repurposed drugs are important in order to have an efficient target concentration as the drugs were implemented for different treatment paradigms.[33]
Table 1: Table illustrates the mechanism of various drug therapies and reasons for the repurposing of the drug.

Vaccines: The Bharat Biotech, the countries pandemic vaccine leaders are collaborating with virologist at the university of Wisconsin –Madison and the vaccine company FluGen, for the project of developing vaccine against corona. They are in a process of developing an intranasal vaccine for COVID 19 called CoroFlu. CoroFlu is in the animal testing phase in the US, and is expected to move to human trials in the next three months. The intranasal route is selected as flu, RSV and corona enter through the naso-region, and hence produce mucosal immunity when given by nasal drop (just one drop is easy to be injected to the nasal route). Bharat biