagglutinin | McKimm-Breschkin *et al*. (2018)[24] |
| | | Rotavirus | Viral morphogenesis | Mahapatro Wang *et al*. (2017)[25] |
| Remdesivir | Hepatitis C, RSC | SARS-CoV-2 | RdRp inhibitor | Dehelean *et al*. (2020)[26] |
| | | EBOV | RdRp inhibitor | Nili *et al*. (2020)[27] |
| Raltegravir | Antiviral | Herpesvirus | Terminase | Yan *et al*. (2014)[28] |

*ND: Not done

amphiphilic drugs like Amiodarone, and the RNA polymerase inhibitor BCX-4430.[37-41]

## Influenza Virus

The influenza virus is included in the family Orthomyxoviridae and is responsible for global epidemics of flu disease. The antiparasitic medication nitazoxanide, currently used for the treatment of influenza, is by far the most advanced example of drug repurposing.[42] A triple-drug combination of clarithromycin, naproxen, and oseltamivir demonstrated potency against severe influenza infection.[11] Dinaciclib, flavopiridol, and PIK-75 have been documented to be highly potent against H7N9 viruses with lower toxicity.[43] Drugs such as dapivirine, naproxen, clarithromycin, and BAY 81-8781 are were reported to possess anti-influenza activity.[44] The efficacy of nalidixic acid and dorzolamide against oseltamivir-resistant influenza has been reported.[45] In a recent study, antibiotic azithromycin exhibited broad-spectrum anti-viral effects against the influenza virus and SARS-CoV-2.[46] The combined treatment of oseltamivir and anti-fungal drug itraconazole yielded stronger anti-viral activities in the influenza virus compared to monotherapy with oseltamivir.[47] Amitriptyline HCl (an anti-depressant drug), azacitidine (an anti-neoplastic drug) significantly decreased the lung injury score and enhanced the survival of H5N1 virus-infected mice.[48] In a recent study, eight compounds (antimycin A, brequinar, 6-azauridine, azaribine, pyrazofurin, AVN-944, mycophenolate mofetil, and mycophenolic acid), previously known as an anti-viral agent against mammarenaviruses exhibited potent anti-influenza

virus activity.[49] Papaverine (presently used for the treatment of heart disease, impotency, and psychosis) and emetine (anti-protozoal drug), exhibited anti-viral activity against the influenza A virus.[50,51] Guanethidine (anti-hypertensive drug), Trametinib (MEK inhibitor and Verdinexor (a selective inhibitor of nuclear export, SINE), exhibited measurable anti-influenza activity in cell culture.[52-54] Anti-fungal therapeutics, posaconazole, and itraconazole were shown to inhibit the *in vitro* and *in vivo* propagation of the influenza virus.[55]

## Dengue virus

Dengue fever is a painful, disabling mosquito-borne infection caused by any of the four-antigenically distinct serotypes of Dengue Virus (DENV). The repositioning of drugs currently used seems to be a successful and alternate approach for accelerated clinical intervention, considering the delay in bringing new drugs in the market and the rapidly spreading nature of DENV.[56] Viral protease inhibitors have been repurposed against Dengue virus infection, such as Nelfinavir, Lopinavir, and Ritonavir.[57] Chloroquine, an anti-malarial medication, has been shown to inhibit DENV-2 replication in Vero cells by plaque assay and qRT-PCR at a dosage of 5 μg/ml.[58] Castanospermine, a natural alkaloid, was active *in vitro* against DENV-1, influenza virus, cytomegalovirus, and HIV-1.[59] Antipsychotic agents (dasatinib, bortezomib, and prochlorperazine) antiparasitic agents (ivermectin, Suramin, Nitazoxanide A), steroid (dexamethasone, prednisolone), and antibiotics (geneticin, narasin, and minocycline) are potent against DENV.[56] Sofosbuvir, a clinically approved anti-hepatitis C virus, blocks DENV replication.[60] Sunitinib and erlotinib, inhibitors of cellular kinases AAK1 and GAK and approved anti-cancer drugs, possess anti-DENV activity.[61] N-desmethylclozapine, fluoxetine hydrochloride, and salmeterol xinafoate were reported as DENV inhibitors by screening a library of pharmacologically active compounds and approved drugs.[62] Two analogues of resveratrol, PNR-4-44, and PNR-5-02, possessed strong anti-DENV activity and targeted viral protein synthesis and replication.[63] Balapiravir and ribavirin, inhibitors of viral RNA-dependent RNA polymerase (RdRp), developed originally as inhibitors of HCV, were effective against DENV.[64] Prochlorperazine, a dopamine D2 receptor antagonist, approved for treating human nausea, vomiting, and headache, is effective against *in vitro* and *in vivo* DENV infection.[17] Nordihydroguaiaretic acid (NDGA), a lipid-lowering drug with antioxidant and anti-inflammatory properties, inhibited DENV infection by targeting replication and assembly of viral RNA.[65] Bioflavonoids, Baicalein, and quercetin exert virucidal activity against DENV by interfering with intracellular replication.[66,67] The natural cinchona alkaloid, Quinine, inhibited DENV replication and viral protein synthesis of DENV RNA in a dose-dependent manner.[68] These studies suggest that repurposing of existing drugs is a promising strategy to treat dengue infection.

## Human Immunodeficiency virus

HIV, which has claimed almost 33 million lives so far, remains a substantial global public health issue. Studies have shown that Chloroquine and its analogue, hydroxyl Chloroquine, can inhibit HIV-1 replication.[69] Zidovudine, the first anti-HIV medication approved by the FDA, was created primarily as an anti-cancer drug in 1964, before being formulated as an anti-HIV product.[70] This was not only the first excellent case of drug repositioning but also the fastest approval period for drugs, completed in 25 months. Therefore, drug repurposing strategy can be crucial for saving time and money associated with the production of new drugs. Several anti-HIV drugs are repurposed candidates for other diseases. For example, cidofovir and ganciclovir have been generally accepted for their capacity to bring about apoptosis in cancer cells.[71,72] Efavirenz has been shown to have significant anti-neoplastic activity against both pancreatic and anaplastic thyroid cancer.[73] Rilpivirine, along with etravirine and efavirenz, was recently reported to inhibit Zika virus infection in the brain.[74] HIV-1 protease inhibitors viz. ritonavir and lopinavir are known to exhibit anti-protozoal activity, in addition to anti-cancer activity and anti-malarial activity.[75,76] Remdesivir, another HIV-1 protease inhibitor, has also shown significant inhibitory potential against several viruses, including filoviruses such as Ebola.[77]

## SARS-CoV-2

Coronaviruses (CoVs) are single-stranded RNA viruses that cause various diseases, such as common cold, respiratory and gastrointestinal infections. The primary challenge about CoV infections includes their substantial death rates, the advent of mutated viral strains capable of human-to-human transmission, and trouble in determining the intermediate host. SARS-CoV-2, causing COVID-19 outbreaks originated in China in late 2019 and later spreads to many countries worldwide. In this scenario, where CoVs poses a significant concern to global public health, the quest for potent therapeutic methods has become a priority for global public health management. The main targets for drug-repurposing studies in SARS-CoV-2

are main protease (mPro), spike protein, and RNA-dependent RNA polymerase (RdRp). Several drugs such as paritaprevir, simeprevir, Saquinavir, ritonavir, remdesivir, delavirdine, cefuroxime, oseltamivir, prevacid, Apixaban, Nelfinavir, glecaprevir, Perampanel, Carprofen, Celecoxib, Alprazolam, Trovafolxacin, Sarafloxacin, Ethyl biscoumacetate, Daunorubicin, ergotamine, bromocriptine, meclocycline, amrubicin, ergoloid, ketotifen-N-glucuronide, N-trifluoroacetyl-adriamycin, and 5a-reductase-inhibitor were proposed as mPro mediated potential inhibitor of SARS-CoV-2.[78-82] The virtual screening of inhibitors against human Transmembrane serine protease 2 (TMPRSS2), which allow spike protein-mediated entry of SARS-CoV-2, predicted benzquercin as the most potent hit.[83] Recently, several compounds, including ivermectin, selamectin, doramectin, theaflavin digallate, suramin sodium, and taraxanthin were predicted to strongly bind to the receptor-binding domain (RBD) of spike protein, suggesting these as possible drug candidates against SARS-CoV-2.[84] Eltrombopag, used for the treatment of thrombocytopenia, interacts with the S2 domain of spike protein, and *in vitro* studies demonstrated that it could interfere with viral entry into host cells.[85] Even though sofosbuvir and remdesivir are anti-virals targeting RdRp of other viruses like HCV, MERS, and SARS, these drugs were proved ineffective against SARS-CoV-2 as confirmed by a recent clinical trial; at the same time, these drugs may shorten recovery time in patients.[86,87] It was predicted that the antiretroviral drug, zidovudine could bind to the newly identified nucleocapsid N-protein.[88] While Hydroxychloroquine was found to be beneficial in inhibiting *in vitro* SARS-CoV-2 infection, the results of preliminary massive-scale randomized clinical trials in COVID-19 failed to demonstrate any survival advantage of such drug therapy.[89,90] The combination of lopinavir/ritonavir used for HIV treatment is a possible candidate for the treatment of COVID-19.[91] In recent months, the need to find drugs to deal with the COVID-19 pandemic has significantly motivated these kinds of studies, even though very few studies provide experimental validation. It is very significant to prove the effectiveness of such drugs in clinical trials as the world desperately hopes to discover a remedy against SARS-CoV-2 as early as possible.

## DRUG REPURPOSING IN BACTERIOLOGY

Bacteria are incredibly successful in gaining drug resistance by genomic modifications such as point mutations and horizontal transfer of genes from the environment. The repurposing of drugs has recently gained interest where antimicrobial resistance poses a well-recognized global health threat. The list of drugs with potential for repurposing as antibacterial agents is given in Table 2.

At least some drugs primarily intended to prevent the growth of cancer also serves as antimicrobials. The antibacterial effect of anti-cancer drugs, 5-fluorouracil, gallium (Ga) compounds, and mitomycin has also been reported previously.[132] Floxuridine, an FDA-approved anti-cancer drug used in the treatment of metastatic carcinoma of the colon, inhibits the growth of *S. aureus*.[98] Denileukin diftitox, an anti-neoplastic agent, currently used to treat T-cell cutaneous lymphoma, enhances the effect of rifampin, isoniazid, and pyrazinamide against infection with *M. tuberculosis* in the mouse model.[99]

Alkylation could be the typical mechanism of action of anti-cancer molecules with antimicrobial activity; however, molecules such as tamoxifen strengthen the host immune system to neutralize them.[133] Mitomycin, FDA approved anti-cancer drug, showed potent antibacterial activity against bacterial pathogens, *Pseudomonas aeruginosa, Staphylococcus aureus*, *Acinetobacter baumannii,* and *Escherichia coli*.[96,97] Moreover, mitomycin eradicates dormant persister cells that are intrinsically tolerant to regular antibiotics.[134] Another alkylating agent and anti-cancer drug, 3-bromopyruvate, shows bactericidal activity against MRSA and possesses the ability to disrupt biofilms.[135] Interestingly, it is also an inhibitor of the New Delhi Metallo-β-lactamase-1 (NDM-1) and reduces the minimal inhibitory concentration (MIC) for several β-lactam antibiotics in *E. coli* strains expressing NDM-1.[136] Other alkylating anti-cancer drugs such as mechlorethamine, chlorambucil, diaziquone, busulfan, thioTEPA, streptozotocin, carmustine, and lomustine also shows promising antibacterial activity.[132] Biofilm inhibition and bacterial quorum sensing interfering activities of Fluoropyrimidine, 5-fluorouracil (5-FU) have been reported previously.[137]

Toremifene, used to treat breast cancer, not only impedes the growth of oral pathogens like *S. mutans* and *P. gingivalis* but also prevents biofilm formation.[94] Antifolate cancer drug methotrexate inhibited the growth of *S. aureus*, *S. arlettae* and *S. sciurii* but only at higher concentrations.[138,139] Another anti-estrogen, Tamoxifen, increases the antibacterial activity of white blood cells and enhances the clearance of MRSA.[95] Sorafenib, a multi-kinase inhibitor used against renal cancer and liver cancer, suppressed the growth of antibiotic-resistant *Klebsiella pneumoniae* strain, suggesting its therapeutic utility against bacterial infection.[140] Furthermore, one of the optimized analogue of Sorafenib, PK150, destroys the persister cells, and it

**Table 2: Drugs with potential for repurposing as antibacterial agents.**

| Drug | Initial use | Repurposed use | References |
|---|---|---|---|
| Pentamidine | Antiprotozoal | Against carbapenemase-producing Enterobacteriaceae | Cebrero *et al*. (2018)[92] |
| Gallium nitrate | Hepatocellular carcinoma | Inhibits *Acinetobacter baumannii* growth and biofilm formation | Chua *et al*. (2006)[93] |
| Toremifene | Breast cancer | Inhibits *Streptococcus mutans* and *Porphyromonas gingivalis,* biofilm inhibition | Gerits *et al*. (2017)[94] |
| Tamoxifen | Anticancer | Increases the antibacterial activity of white blood cells against Methicillin-resistant *Staphylococcus aureus* (MRSA) | Corriden *et al*. (2015)[95] |
| Mitomycin C | Anticancer | Antibacterial activity against *Pseudomonas aeruginosa, Staphylococcus aureus*, *A. baumannii* | Reich *et al*. (1961),[96] Cruz-Muñiz *et al*. (2017)[97] |
| Floxuridine | Anticancer | Inhibits *S. aureus* | Yeo *et al*. (2018)[98] |
| Denileukin diftitox | Anticancer | Inhibits *Mycobacterium tuberculosis* | Gupta *et al*. (2017)[99] |
| Compound TS262 | Anticancer | Inhibits *A. baumannii* | Alves *et al*. (2020)[100] |
| Naftifine | Antifungal | Reduces the virulence of *S. aureus* | Chen *et al*. (2016)[101] |
| Clotrimazole | Antifungal | Inhibits *Staphylococcus pseudintermedius* | Frosini *et al*. (2017)[102] |
| Miconazole | Antifungal | Active against *Streptococcus spp, Staphylococcus spp, Enterococcus spp* | Nenoff *et al*. (2017)[103] |
| Statins | Antihyperlipidemic | Active against several Gram-positive bacteria and Gram-negative bacteria | Ko *et al*. (2017)[104] |
| Aspirin | NSAID | Active against several Gram-positive bacteria and Gram-negative bacteria | Ahmed *et al*. (2016),[105] Konreddy *et al*. (2019)[106] |
| Diflunisal | NSAID | Reduce *S. aureus* cytotoxicity | Hendrix *et al*. (2016)[107] |
| Ibuprofen | NSAID | Active against *S. aureus* | Öztürk *et al*. (2021)[108] |
| Celecoxib | NSAID | Active against *S. aureus, Bacillus anthracis, Bacillus subtilis*, and *Mycobacterium smegmatis* | Thangamani *et al*. (2015)[109] |
| Mefenamic acid | NSAID | Synergistic activity with chloramphenicol and cefuroxime against MRSA | Chan *et al*. (2017)[110] |
| Salicylamide | NSAID | Active against *Neisseria gonorrhoeae* | Alhashimi *et al*. (2019)[111] |
| Ebselen | Anti-inflammatory, anti-oxidant | Active against *B. subtilis*, *B. cereus*, *M. tuberculosis*, *S. aureus*, *E. coli* | Gustafsson *et al*. (2016),[112] Dong *et al*. (2019)[113] |
| Artesunate | Antimalarial | Active against *M. tuberculosis* | Choi *et al*. (2017)[114] |
| Artemisinin | Antimalarial | Active against *Fusobacterium nucleatum subsp. polymorphum, Fusobacterium nucleatum subsp. animalis,* and *Prevotella intermedia* | Kim *et al*. (2015)[115] |
| Niclosamide | Antiparasitic | Anti-virulence and anti-biofilm activity against *P. aeruginosa* | Imperi *et al*. (2013)[116] |
| Auranofin | Antiparasitic | Inhibits *Enterococcus faecium, S. aureus, Enterococcus faecalis, Streptococcus pneumoniae,* and *Streptococcus agalactiae* | Harbut *et al*. (2015)[117] |
| Oxyclozanide | Antiparasitic | Against MRSA | Rajamuthiah *et al*. (2015)[118] |
| Nitazoxanide | Antiparasitic | Against *M. tuberculosis* | de Carvalho *et al*. (2009)[119] |
| Rafoxanide | | Inhibits *A. baumannii* | Domínguez *et al*. (2020)[120] |
| Zidovudine | Antiviral | Against carbapenem-resistant *Enterobacteriaceae* | Doléans *et al*. (2011)[121] |
| Ribavirin | Antiviral | Reduces *V. cholerae* pathogenesis | Mandal *et al*. (2016)[122] |
| DIBI | Thalassemia treatment | Inhibits *S. aureus* | Parquet *et al*. (2018)[123] |
| Ivacaftor | Cystic fibrosis | Inhibits *S. aureus*, *S. pneumoniae* | Reznikov *et al*. (2014)[124] |
| Zafirlukast | Antiasthma drug | Antibacterial and antibiofilm activity against Gram-positive pathogens | Gerits *et al*. (2017)[94] |
| Glatiramer Acetate | Multiple sclerosis | Inhibits *E. coli*, *P. aeruginosa* | Christiansen *et al*. (2017)[125] |
| Penfluridol | Antipsychotic | Prevent biofilm formation of *E. faecalis* | Zeng *et al*. (2021)[126] |
| Ethoxzolamide | Diuretic | Inhibits *H. pylori* | Rahman *et al*. (2020)[127] |
| ticagrelor | Antiplatelet therapy | Inhibits *Clostridioides difficile* | Phanchana *et al*. (2020)[128] |
| Sitagliptin | Diabetes mellitus type II | Anti-virulence agent against *S. marcescens* | Abbas *et al*. (2020)[129] |
| SCR0911 | Cytochrome $bc_1$ inhibitor | Inhibits *M. tuberculosis* | Chong *et al*. (2020)[130] |
| Griseofulvin | Antifungal | Several Gram-negative and Gram-positive bacteria | Geronikaki *et al*. (2020)[131] |
| Salicylamide | NSAID | *Neisseria gonorrhoeae* | Alhashimi *et al*. (2019)[111] |

failed to induce resistance upon continuous exposure of *S. aureus,* indicating its therapeutic potential.[141]

Diverse class of anti-fungal drugs viz. naftifine, miconazole, clotrimazole, and ciclopirox displayed intense antimicrobial activities against Gram-positive and Gram-negative pathogens like *Microsporum canis, Micrococcus luteus, Propionibacterium acnes,* MRSA, *Malassezia furfur, Chryseobacterium aquaticum, Trichophyton mentagrophytes, Candida albicans, Trichophyton rubrum, Epidermophyton floccosum,* and *P. aeruginosa*.[106,142] Clotrimazole is an FDA-approved imidazole derivate with broad-spectrum anti-fungal activity, showed less MIC50 and MIC90 (0.5-1mg/L) for methicillin-sensitive and methicilin resistant strains of *Staphylococcus pseudintermedius*, supporting its use through drug repurposing.[102] Miconazole, traditionally used for skin, nail, and vaginal infections, showed antimicrobial properties against Gram-positive bacteria *Streptococcus* spp., *Staphylococcus* spp., *Enterococcus* spp., and *Corynebacterium* spp., with MIC value ranging between 0.78 and 6.25 μg/mL.[103] Naftifine, another FDA-approved anti-fungal competitively inhibited diapophytoene desaturase, an enzyme involved in carotenoid pigment synthesis, thereby reduces the virulence of *S. aureus*.[102] Therefore, naftifine can be considered as a promising repurposed anti-virulence drug against *S. aureus*.

Statins inhibit HMG-CoA reductase, involved in the cholesterol biosynthetic pathway. Statins viz. atorvastatin, fluvastatin, simvastatin, and rosuvastatin exhibit antimicrobial activity against Gram-positive bacteria (*Streptococcus, Staphylococcus,* and *Enterococci*) and Gram-negative bacteria (*Moraxella catarrhalis, Haemophilus influenzae*, *Porphyromonas gingivalis* and *Aggregatibacter inomycetemcomitans, Enterobacter aerogenes*, *Citrobacter freundii*, *Enterobacter cloacae*, *Klebsiella pneumoniae, Proteus mirabilis, and E. coli*).[104] Simvastatin is one of the most potent antimicrobial agents among statins, showing potent antibacterial activity against Gram-positive and Gram-negative pathogens and inhibited established *staphylococcal* biofilms.[109]

Interestingly, investigators have also explored the efficacy of existing FDA-approved anti-inflammatory drugs against bacterial pathogens. For example, non-steroidal anti-inflammatory drugs (NSAIDs) such as diclofenac sodium, ibuprofen, indomethacin, and aspirin, exhibited antibacterial activity against *E. coli*, Coagulase-negative *Staphylococci* (CoNS), *S. aureus*, *Klebsiella* spp., *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Streptococci* spp., *Proteus* spp. and *Bacillus* spp.[105] Diflunisal, an FDA-approved NSAID is reported to reduce *S. aureus* cytotoxicity, inhibit skeletal cell death, and prevent bone destruction during staphylococcal osteomyelitis.[107] Further, it is reported that diflunisal inhibits the growth of *Helicobacter pylori,* indicating its usefulness in drug repurposing.[143]

The organo-selenium compound ebselen is a topical antibacterial agent in the animal model of MDR *S. aureus* skin infection.[113] Gustafsson *et al.* evaluated the library of ebselen analogue against *B. anthracis M. tuberculosis, S. aureus, B. subtilis,* and *B. cereus* and reported its potential activity in terms of low MIC.[112] These reports suggest the suitability of ebselen as a novel repurposed drug.

Artemisinin is a sesquiterpene lactone anti-malarial drug. Bacterial species like *Fusobacterium nucleatum subsp. polymorphum,* periodontopathic microorganisms such as *Fusobacterium nucleatum subsp. animalis,* and *Prevotella intermedia* were found susceptible to artemisinin.[115] Artemisinin derivatives, artesunate, and dihydroartemisinin exhibited more potent antibacterial activity against *E. coli* than artemisinin.[144] Moreover, artesunate demonstrated selective anti-Mtb activity relative to artemisinin, indicating its effectiveness as a next-generation tuberculosis medication.[114]

Investigators have also demonstrated the potential antibacterial efficacy of antiparasitic agents like auranofin, niclosamide, nitazoxanide, and oxyclozanide against Gram-positive bacteria. Auranofin, an FDA-approved drug for rheumatoid arthritis, exhibited a strong antibacterial effect against several Gram-positive bacteria, including *Enterococcus faecium, S. aureus, Enterococcus faecalis, Streptococcus pneumoniae,* and *Streptococcus agalactiae*.[117] Niclosamide is a benzamide anthelmintic drug used against tapeworm infestation. Imperi *et al.* (2013)[116] demonstrated the anti-virulence and anti-biofilm activity of niclosamide in *P. aeruginosa*. It was earlier reported that nitazoxanide inhibits replicating and nonreplicating forms of Mtb; however, the bactericidal activity could not be validated in the recently conducted phase II clinical trials.[119,145] Oxyclozanide, a salicylanilide anthelmintic drug used against fascioliasis in ruminants, exhibited potent antibacterial activity against MRSA with low MIC values.[118] Overall, these studies suggest that antiparasitic drugs can be successfully repurposed for antimicrobial use. Other salicylanilides, rafoxanide, and closantel have also shown promising antibacterial activity.[146] Anti-helminthic drugs such as moxidectin, ivermectin, and selamectin displayed potency against *M. tuberculosis* and *M. ulcerans*.[147,148]

Few anti-viral drugs, viz. ribavirin and zidovudine have also emerged as drug repurposing candidates. Ribavirin, used for treating hepatitis C, RSV, and viral hemorrhagic fever, binds to virulence activator, AphB and reduced *Vibrio cholerae* pathogenesis in animal models.[122] Zidovudine exhibited synergistic activity

with Tigecycline to treat systemic carbapenem-resistant enterobacteriaceae infections.[121]

## DRUG REPURPOSING IN MYCOLOGY

Mebendazole, an anti-helminthic drug, prevented the growth of the fungi *Cryptococcus* spp.[149] Quinacrine exhibited synergistic action with caspofungin or amphotericin B and inhibited the growth of *Candida albicans*.[150] An anti-metabolite drug used for colorectal cancer, floxuridine demonstrated anti-fungal activity against *Exserohilum rostratum*.[151] Similarly, some anti-inflammatory and immunosuppressive drugs such as aspirin, ibuprofen, and tacrolimus possessed an anti-fungal effect against *Cryptococcus neoformans, Cryptococcus gattii*, and *E. rostratum*.[151,152] The synergy and anti-fungal efficacy of the antipsychotic drug, bromperidol with various azoles like posaconazole, voriconazole, itraconazole, and ketoconazole have been reported previously against *C. albicans, C. glabrata*, and *Aspergillus terreus*.[153]

## DRUG REPURPOSING IN ONCOLOGY

The pharmaceutical industry is developing new cancer therapies, but the process of getting these drugs into the market is slow and costly. The re-use of available approved non-cancer medications as new anti-cancer therapies is a relatively untapped, affordable, and secure strategy. Drug repurposing has the potential to make clinically meaningful improvements to oncology and will bring significant long-term economic and social benefits to sustainable health care systems. The list of drugs with potential for repurposing as anti-cancer agents are given in Table 3.

The interferons are anti-viral agents repurposed for the control of leukaemias and solid cancers. IFN-α has been used to treat hairy cell leukaemia, CML, and myelofibrosis for several years.[169,170] IFNs co-formulation has also been suggested to improve temozolomide therapy by inhibiting the repair enzyme MGMT.[171] Cytokines such as TNF48 and IL2 have also been repurposed, but with limited clinical success due to high toxicity.[172] Investigators have also attempted to repurpose other drugs such as statins, disulfiram, nelfinivir, saracatinib, propranolol, abivertinib, leucovorin, artemisinin, and mibefradil. Statins demonstrate anti-cancer properties by inhibiting the function of small GTP-binding proteins Ras, Rho, and Rac.[173] Disulfiram (DSF) was the first drug developed to treat alcoholism. However, studies suggest that DSF can be effectively repurposed for the treatment of human cancers.[174] Research on nelfinivir demonstrated that it is a valuable drug for cancer treatment, and the mechanism of anti-cancer activity is mediated by activation of endoplasmic reticulum stress-pathway and Akt inhibition pathways.[175] Saracatinib is an Src/Abl kinase inhibitor possessing an antitumor against gastric cancer cell lines. Cotreatment of saracatinib with 5-Flurouracil resulted in enhanced anti-cancer activity in the mouse model, indicating its applicability as a repurposed drug in the future.[176] Studies have shown the efficacy of a non-selective beta-blocker, propranolol as an anti-metastatic agent, particularly relevant to breast cancer.[177] Abivertinib, an inhibitor of Bruton tyrosine kinase, has shown promising anti-cancer effects against acute myeloid leukaemia in preclinical studies.[144] Side effects of methotrexate and other chemotherapy medications can be controlled by leucovorin (folinic acid), initially developed to treat pernicious and megaloblastic anemia. The treatment of colorectal cancer using combinations of leucovorin with 5-fluorouracil and either oxaliplatin or irinotecan is reported previously.[178] Recently, dihydroartemisinin (DHA), a semisynthetic artemisinin derivative, has been reported to show anti-cancer activity against several cancer types, including colorectal cancer.[179] Mibefradil, a T-type $Ca^{2+}$ channel blocker, retard cell division and stimulate cell apoptosis in leukaemia cell lines.[180] The anti-cancer properties of mebendazole, a well-known anti-helminthic drug, have been elucidated in various studies.[181] Rapamycin, an immunosuppressant, has also been proved to possess anti-leukemic effects.[182] To conclude, the high quality of research on repurposing compounds is remarkable and has helped to improve survival and mitigate the impact of chemotherapy on cancer patients.

## CHALLENGES FOR DRUG REPURPOSING

The drug repurposing approach has achieved some remarkable success in the past, for example, raloxifene, initially used for osteoporosis was subsequently approved by the FDA for invasive breast cancer, and Sildenafil, initially used for angina, was repurposed and became the foremost product to treat erectile dysfunction. On the other hand, some repurposed drugs have failed at the level of phase III trials (for example, latrepirdine, an antihistamine repurposed for Huntington's disease, failed in phase III trials). No one can deny the fact that the majority of drug development projects fail during human clinical trials. Despite all hurdles, the search for the novel, effective, safe, and inexpensive drug should continue with the highest priority. The lack of sufficient funds and interest from the pharmaceutical industry is another obstacle for drug repurposing research. Lastly,

**Table 3: Drugs with potential for repurposing as anticancer agents.**

| Drug | Initial use | Repurposed use | References |
|---|---|---|---|
| Indomethacin | Rheumatic disease | Colorectal cancer | Zhang *et al.* (2011),[154] Zhang *et al.* (2020)[155] |
| Quinacrine | Malaria, giardiasis, rheumatoid arthritis | Prostatic, and non-small cell lung cancer | Kanai *et al.* (2014)[156] |
| Curcumin | Dermatological diseases | Pancreatic, breast, and prostate cancer, multiple myeloma | Aggarwal *et al.* (2020),[50] Tuli *et al.* (2019)[157] |
| Genistein | Menopause, osteoporosis, obesity | Prostate, ovarian, and colorectal cancer | Pounds *et al.* (2017)[158] |
| Itraconazole | Antifungal agent | Prostate, and lung cancer | Xu *et al.* (2019)[159] |
| Berberine | Bacterial diarrhea | Breast, gastric, colorectal, and lung cancer | Li *et al.* (2014)[160] |
| Niclosamide | Antihelminthic drug | Colorectal, and prostate cancer | Bai *et al.* (2011)[161] |
| Triamterene | Diuretic | Acute myelocytic leukemia | Kanai *et al.* (2014)[156] |
| Mebendazole | Intestinal helminthiasis | Glioblastoma multiforme | Agarwal *et al.* (2005)[162] |
| Prazosin | Hypertension | Adrenal incidentalomas | Srirangam *et al.* (2011)[163] |
| Ritonavir | Human immunodeficiency virus | Breast cancer, Kaposi's sarcoma, ovarian cancer | Zhang *et al.* (2018)[164] |
| Artemisinin and related-derivatives | Malaria | Brain, liver, cervical, breast, colorectal, and lung cancer, leukemia | Verbaanderd *et al.* (2017)[165] |
| Chloroquine and related-derivatives | Malaria, rheumatoid arthritis | Pancreatic, breast cancer, chondrosarcoma | Elwood *et al.* (2018)[166] |
| Aspirin | Pain, fever | Gastrointestinal, and esophageal cancer | Viola *et al.* (2018)[167] |
| Disulfiram | Alcohol-aversion drug | Prostate, and breast cancer, melanoma | Lu *et al.* (2021)[168] |
| Rapamycin | Immunosuppressant, anti-restenosis agent | Rectum, breast, and prostate cancer | Kanai *et al.* (2014)[156] |

a range of legal and intellectual property barriers have a significant effect on the future benefit expected from the repurposed product.

## CONCLUSION

Multiple disease outbreaks already afflict the global health care system with a lack of effective drugs to prevent transmission of the pathogen. The drugs used to treat recently emerged infectious agents like SARS-CoV-2 are not very successful, and it is a formidable challenge to develop vaccines for all diseases. In this context, there is an immense requirement to repurpose the available drugs using solid shreds of evidence. Therefore, assessing the repurposing potency of existing drugs and the synergism of two or more known drugs can offer an excellent and practical approach for the development of new therapeutic agents. The drug repositioning approach provides a substantial decrease in research and development costs, quick testing, a higher likelihood of success in the market, and reduced investment risk. Due to this fact, drug scientists and pharmaceutical companies are immensely interested and benefited, allowing the implementation of novel repositioning strategy methods in drug development programs. Besides, virtual screening, structure-based drug design, pharmacophore modelling, and artificial intelligence (AI) technology will further speed up the drug discovery phase. Further, the drug repositioning strategy has become very useful to determine the undefined mechanism of drug action by exploring novel pathways or off-targets. Finally, drug repurposing strategy can be efficiently used in the discovery of new drugs, and it offers immense potential.

## ACKNOWLEDGEMENT

The authors are extremely grateful to former Principal, Dr. Aravind Krishnan K, Principal, and Dr. Sajeeb Khan A, Head, Dept. of Zoology Government College for Women, Trivandrum for providing necessary facilities.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## Financial Support and Sponsorship

Research funding under Performance Linked Encouragement for Academic Studies and Endeavour (PLEASE) scheme, Directorate of Higher Education, Govt. of Kerala awarded to Praveen Kumar is duly acknowledged.

## REFERENCES

1. Naylor S, Kauppi M, Schonfeld JM. Therapeutic drug repurposing, repositioning and rescue: Part II: Business review. Drug Discov World. 2015;16:57-72.
2. Talevi A, Bellera CL. Challenges and opportunities with drug repurposing: Finding strategies to find alternative uses of therapeutics. Expert Opin Drug Discov. 2020;15(4):397-401. doi: 10.1080/17460441.2020.1704729, PMID 31847616.
3. Li Q, Kang C. Progress in developing inhibitors of SARS-CoV-2 3C-like protease. Microorganisms. 2020;8(8):1250. doi: 10.3390/microorganisms8081250, PMID 32824639.
4. Agrawal P. Advantages and challenges in drug Re-profiling. J Pharmacovigilance. 2015;s2. doi: 10.4172/2329-6887.S2-e002.
5. Retallack H, Di Lullo E, Arias C, Knopp KA, Laurie MT, Sandoval-Espinosa C, *et al*. Zika virus cell tropism in the developing human brain and inhibition by azithromycin. Proc Natl Acad Sci U S A. 2016;113(50):14408-13. doi: 10.1073/pnas.1618029113, PMID 27911847.
6. Rausch K, Hackett BA, Weinbren NL, Reeder SM, Sadovsky Y, Hunter CA, *et al*. Screening bioactives reveals Nanchangmycin as a broad spectrum antiviral active against Zika virus. Cell Rep. 2017;18(3):804-15. doi: 10.1016/j.celrep.2016.12.068, PMID 28099856.
7. Costa VV, Del Sarto JL, Rocha RF, Silva FR, Doria JG, Olmo IG, *et al*. N-methyl-d-aspartate (NMDA) receptor blockade prevents neuronal death induced by Zika virus infection. mBio. 2017;8(2). doi: 10.1128/mBio.00350-17, PMID 28442607.
8. Hasanagic S, Serdarevic F. Potential role of memantine in the prevention and treatment of COVID-19: Its antagonism of nicotinic acetylcholine receptors and beyond. Eur Respir J. 2020;56(2). doi: 10.1183/13993003.01610-2020, PMID 32554535.
9. Yuan S, Chan JF-W, Den-Haan H, Chik KK-H, Zhang AJ, Chan CC-S, *et al*. Structure-based discovery of clinically approved drugs as Zika virus NS2B-NS3 protease inhibitors that potently inhibit Zika virus infection *in vitro* and *in vivo*. Antiviral Res. 2017;145:33-43. doi: 10.1016/j.antiviral.2017.07.007, PMID 28712942.
10. Kamiyama N, Soma R, Hidano S, Watanabe K, Umekita H, Fukuda C, *et al*. Ribavirin inhibits Zika virus (ZIKV) replication *in vitro* and suppresses viremia in ZIKV-infected STAT1-deficient mice. Antiviral Res. 2017;146:1-11. doi: 10.1016/j.antiviral.2017.08.007, PMID 28818572.
11. Xu M, Lee EM, Wen Z, Cheng Y, Huang WK, Qian X, *et al*. Identification of small-molecule inhibitors of Zika virus infection and induced neural cell death via a drug repurposing screen. Nat Med. 2016;22(10):1101-7. doi: 10.1038/nm.4184, PMID 27571349.
12. Li Z, Brecher M, Deng YQ, Zhang J, Sakamuru S, Liu B, *et al*. Existing drugs as broad-spectrum and potent inhibitors for Zika virus by targeting NS2B-NS3 interaction. Cell Res. 2017;27(8):1046-64. doi: 10.1038/cr.2017.88, PMID 28685770.
13. Zhou T, Tan L, Cederquist GY, Fan Y, Hartley BJ, Mukherjee S, *et al*. High-content screening in hPSC-neural progenitors identifies drug candidates that inhibit Zika virus infection in fetal-like organoids and adult brain. Cell Stem Cell. 2017;21(2):274-283.e5. doi: 10.1016/j.stem.2017.06.017, PMID 28736217.
14. Barrows NJ, Campos RK, Powell ST, Prasanth KR, Schott-Lerner G, Soto-Acosta R, *et al*. A screen of FDA-approved drugs for inhibitors of Zika virus infection. Cell Host Microbe. 2016;20(2):259-70. doi: 10.1016/j.chom.2016.07.004, PMID 27476412.
15. Zhang S, Yi C, Li C, Zhang F, Peng J, Wang Q, *et al*. Chloroquine inhibits endosomal viral RNA release and autophagy-dependent viral replication and effectively prevents maternal to fetal transmission of Zika virus. Antiviral Res. 2019;169:104547. doi: 10.1016/j.antiviral.2019.104547.
16. Bullard-Feibelman KM, Govero J, Zhu Z, Salazar V, Veselinovic M, Diamond MS, *et al*. The FDA-approved drug sofosbuvir inhibits Zika virus infection. Antiviral Res. 2017;137:134-40. doi: 10.1016/j.antiviral.2016.11.023, PMID 27902933.
17. Simanjuntak Y, Liang JJ, Lee YL, Lin YL. Repurposing of prochlorperazine for use against dengue virus infection. J Infect Dis. 2015;211(3):394-404. doi: 10.1093/infdis/jiu377, PMID 25028694.
18. He S, Lin B, Chu V, Hu Z, Hu X, Xiao J, *et al*. Repurposing of the antihistamine chlorcyclizine and related compounds for treatment of hepatitis C virus infection. Sci Transl Med. 2015;7(282):282ra49. doi: 10.1126/scitranslmed.3010286, PMID 25855495.
19. Wang S, Liu Y, Guo J, Wang P, Zhang L, Xiao G, *et al*. Screening of FDA-approved drugs for inhibitors of Japanese encephalitis virus infection. J Virol. 2017;91(21). doi: 10.1128/JVI.01055-17, PMID 28814523.
20. Plaze M, Attali D, Prot M, Petit AC, Blatzer M, Vinckier F, *et al*. Inhibition of the replication of SARS-CoV-2 in human cells by the FDA-approved drug chlorpromazine. Int J Antimicrob Agents. 2021;57(3):106274. doi: 10.1016/j.ijantimicag.2020.106274.
21. Sissoko D, Laouenan C, Folkesson E, M'Lebing AB, Beavogui AH, Baize S, *et al*. JIKI Study Group. Experimental Treatment with favipiravir for Ebola Virus Disease (the JIKI Trial): A Historically Controlled, Single-Arm Proof-of-Concept Trial in Guinea. PLOS Med. 2016;13(3):e1001967. doi: 10.1371/journal.pmed.1001967, PMID 26930627.
22. Morales-Ortega A, Bernal-Bello D, Llarena-Barroso C, Frutos-Pérez B, Duarte-Millán MÁ, García de Viedma-García V, *et al*. Imatinib for COVID-19: A case report. Clin Immunol. 2020;218:108518. doi: 10.1016/j.clim.2020.108518.
23. Emadi A, Chua JV, Talwani R, Bentzen SM, Baddley J. Safety and Efficacy of imatinib for Hospitalized Adults with COVID-19: A structured summary of a study protocol for a randomised controlled trial. Trials. 2020;21(1):897. doi: 10.1186/s13063-020-04819-9, PMID 33115543.
24. McKimm-Breschkin JL, Jiang S, Hui DS, Beigel JH, Govorkova EA, Lee N. Prevention and treatment of respiratory viral infections: presentations on antivirals, traditional therapies and host-directed interventions at the 5th ISIRV Antiviral Group conference. Antiviral Res. 2018;149:118-42. doi: 10.1016/j.antiviral.2017.11.013, PMID 29162476.
25. Mahapatro S, Mahilary N, Satapathy AK, Das RR. Nitazoxanide in acute rotavirus diarrhea: A randomized control trial from a developing country. J Trop Med. 2017;2017:7942515. doi: 10.1155/2017/7942515.
26. Dehelean CA, Lazureanu V, Coricovac D, Mioc M, Oancea R, Marcovici I, *et al*. SARS-CoV-2: Repurposed Drugs and Novel Therapeutic Approaches-Insights into Chemical Structure-Biological Activity and Toxicological Screening. J Clin Med. 2020;9(7):2084. doi: 10.3390/jcm9072084, PMID 32630746.
27. Nili A, Farbod A, Neishabouri A, Mozafarihashjin M, Tavakolpour S, Mahmoudi H. Remdesivir: A beacon of hope from Ebola virus disease to COVID-19. Rev Med Virol. 2020;30(6):1-13. doi: 10.1002/rmv.2133, PMID 33210457.
28. Yan Z, Bryant KF, Gregory SM, Angelova M, Dreyfus DH, Zhao XZ, *et al*. HIV integrase inhibitors block replication of alpha-, beta-, and gammaherpesviruses. mBio. 2014;5(4):e01318-14. doi: 10.1128/mBio.01318-14. PMID 24987091.
29. Mercorelli B, Palù G, Loregian A. Drug repurposing for viral infectious diseases: How far are we? Trends Microbiol. 2018;26(10):865-76. doi: 10.1016/j.tim.2018.04.004, PMID 29759926.
30. Wikan N, Smith DR. Zika virus: History of a newly emerging arbovirus. Lancet Infect Dis. 2016;16(7):e119-26. doi: 10.1016/S1473-3099(16)30010-X, PMID 27282424.
31. Delvecchio R, Higa LM, Pezzuto P, Valadão AL, Garcez PP, Monteiro FL, *et al*. Chloroquine, an endocytosis blocking agent, inhibits Zika virus infection in different cell models. Viruses. 2016;8(12):322. doi: 10.3390/v8120322, PMID 27916837.
32. Yang S, Xu M, Lee EM, Gorshkov K, Shiryaev SA, He S, *et al*. Emetine inhibits Zika and Ebola virus infections through two molecular mechanisms: Inhibiting viral replication and decreasing viral entry. Cell Discov. 2018;4(1):31. doi: 10.1038/s41421-018-0034-1, PMID 29872540.

33. Kim JA, Seong RK, Kumar M, Shin OS. Favipiravir and ribavirin inhibit replication of Asian and African strains of Zika virus in different cell models. Viruses. 2018;10(2):72. doi: 10.3390/v10020072, PMID 29425176.
34. Liu G, Wong G, Su S, Bi Y, Plummer F, Gao GF, *et al*. Clinical evaluation of Ebola Virus Disease Therapeutics. Trends Mol Med. 2017;23(9):820-30. doi: 10.1016/j.molmed.2017.07.002, PMID 28822631.
35. Warren TK, Jordan R, Lo MK, Ray AS, Mackman RL, Soloveva V, *et al*. Therapeutic efficacy of the small molecule GS-5734 against Ebola virus in rhesus monkeys. Nature. 2016;531(7594):381-5. doi: 10.1038/nature17180, PMID 26934220.
36. Sheahan TP, Sims AC, Graham RL, Menachery VD, Gralinski LE, Case JB, *et al*. Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. Sci Transl Med. 2017;9(396):eaal3653. doi: 10.1126/scitranslmed.aal3653, PMID 28659436.
37. Kouznetsova J, Sun W, Martínez-Romero C, Tawa G, Shinn P, Chen CZ, *et al*. Identification of 53 compounds that block Ebola virus-like particle entry via a repurposing screen of approved drugs. Emerg Microbes Infect. 2014;3(12):e84. doi: 10.1038/emi.2014.88, PMID 26038505.
38. Johansen LM, DeWald LE, Shoemaker CJ, Hoffstrom BG, Lear-Rooney CM, Stossel A, *et al*. A screen of approved drugs and molecular probes identifies therapeutics with anti–Ebola virus activity. Sci Transl Med. 2015;7(290):290ra89. doi: 10.1126/scitranslmed.aaa5597, PMID 26041706.
39. Wang Y, Cui R, Li G, Gao Q, Yuan S, Altmeyer R, *et al*. Teicoplanin inhibits Ebola Pseudovirus infection in cell culture. Antiviral Res. 2016;125:1-7. doi: 10.1016/j.antiviral.2015.11.003, PMID 26585243.
40. Salata C, Baritussio A, Munegato D, Calistri A, Ha HR, Bigler L, *et al*. Amiodarone and metabolite MDEA inhibit Ebola virus infection by interfering with the viral entry process. Pathog Dis. 2015;73(5):ftv032. doi: 10.1093/femspd/ftv032, PMID 25933611.
41. Taylor R, Kotian P, Warren T, Panchal R, Bavari S, Julander J, *et al*. BCX4430 – A broad-spectrum antiviral adenosine nucleoside analog under development for the treatment of Ebola virus disease. J Infect Public Health. 2016;9(3):220-6. doi: 10.1016/j.jiph.2016.04.002, PMID 27095300.
42. Haffizulla J, Hartman A, Hoppers M, Resnick H, Samudrala S, *et al*. US Nitazoxanide Influenza Clinical Study Group. Effect of nitazoxanide in adults and adolescents with acute uncomplicated influenza: A double-blind, randomised, placebo-controlled, phase 2b/3 trial. Lancet Infect Dis. 2014;14(7):609-18. doi: 10.1016/S1473-3099(14)70717-0, PMID 24852376.
43. Perwitasari O, Yan X, O'Donnell J, Johnson S, Tripp RA. Repurposing kinase inhibitors as antiviral agents to control influenza A virus replication. Assay Drug Dev Technol. 2015;13(10):638-49. doi: 10.1089/adt.2015.0003.drrr, PMID 26192013.
44. Mani D, Wadhwani A, Krishnamurthy PT. Drug repurposing in antiviral research: A current scenario. J Young Pharm. 2019;11(2):117-21. doi: 10.5530/jyp.2019.11.26.
45. Bao J, Marathe B, Govorkova EA, Zheng JJ. Drug repurposing identifies inhibitors of oseltamivir-resistant influenza viruses. Angew Chem Int Ed Engl. 2016;55(10):3438-41. doi: 10.1002/anie.201511361, PMID 26833677.
46. Du X, Zuo X, Meng F, Han C, Ouyang W, Han Y, *et al*. Direct inhibitory effect on viral entry of influenza A and SARS-CoV-2 viruses by azithromycin. Cell Prolif. 2021;54(1):e12953. doi: 10.1111/cpr.12953, PMID 33211371.
47. Schloer S, Goretzko J, Pleschka S, Ludwig S, Rescher U. Combinatory treatment with oseltamivir and itraconazole targeting both virus and host factors in influenza A virus infection. Viruses. 2020;12(7). doi: 10.3390/v12070703, PMID 32610711.
48. Huang F, Zhang C, Liu Q, Zhao Y, Zhang Y, Qin Y, *et al*. Identification of amitriptyline HCl, flavin adenine dinucleotide, azacitidine and calcitriol as repurposing drugs for influenza A H5N1 virus-induced lung injury. PLOS Pathog. 2020;16(3):e1008341. doi: 10.1371/journal.ppat.1008341, PMID 32176725.
49. Park JG, Ávila-Pérez G, Nogales A, Blanco-Lobo P, De la Torre JC, Martínez-Sobrido L. Identification and characterization of novel compounds with broad-spectrum antiviral activity against influenza A and B viruses. J Virol. 2020;94(7):e02149-19. doi: 10.1128/JVI.02149-19, PMID 31941776.
50. Aggarwal M, Leser GP, Lamb RA. Repurposing papaverine as an antiviral agent against influenza viruses and paramyxoviruses. J Virol. 2020;94(6):e01888-19. doi: 10.1128/JVI.01888-19, PMID 31896588.
51. Andersen PI, Krpina K, Ianevski A, Shtaida N, Jo E, Yang J, *et al*. Novel antiviral activities of Obatoclax, emetine, niclosamide, Brequinar, and homoharringtonine. Viruses. 2019;11(10):964. doi: 10.3390/v11100964, PMID 31635418.
52. Radosevic D, Sencanski M, Perovic V, Veljkovic N, Prljic J, Veljkovic V, *et al*. Virtual screen for repurposing of drugs for candidate influenza a M2 ion-channel inhibitors. Front Cell Infect Microbiol. 2019;9:67. doi: 10.3389/fcimb.2019.00067, PMID 30972303.
53. Schräder T, Dudek SE, Schreiber A, Ehrhardt C, Planz O, Ludwig S. The clinically approved MEK inhibitor trametinib efficiently blocks influenza A virus propagation and cytokine expression. Antiviral Res. 2018;157:80-92. doi: 10.1016/j.antiviral.2018.07.006, PMID 29990517.
54. Pickens JA, Tripp RA. Verdinexor targeting of CRM1 is a promising therapeutic approach against RSV and influenza viruses. Viruses. 2018;10(1). doi: 10.3390/v10010048, PMID 29361733.
55. Schloer S, Goretzko J, Kühnl A, Brunotte L, Ludwig S, Rescher U. The clinically licensed antifungal drug itraconazole inhibits influenza virus *in vitro* and *in vivo*. Emerg Microbes Infect. 2019;8(1):80-93. doi: 10.1080/22221751.2018.1559709, PMID 30866762.
56. Botta L, Rivara M, Zuliani V, Radi M. Drug repurposing approaches to fight dengue virus infection and related diseases. Front Biosci (Landmark Ed). 2018;23(6):997-1019. doi: 10.2741/4630, PMID 28930586.
57. Bhakat S, Delang L, Kaptein S, Neyts J, Leyssen P, Jayaprakash V. Reaching beyond HIV/HCV: Nelfinavir as a potential starting point for broad-spectrum protease inhibitors against dengue and Chikungunya virus. RSC Adv. 2015;5(104):85938-49. doi: 10.1039/C5RA14469H.
58. Farias KJS, Machado PRL, Da Fonseca BAL. Chloroquine inhibits dengue virus type 2 replication in Vero cells but not in C6/36 cells. Scientific World Journal. 2013;2013:282734. doi: 10.1155/2013/282734.
59. Whitby K, Pierson TC, Geiss B, Lane K, Engle M, Zhou Y, *et al*. Castanospermine, a potent inhibitor of dengue virus infection *in vitro* and *in vivo*. J Virol. 2005;79(14):8698-706. doi: 10.1128/JVI.79.14.8698-8706.2005, PMID 15994763.
60. Xu H-T, Colby-Germinario SP, Hassounah SA, Fogarty C, Osman N, Palanisamy N, *et al*. Evaluation of Sofosbuvir (β-D-2′-deoxy-2′-α-fluoro-2′-β-C-methyluridine) as an inhibitor of dengue virus replication # [sci rep:2017:7(1):6345]. Sci Rep. 2017;7(1). doi: 10.1038/s41598-017-06612-2.
61. Pu SY, Xiao F, Schor S, Bekerman E, Zanini F, Barouch-Bentov R, *et al*. Feasibility and biological rationale of repurposing sunitinib and erlotinib for dengue treatment. Antiviral Res. 2018;155:67-75. doi: 10.1016/j.antiviral.2018.05.001, PMID 29753658.
62. Medigeshi GR, Kumar R, Dhamija E, Agrawal T, Kar M. N-Desmethylclozapine, fluoxetine, and salmeterol inhibit postentry stages of the dengue virus life cycle. Antimicrob Agents Chemother. 2016;60(11):6709-18. doi: 10.1128/AAC.01367-16, PMID 27572397.
63. Han YS, Penthala NR, Oliveira M, Mesplède T, Xu H, Quan Y, *et al*. Identification of resveratrol analogs as potent anti-dengue agents using a cell-based assay. J Med Virol. 2017;89(3):397-407. doi: 10.1002/jmv.24660, PMID 27509184.
64. Beesetti H, Khanna N, Swaminathan S. Investigational drugs in early development for treating dengue infection. Expert Opin Investig Drugs. 2016;25(9):1059-69. doi: 10.1080/13543784.2016.1201063, PMID 27322111.
65. Soto-Acosta R, Bautista-Carbajal P, Syed GH, Siddiqui A, Del Angel RM. Nordihydroguaiaretic acid (NDGA) inhibits replication and viral morphogenesis of dengue virus. Antiviral Res. 2014;109:132-40. doi: 10.1016/j.antiviral.2014.07.002, PMID 25017471.
66. Zandi K, Teoh BT, Sam SS, Wong PF, Mustafa MR, Abubakar S. Novel antiviral activity of baicalein against dengue virus. BMC Complement Altern Med. 2012;12:214. doi: 10.1186/1472-6882-12-214, PMID 23140177.
67. Zandi K, Teoh BT, Sam SS, Wong PF, Mustafa MR, Abubakar S. Antiviral activity of four types of bioflavonoid against dengue virus type-2. Virol J. 2011;8:560. doi: 10.1186/1743-422X-8-560, PMID 22201648.
68. Malakar S, Sreelatha L, Dechtawewat T, Noisakran S, Yenchitsomanus PT, Chu JJH, *et al*. Drug repurposing of quinine as antiviral against dengue virus infection. Virus Res. 2018;255:171-8. doi: 10.1016/j.virusres.2018.07.018, PMID 30055216.

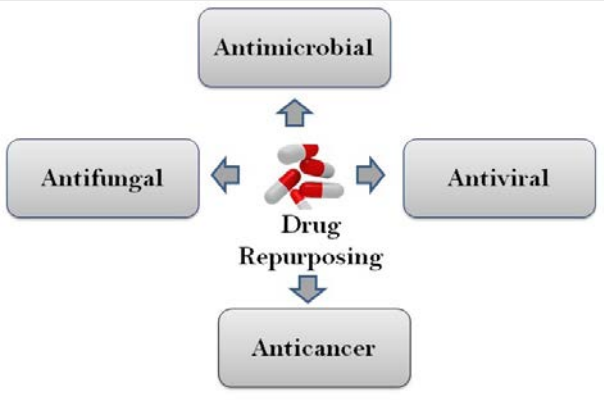
69. Savarino A, Shytaj IL. Chloroquine and beyond: Exploring anti-rheumatic drugs to reduce immune hyperactivation in HIV/AIDS. Retrovirology. 2015;12:51. doi: 10.1186/s12977-015-0178-0, PMID 26084487.
70. Fischl MA, Richman DD, Grieco MH, Gottlieb MS, Volberding PA, Laskin OL, *et al*. The efficacy of azidothymidine (AZT) in the treatment of patients with AIDS and AIDS-related complex. A double-blind, placebo-controlled trial. N Engl J Med. 1987;317(4):185-91. doi: 10.1056/NEJM198707233170401, PMID 3299089.
71. Chemaly RF, Hill JA, Voigt S, Peggs KS. *In vitro* comparison of currently available and investigational antiviral agents against pathogenic human double-stranded DNA viruses: A systematic literature review. Antiviral Res. 2019;163:50-8. doi: 10.1016/j.antiviral.2019.01.008, PMID 30677427.
72. Hadaczek P, Ozawa T, Soroceanu L, Yoshida Y, Matlaf L, Singer E, *et al*. Cidofovir: A novel antitumor agent for glioblastoma. Clin Cancer Res. 2013;19(23):6473-83. doi: 10.1158/1078-0432.CCR-13-1121, PMID 24170543.
73. Hecht M, Erber S, Harrer T, Klinker H, Roth T, Parsch H, *et al*. Efavirenz has the highest anti-proliferative effect of non-nucleoside reverse transcriptase inhibitors against pancreatic cancer cells. PLOS ONE. 2015;10(6):e0130277. doi: 10.1371/journal.pone.0130277, PMID 26086472.
74. Sariyer IK, Gordon J, Burdo TH, Wollebo HS, Gianti E, Donadoni M, *et al*. Suppression of Zika virus infection in the brain by the antiretroviral drug Rilpivirine. Mol Ther. 2019;27(12):2067-79. doi: 10.1016/j.ymthe.2019.10.006, PMID 31653397.
75. Dunn LA, Andrews KT, McCarthy JS, Wright JM, Skinner-Adams TS, Upcroft P, *et al*. The activity of protease inhibitors against Giardia duodenalis and metronidazole-resistant Trichomonas vaginalis. Int J Antimicrob Agents. 2007;29(1):98-102. doi: 10.1016/j.ijantimicag.2006.08.026, PMID 17137752.
76. Andrews KT, Fairlie DP, Madala PK, Ray J, Wyatt DM, Hilton PM, *et al*. Potencies of human immunodeficiency virus protease inhibitors *in vitro* against Plasmodium falciparum and *in vivo* against murine malaria. Antimicrob Agents Chemother. 2006;50(2):639-48. doi: 10.1128/AAC.50.2.639-648.2006, PMID 16436721.
77. Tchesnokov EP, Feng JY, Porter DP, Götte M. Mechanism of inhibition of Ebola virus RNA-dependent RNA polymerase by Remdesivir. Viruses. 2019;11(4):326. doi: 10.3390/v11040326, PMID 30987343.
78. Alamri MA, Ul Qamar T M, Mirza MU, Bhadane R, Alqahtani SM, Muneer I, *et al*. Pharmacoinformatics and molecular dynamics simulation studies reveal potential covalent and FDA-approved inhibitors of SARS-CoV-2 main protease 3CLpro. J Biomol Struct Dyn. 2020;1–13.
79. Al-Khafaji K, Al-Duhaidahawi D, Taskin Tok T. Using integrated computational approaches to identify safe and rapid treatment for SARS-CoV-2. J Biomol Struct Dyn. 2020:1-9. doi: 10.1080/07391102.2020.1764392.
80. Fischer A, Sellner M, Neranjan S, Smieško M, Lill MA. Potential inhibitors for novel coronavirus protease identified by virtual screening of 606 million compounds. Int J Mol Sci. 2020;21(10):3626. doi: 10.3390/ijms21103626, PMID 32455534.
81. Gimeno A, Mestres-Truyol J, Ojeda-Montes MJ, Macip G, Saldivar-Espinoza B, Cereto-Massagué A, *et al*. Prediction of novel inhibitors of the main protease (M-pro) of SARS-CoV-2 through consensus docking and drug reposition. Int J Mol Sci. 2020;21(11):3793. doi: 10.3390/ijms21113793, PMID 32471205.
82. Jiménez-Alberto A, Ribas-Aparicio RM, Aparicio-Ozores G, Castelán-Vega JA. Virtual screening of approved drugs as potential SARS-CoV-2 main protease inhibitors. Comput Biol Chem. 2020;88:107325. doi: 10.1016/j.compbiolchem.2020.107325.
83. Singh N, Decroly E, Khatib AM, Villoutreix BO. Structure-based drug repositioning over the human TMPRSS2 protease domain: Search for chemical probes able to repress SARS-CoV-2 Spike protein cleavages. Eur J Pharm Sci. 2020;153:105495. doi: 10.1016/j.ejps.2020.105495.
84. de Oliveira OV, Rocha GB, Paluch AS, Costa LT. Repurposing approved drugs as inhibitors of SARS-CoV-2 S-protein from molecular modeling and virtual screening. J Biomol Struct Dyn. 2021;39(11):3924-33. doi: 10.1080/07391102.2020.1772885, PMID 32448085.
85. Feng S, Luan X, Wang Y, Wang H, Zhang Z, Wang Y, *et al*. Eltrombopag is a potential target for drug intervention in SARS-CoV-2 spike protein. Infect Genet Evol. 2020;85:104419. doi: 10.1016/j.meegid.2020.104419.
86. Wang Y, Zhang D, Du G, Du R, Zhao J, Jin Y, *et al*. Remdesivir in adults with severe COVID-19: A randomised, double-blind, placebo-controlled, multicentre trial. Lancet. 2020;395(10236):1569-78. doi: 10.1016/S0140-6736(20)31022-9, PMID 32423584.
87. Kaddoura M, Allbrahim M, Hijazi G, Soudani N, Audi A, Alkalamouni H, *et al*. COVID-19 therapeutic options under investigation. Front Pharmacol. 2020;11:1196. doi: 10.3389/fphar.2020.01196, PMID 32848795.
88. Yadav R, Choudhury C, Kumar Y, Bhatia A. Virtual repurposing of ursodeoxycholate and chenodeoxycholate as lead candidates against SARS-Cov2-Envelope protein: A molecular dynamics investigation. J Biomol Struct Dyn. 2020:1-12. doi: 10.1080/07391102.2020.1868339. PMID 33382021.
89. Liu J, Cao R, Xu M, Wang X, Zhang H, Hu H, *et al*. Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection *in vitro*. Cell Discov. 2020;6(1):16. doi: 10.1038/s41421-020-0156-0, PMID 32194981.
90. Khuroo MS. Chloroquine and hydroxychloroquine in coronavirus disease 2019 (COVID-19). Facts, fiction and the hype: A critical appraisal. Int J Antimicrob Agents. 2020;56(3):106101. doi: 10.1016/j.ijantimicag.2020.106101.
91. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, *et al*. A trial of lopinavir–ritonavir in adults hospitalized with severe Covid-19. N Engl J Med. 2020;382(19):1787-99. doi: 10.1056/NEJMoa2001282, PMID 32187464.
92. Cebrero-Cangueiro T, Álvarez-Marín R, Labrador-Herrera G, Smani Y, Cordero-Matía E, Pachón J, *et al*. *In vitro* Activity of pentamidine Alone and in Combination With aminoglycosides, tigecycline, rifampicin, and doripenem Against Clinical Strains of carbapenemase-Producing and/or colistin-Resistant Enterobacteriaceae. Front Cell Infect Microbiol. 2018;8:363. doi: 10.3389/fcimb.2018.00363, PMID 30406040.
93. Chua MS, Bernstein LR, Li R, So SKS. Gallium maltolate is a promising chemotherapeutic agent for the treatment of hepatocellular carcinoma. Anticancer Res. 2006;26(3A):1739-43. PMID 16827101.
94. Gerits E, Van der Massen I, Vandamme K, De Cremer K, De Brucker K, Thevissen K, *et al*. *In vitro* activity of the antiasthmatic drug zafirlukast against the oral pathogens *Porphyromonas gingivalis* and *Streptococcus mutans*. FEMS Microbiol Lett. 2017;364(2). doi: 10.1093/femsle/fnx005, PMID 28087617.
95. Corriden R, Hollands A, Olson J, Derieux J, Lopez J, Chang JT, *et al*. Tamoxifen augments the innate immune function of neutrophils through modulation of intracellular ceramide. Nat Commun. 2015;6(1):8369. doi: 10.1038/ncomms9369, PMID 26458291.
96. Reich E, Shatkin AJ, Tatum EL. Bacteriocidal action of mitomycin C. Biochim Biophys Acta. 1961;53(1):132-49. doi: 10.1016/0006-3002(61)90800-9.
97. Cruz-Muñiz MY, López-Jacome LE, Hernández-Durán M, Franco-Cendejas R, Licona-Limón P, Ramos-Balderas JL, *et al*. Repurposing the anticancer drug mitomycin C for the treatment of persistent *Acinetobacter baumannii* infections. Int J Antimicrob Agents. 2017;49(1):88-92. doi: 10.1016/j.ijantimicag.2016.08.022, PMID 27939675.
98. Yeo WS, Arya R, Kim KK, Jeong H, Cho KH, Bae T. The FDA-approved anti-cancer drugs, streptozotocin and floxuridine, reduce the virulence of Staphylococcus aureus. Sci Rep. 2018;8(1):2521. doi: 10.1038/s41598-018-20617-5. PMID 29410445.
99. Gupta S, Cheung L, Pokkali S, Winglee K, Guo H, Murphy JR, *et al*. Suppressor cell-depleting immunotherapy with denileukin diftitox is an effective Host-Directed Therapy for Tuberculosis. J Infect Dis. 2017;215(12):1883-7. doi: 10.1093/infdis/jix208, PMID 28863467.
100. Alves Ferreira D, Martins LMDRS, Fernandes AR, Martins M. A tale of two ends: Repurposing metallic compounds from anti-tumour agents to effective antibacterial activity. Antibiotics;9(6):321. doi: 10.3390/antibiotics9060321.
101. Chen F, Di H, Wang Y, Cao Q, Xu B, Zhang X, *et al*. Small-molecule targeting of a diapophytoene desaturase inhibits S. aureus virulence. Nat Chem Biol. 2016;12(3):174-9. doi: 10.1038/nchembio.2003, PMID 26780405.
102. Frosini SM, Bond R. Activity *in vitro* of clotrimazole against canine methicillin-resistant and susceptible *Staphylococcus pseudintermedius*. Antibiotics (Basel). 2017;6(4). doi: 10.3390/antibiotics6040029, PMID 29165345.
103. Nenoff P, Koch D, Krüger C, Drechsel C, Mayser P. New insights on the antibacterial efficacy of miconazole *in vitro*. Mycoses. 2017;60(8):552-7. doi: 10.1111/myc.12620, PMID 28370366.
104. Ko HHT, Lareu RR, Dix BR, Hughes JD. Statins: Antimicrobial resistance breakers or makers? Peer J. 2017;5:e3952. doi: 10.7717/peerj.3952, PMID 29085751.

105. Eman FA, Rehab MAE, Abo BFA, Nancy GF, Neveen AA, Gamal FMG. Evaluation of antibacterial activity of some non-steroidal anti-inflammatory drugs against *Escherichia coli* causing urinary tract infection. Afr J Microbiol Res. 2016;10(34):1408-16. doi: 10.5897/AJMR2016.8179.
106. Konreddy AK, Rani GU, Lee K, Choi Y. Recent drug-repurposing-driven advances in the discovery of novel antibiotics. Curr Med Chem. 2019;26(28):5363-88. doi: 10.2174/0929867325666180706101404, PMID 29984648.
107. Hendrix AS, Spoonmore TJ, Wilde AD, Putnam NE, Hammer ND, Snyder DJ, *et al*. Repurposing the nonsteroidal anti-inflammatory drug diflunisal as an Osteoprotective, antivirulence therapy for *Staphylococcus aureus* osteomyelitis. Antimicrob Agents Chemother. 2016;60(9):5322-30. doi: 10.1128/AAC.00834-16, PMID 27324764.
108. ÖztÜrk İ, Eraç Y, Ballar Kırmızibayrak P, Ermertcan Ş. Nonsteroidal anti-inflammatory drugs alter antibiotic susceptibility and expression of virulence-related genes and protein A of Staphylococcus aureus. Turk J Med Sci. 2021;51(2):835-47. doi: 10.3906/sag-2003-60, PMID 33078603.
109. Thangamani S, Mohammad H, Abushahba MFN, Hamed MI, Sobreira TJP, Hedrick VE, *et al*. Exploring simvastatin, an antihyperlipidemic drug, as a potential topical antibacterial agent [sci rep:16407]. Sci Rep. 2015;5:16407. doi: 10.1038/srep16407, PMID 26553420.
110. Chan EWL, Yee ZY, Raja I, Yap JKY. Synergistic effect of non-steroidal anti-inflammatory drugs (NSAIDs) on antibacterial activity of cefuroxime and chloramphenicol against methicillin-resistant *Staphylococcus aureus*. J Glob Antimicrob Resist. 2017;10:70-4. doi: 10.1016/j.jgar.2017.03.012, PMID 28673701.
111. Alhashimi M, Mayhoub A, Seleem MN. Repurposing salicylamide for combating multidrug-resistant Neisseria gonorrhoeae. Antimicrob Agents Chemother. 2019;63(12):e01225-19. doi: 10.1128/AAC.01225-19, PMID 31570391.
112. Gustafsson TN, Osman H, Werngren J, Hoffner S, Engman L, Holmgren A. Ebselen and analogs as inhibitors of *Bacillus anthracis* thioredoxin reductase and bactericidal antibacterials targeting Bacillus species, *Staphylococcus aureus* and *Mycobacterium tuberculosis*. Biochim Biophys Acta. 2016;1860(6):1265-71. doi: 10.1016/j.bbagen.2016.03.013, PMID 26971857.
113. Dong C, Zhou J, Wang P, Li T, Zhao Y, Ren X, *et al*. Topical therapeutic efficacy of ebselen against multidrug-resistant *Staphylococcus aureus* LT-1 targeting thioredoxin reductase. Front Microbiol. 2019;10:3016. doi: 10.3389/fmicb.2019.03016, PMID 32010088.
114. Choi WH. Novel pharmacological activity of artesunate and artemisinin: Their potential as anti-tubercular agents. J Clin Med. 2017;6(3). doi: 10.3390/jcm6030030, PMID 28287416.
115. Kim WS, Choi WJ, Lee S, Kim WJ, Lee DC, Sohn UD, *et al*. Anti-inflammatory, antioxidant and antimicrobial effects of artemisinin extracts from *Artemisia annua* L. Korean J Physiol Pharmacol. 2015;19(1):21-7. doi: 10.4196/kjpp.2015.19.1.21, PMID 25605993.
116. Imperi F, Massai F, Ramachandran Pillai CR, Longo F, Zennaro E, Rampioni G, *et al*. New life for an old drug: The anthelmintic drug niclosamide inhibits Pseudomonas aeruginosa quorum sensing. Antimicrob Agents Chemother. 2013 Feb;57(2):996-1005. doi: 10.1128/AAC.01952-12, PMID 23254430.
117. Harbut MB, Vilchèze C, Luo X, Hensler ME, Guo H, Yang B, *et al*. Auranofin exerts broad-spectrum bactericidal activities by targeting thiol-redox homeostasis. Proc Natl Acad Sci U S A. 2015;112(14):4453-8. doi: 10.1073/pnas.1504022112, PMID 25831516.
118. Rajamuthiah R, Fuchs BB, Conery AL, Kim W, Jayamani E, Kwon B, *et al*. Repurposing salicylanilide anthelmintic drugs to combat drug resistant *Staphylococcus aureus*. PLOS ONE. 2015;10(4):e0124595. doi: 10.1371/journal.pone.0124595, PMID 25897961.
119. De Carvalho LPS, Lin G, Jiang X, Nathan C. Nitazoxanide kills replicating and non-replicating *Mycobacterium tuberculosis* and evades resistance. J Med Chem. 2009;52(19):5789-92. doi: 10.1021/jm9010719, PMID 19736929.
120. Domínguez AV, Mejías MEJ, Smani Y. Drugs repurposing for multi-drug resistant bacterial infections. Drug repurposing - hypothesis, molecular aspects and therapeutic applications. Vol. 97; 2020.
121. Doléans-Jordheim A, Bergeron E, Bereyziat F, Ben-Larbi S, Dumitrescu O, Mazoyer MA, *et al*. Zidovudine (AZT) has a bactericidal effect on enterobacteria and induces genetic modifications in resistant strains. Eur J Clin Microbiol Infect Dis. 2011;30(10):1249-56. doi: 10.1007/s10096-011-1220-3, PMID 21494911.
122. Mandal RS, Ta A, Sinha R, Theeya N, Ghosh A, Tasneem M, *et al*. Ribavirin suppresses bacterial virulence by targeting LysR-type transcriptional regulators [sci rep:39454]. Sci Rep. 2016;6(1):39454. doi: 10.1038/srep39454, PMID 27991578.
123. Parquet MDC, Savage KA, Allan DS, Davidson RJ, Holbein BE. Novel iron-chelator DIBI inhibits *Staphylococcus aureus* growth, suppresses experimental MRSA infection in mice and enhances the activities of diverse antibiotics *in vitro*. Front Microbiol. 2018;9:1811. doi: 10.3389/fmicb.2018.01811, PMID 30154764.
124. Reznikov LR, Abou Alaiwa MH, Dohrn CL, Gansemer ND, Diekema DJ, Stoltz DA, *et al*. Antibacterial properties of the CFTR potentiator ivacaftor. J Cyst Fibros. 2014;13(5):515-9. doi: 10.1016/j.jcf.2014.02.004, PMID 24618508.
125. Christiansen SH, Murphy RA, Juul-Madsen K, Fredborg M, Hvam ML, Axelgaard E, *et al*. The Immunomodulatory Drug Glatiramer Acetate is Also an Effective Antimicrobial Agent that Kills Gram-negative Bacteria. Sci Rep. 2017;7(1):15653. doi: 10.1038/s41598-017-15969-3. PMID 29142299.
126. Zeng X, She P, Zhou L, Li S, Hussain Z, Chen L, *et al*. Drug repurposing: Antimicrobial and antibiofilm effects of penfluridol against *Enterococcus faecalis*. MicrobiologyOpen. 2021;10(1):e1148. doi: 10.1002/mbo3.1148, PMID 33345466.
127. Rahman MM, Tikhomirova A, Modak JK, Hutton ML, Supuran CT, Roujeinikova A. Antibacterial activity of ethoxzolamide against *Helicobacter pylori* strains SS1 and 26695. Gut Pathog. 2020;12:20. doi: 10.1186/s13099-020-00358-5, PMID 32318117.
128. Phanchana M, Phetruen T, Harnvoravongchai P, Raksat P, Ounjai P, Chankhamhaengdecha S, *et al*. Repurposing a platelet aggregation inhibitor ticagrelor as an antimicrobial against Clostridioides difficile. Sci Rep. 2020;10(1):6497. doi: 10.1038/s41598-020-63199-x. PMID 32300130.
129. Abbas HA, Hegazy WAH. Repurposing anti-diabetic drug "sitagliptin" as a novel virulence attenuating agent in *Serratia marcescens*. PLOS ONE. 2020;15(4):e0231625. doi: 10.1371/journal.pone.0231625, PMID 32298346.
130. Chong SMS, Manimekalai MSS, Sarathy JP, Williams ZC, Harold LK, Cook GM, *et al*. Antituberculosis Activity of the Antimalaria cytochrome bcc oxidase Inhibitor SCR0911. ACS Infect Dis. 2020;6(4):725-37. doi: 10.1021/acsinfecdis.9b00408, PMID 32092260.
131. Geronikaki A, Kartsev V, Petrou A, Akrivou MG, Vizirianakis IS, Chatzopoulou FM, *et al*. Antibacterial activity of griseofulvin analogues as an example of drug repurposing. Int J Antimicrob Agents. 2020;55(3):105884. doi: 10.1016/j.ijantimicag.2020.105884.
132. Soo VWC, Kwan BW, Quezada H, Castillo-Juárez I, Pérez-Eretza B, García-Contreras SJ, *et al*. Repurposing of anticancer drugs for the treatment of bacterial infections. Curr Top Med Chem. 2017;17(10):1157-76. doi: 10.2174/1568026616666160930131737, PMID 27697046.
133. Quezada H, Martínez-Vázquez M, López-Jácome E, González-Pedrajo B, Andrade Á, Fernández-Presas AM, *et al*. Repurposed anti-cancer drugs: The future for anti-infective therapy? Expert Rev Anti Infect Ther. 2020;18(7):609-12. doi: 10.1080/14787210.2020.1752665, PMID 32290720.
134. Kwan BW, Chowdhury N, Wood TK. Combatting bacterial infections by killing persister cells with mitomycin C. Environ Microbiol. 2015;17(11):4406-14. doi: 10.1111/1462-2920.12873, PMID 25858802.
135. Visca P, Pisa F, Imperi F. The antimetabolite 3-bromopyruvate selectively inhibits *Staphylococcus aureus*. Int J Antimicrob Agents. 2019;53(4):449-55. doi: 10.1016/j.ijantimicag.2018.11.008, PMID 30472291.
136. Kang PW, Su JP, Sun LY, Gao H, Yang KW. 3-bromopyruvate as a potent covalently reversible inhibitor of New Delhi metallo-β-lactamase-1 (NDM-1). Eur J Pharm Sci. 2020;142:105161. doi: 10.1016/j.ejps.2019.105161.
137. Ueda A, Attila C, Whiteley M, Wood TK. Uracil influences quorum sensing and biofilm formation in *Pseudomonas aeruginosa* and fluorouracil is an antagonist. Microb Biotechnol. 2009;2(1):62-74. doi: 10.1111/j.1751-7915.2008.00060.x, PMID 21261882.
138. Kruszewska H, Zareba T, Tyski S. Antimicrobial activity of selected non-antibiotics-activity of methotrexate against *Staphylococcus aureus* strains. Acta Pol Pharm. 2000;57;Suppl:117-9. PMID 11293238.
139. Mammen M, Mohanan AG, Kumar P. Computational and Experimental Validation of Methotrexate as Staphylococcal - DHFR inhibitor. Curr Trends Biotechnol Pharm. 2020;14(4):396-402. doi: 10.5530/ctbp.2020.4.41.

140. Roberts JL, Tavallai M, Nourbakhsh A, Fidanza A, Cruz-Luna T, Smith E, *et al*. GRP78/dna K is a target for Nexavar/Stivarga/Votrient in the treatment of human malignancies, viral infections and bacterial diseases. J Cell Physiol. 2015;230(10):2552-78. d oi: 10.1002/jcp.25014, PMID 25858032.
141. Le P, Kunold E, Macsics R, Rox K, Jennings MC, Ugur I, *et al*. Repurposing human kinase inhibitors to create an antibiotic active against drug-resistant *Staphylococcus aureus*, persisters and biofilms. Nat Chem. 2020;12(2):145-58. doi: 10.1038/s41557-019-0378-7, PMID 31844194.
142. Burnett BP, Mitchell CM. Antimicrobial activity of iodoquinol 1%-hydrocortisone acetate 2% gel against ciclopirox and clotrimazole. Cutis. 2008;82(4):273-80. PMID 19055171.
143. Pandey P, Verma V, Gautam G, Kumari N, Dhar SK, Gourinath S. Targeting the β-clamp in Helicobacter pylori with FDA-approved drugs reveals micromolar inhibition by diflunisal. FEBS Lett. 2017;591(15):2311-22. doi: 10.1002/1873-3468.12734, PMID 28656718.
144. Huang S, Pan J, Jin J, Li C, Li X, Huang J, *et al*. Abivertinib, a novel BTK inhibitor: Anti-Leukemia effects and synergistic efficacy with homoharringtonine in acute myeloid leukemia. Cancer Lett. 2019;461:132-43. doi: 10.1016/j.canlet.2019.07.008, PMID 31310800.
145. Walsh KF, McAulay K, Lee MH, Vilbrun SC, Mathurin L, Jean Francois DJ, *et al*. Early bactericidal activity trial of nitazoxanide for pulmonary tuberculosis. Antimicrob Agents Chemother. 2020;64(5). doi: 10.1128/AAC.01956-19, PMID 32071052.
146. Gooyit M, Janda KD. Reprofiled anthelmintics abate hypervirulent stationary-phase Clostridium difficile. Sci Rep. 2016;6:33642. doi: 10.1038/srep33642. PMID 27633064.
147. Lim LE, Vilchèze C, Ng C, Jacobs WR, Ramón-García S, Thompson CJ. Anthelmintic avermectins kill *Mycobacterium tuberculosis*, including multidrug-resistant clinical strains. Antimicrob Agents Chemother. 2013;57(2):1040-6. doi: 10.1128/AAC.01696-12, PMID 23165468.
148. Omansen TF, Porter JL, Johnson PDR, Van der Werf TS, Stienstra Y, Stinear TP. *In-vitro* activity of avermectins against *Mycobacterium ulcerans*. PLOS Negl Trop Dis. 2015;9(3):e0003549. doi: 10.1371/journal.pntd.0003549, PMID 25742173.
149. Joffe LS, Schneider R, Lopes W, Azevedo R, Staats CC, Kmetzsch L, *et al*. The anti-helminthic compound mebendazole has multiple antifungal effects against *Cryptococcus neoformans*. Front Microbiol. 2017;8:535. doi: 10.3389/fmicb.2017.00535, PMID 28400768.
150. Kulkarny VV, Chavez-Dozal A, Rane HS, Jahng M, Bernardo SM, Parra KJ, *et al*. Quinacrine inhibits *Candida albicans* growth and filamentation at neutral pH. Antimicrob Agents Chemother. 2014;58(12):7501-9. doi: 10.1128/AAC.03083-14, PMID 25288082.
151. Sun W, Park YD, Sugui JA, Fothergill A, Southall N, Shinn P, McKew JC, *et al*. Rapid identification of antifungal compounds against *Exserohilum rostratum* using high throughput drug repurposing screens. PLOS ONE. 2013;8(8):e70506. doi: 10.1371/journal.pone.0070506, PMID 23990907.
152. Ogundeji AO, Pohl CH, Sebolai OM. Repurposing of aspirin and ibuprofen as candidate anti-cryptococcus drugs. Antimicrob Agents Chemother. 2016;60(8):4799-808. doi: 10.1128/AAC.02810-15, PMID 27246782.
153. Holbrook SYL, Garzan A, Dennis EK, Shrestha SK, Garneau-Tsodikova S. Repurposing antipsychotic drugs into antifungal agents: Synergistic combinations of azoles and Bromperidol derivatives in the treatment of various fungal infections. Eur J Med Chem. 2017;139:12-21. doi: 10.1016/j.ejmech.2017.07.030, PMID 28797882.
154. Zhang YJ, Bao YJ, Dai Q, Yang WY, Cheng P, Zhu LM, *et al*. MTOR signaling is involved in indomethacin and nimesulide suppression of colorectal cancer cell growth via a COX-2 independent pathway. Ann Surg Oncol. 2011;18(2):580-8. doi: 10.1245/s10434-010-1268-9, PMID 20803081.
155. Zhang Z, Zhou L, Xie N, Nice EC, Zhang T, Cui Y, *et al*. Overcoming cancer therapeutic bottleneck by drug repurposing. Signal Transduct Target Ther. 2020;5(1):113. doi: 10.1038/s41392-020-00213-8, PMID 32616710.
156. Kanai M. Therapeutic applications of curcumin for patients with pancreatic cancer. World J Gastroenterol. 2014;20(28):9384-91. doi: 10.3748/wjg.v20.i28.9384, PMID 25071333.
157. Tuli HS, Tuorkey MJ, Thakral F, Sak K, Kumar M, Sharma AK, *et al*. Molecular mechanisms of action of genistein in cancer: Recent advances. Front Pharmacol. 2019;10:1336. doi: 10.3389/fphar.2019.01336, PMID 31866857.
158. Pounds R, Leonard S, Dawson C, Kehoe S. Repurposing itraconazole for the treatment of cancer. Oncol Lett. 2017;14(3):2587-97. doi: 10.3892/ol.2017.6569, PMID 28927025.
159. Xu J, Long Y, Ni L, Yuan X, Yu N, Wu R, *et al*. Anticancer effect of berberine based on experimental animal models of various cancers: A systematic review and meta-analysis. BMC Cancer. 2019;19(1):589. doi: 10.1186/s12885-019-5791-1, PMID 31208348.
160. Li Y, Li PK, Roberts MJ, Arend RC, Samant RS, Buchsbaum DJ. Multi-targeted therapy of cancer by niclosamide: A new application for an old drug. Cancer Lett. 2014;349(1):8-14. doi: 10.1016/j.canlet.2014.04.003, PMID 24732808.
161. Bai RY, Staedtke V, Aprhys CM, Gallia GL, Riggins GJ. Antiparasitic mebendazole shows survival benefit in 2 preclinical models of glioblastoma multiforme. Neuro Oncol. 2011;13(9):974-82. doi: 10.1093/neuonc/nor077, PMID 21764822.
162. Agarwal A, Gupta S, Mishra AK, Singh N, Mishra SK. Normotensive pheochromocytoma: Institutional experience. World J Surg. 2005;29(9):1185-8. doi: 10.1007/s00268-005-7839-4, PMID 16091986.
163. Srirangam A, Milani M, Mitra R, Guo Z, Rodriguez M, Kathuria H, *et al*. The human immunodeficiency virus protease inhibitor ritonavir inhibits lung cancer cells, in part, by inhibition of survivin. J Thorac Oncol. 2011;6(4):661-70. doi: 10.1097/JTO.0b013e31820c9e3c, PMID 21270666.
164. Zhang Y, Xu G, Zhang S, Wang D, Saravana Prabha P, Zuo Z. Antitumor research on artemisinin and its bioactive derivatives. Nat Prod Bioprospect. 2018;8(4):303-19. doi: 10.1007/s13659-018-0162-1, PMID 29633188.
165. Verbaanderd C, Maes H, Schaaf MB, Sukhatme VP, Pantziarka P, Sukhatme V, *et al*. Repurposing Drugs in Oncology (ReDO)-chloroquine and hydroxychloroquine as anti-cancer agents. Ecancermedicalscience. 2017;11:781. doi: 10.3332/ecancer.2017.781, PMID 29225688.
166. Elwood PC, Pickering JE, Morgan G, Galante J, Weightman AL, Morris D, *et al*. Systematic review update of observational studies further supports aspirin role in cancer treatment: Time to share evidence and decision-making with patients? PLOS ONE. 2018;13(9):e0203957. doi: 10.1371/journal.pone.0203957, PMID 30252883.
167. Viola-Rhenals M, Patel KR, Jaimes-Santamaria L, Wu G, Liu J, Dou QP. Recent advances in Antabuse (disulfiram): The importance of its metal-binding ability to its anticancer activity. Curr Med Chem. 2018;25(4):506-24. doi: 10.2174/0929867324666171023161121, PMID 29065820.
168. Lu C, Li X, Ren Y, Zhang X. Disulfiram: A novel repurposed drug for cancer therapy. Cancer Chemother Pharmacol. 2021;87(2):159-72. doi: 10.1007/s00280-020-04216-8, PMID 33426580.
169. Silva WFD, Teixeira LLC, Rocha V, Buccheri V. Current role of interferon in hairy cell leukemia therapy: A timely decision. Hematol Transfus Cell Ther. 2019;41(1):88-90. doi: 10.1016/j.htct.2018.04.004. PMID 30793110.
170. Bewersdorf JP, Giri S, Wang R, Podoltsev N, Williams RT, Rampal RK, *et al*. Interferon therapy in myelofibrosis: Systematic review and meta-analysis. Clin Lymphoma Myeloma Leuk. 2020;20(10):e712-23. doi: 10.1016/j.clml.2020.05.018, PMID 32669244.
171. Vázquez-Blomquist D, Leenstra S, Van der Kaaij M, Villarreal A, Bello-Rivero I. A co-formulation of interferons type I and II enhances temozolomide response in glioblastoma with unmethylated MGMT promoter status. Mol Biol Rep. 2020;47(7):5263-71. doi: 10.1007/s11033-020-05604-2, PMID 32607953.
172. Schein CH. Repurposing approved drugs for cancer therapy. Br Med Bull. 2021;137(1):13-27. doi: 10.1093/bmb/ldaa045, PMID 33517358.
173. Altwairgi AK. Statins are potential anticancerous agents (review) [review]. Oncol Rep. 2015;33(3):1019-39. doi: 10.3892/or.2015.3741, PMID 25607255.
174. Jiao Y, Hannafon BN, Ding WQ. Disulfiram's anticancer activity: Evidence and mechanisms. Anti-cancer agents Med Chem. 2016;16(11):1378-84. doi: 10.2174/1871520615666160504095040, PMID 27141876.
175. Koltai T. Nelfinavir and other protease inhibitors in cancer: Mechanisms involved in anticancer activity. F1000Res. 2015;4:9. doi: 10.12688/f1000research.5827.2, PMID 26097685.
176. Nam HJ, Im SA, Oh DY, Elvin P, Kim HP, Yoon YK, *et al*. Antitumor activity of saracatinib (AZD0530), a c-Src/Abl kinase inhibitor, alone or in combination with chemotherapeutic agents in gastric cancer. Mol Cancer Ther. 2013;12(1):16-26. doi: 10.1158/1535-7163.MCT-12-0109, PMID 23144237.

177. Pantziarka P, Bryan BA, Crispino S, Dickerson EB. Propranolol and breast cancer-a work in progress. Ecancermedical Science. 2018;12:ed82. doi: 10.3332/ecancer.2018.ed82, PMID 30034523.
178. Kalofonos HP, Aravantinos G, Kosmidis P, Papakostas P, Economopoulos T, Dimopoulos M, *et al*. Irinotecan or oxaliplatin combined with leucovorin and 5-fluorouracil as first-line treatment in advanced colorectal cancer: A multicenter, randomized, phase II study. Ann Oncol. 2005;16(6):869-77. doi: 10.1093/annonc/mdi193, PMID 15855226.
179. Yao Z, Bhandari A, Wang Y, Pan Y, Yang F, Chen R, *et al*. Dihydroartemisinin potentiates antitumor activity of 5-fluorouracil against a resistant colorectal cancer cell line. Biochem Biophys Res Commun. 2018;501(3):636-42. doi: 10.1016/j.bbrc.2018.05.026, PMID 29738772.
180. Huang W, Lu C, Wu Y, Ouyang S, Chen Y. T-type calcium channel antagonists, mibefradil and NNC-55-0396 inhibit cell proliferation and induce cell apoptosis in leukemia cell lines. J Exp Clin Cancer Res. 2015;34(1):54. doi: 10.1186/s13046-015-0171-4, PMID 25989794.
181. Guerini AE, Triggiani L, Maddalo M, Bonù ML, Frassine F, Baiguini A, *et al*. Mebendazole as a candidate for drug repurposing in oncology: An extensive review of current literature. Cancers. 2019;11(9):1284. doi: 10.3390/cancers11091284, PMID 31480477.
182. Sillaber C, Mayerhofer M, Böhm A, Vales A, Gruze A, Aichberger KJ, *et al*. Evaluation of antileukaemic effects of rapamycin in patients with imatinib-resistant chronic myeloid leukaemia. Eur J Clin Investig. 2008;38(1):43-52. doi: 10.1111/j.1365-2362.2007.01892.x, PMID 18173550.

## PICTORIAL ABSTRACT




## SUMMARY

- Drug repurposing is identifying new uses of already existing drugs to reduce the time, cost and effort.
- Recently, this research strategy has secured significant momentum in the field of drug discovery, especially during pandemics like COVID-19.
- Assessing the repurposing potency of existing drugs and the synergism of two or more known drugs can offer an excellent and practical approach for the development of new therapeutic agents.
- Drug repurposing strategy can be efficiently used in the discovery of new drugs, and it offers immense potential.

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**Cite this article:** Kumar P, Mammen M, Madhusoodhanan A, Mohanan AG, Kumar PR, Anilkumar AK, *et al*. Drug Repurposing: A Potentially Emerging Discipline. Indian J of Pharmaceutical Education and Research. 2022;56(2s):s121-s136.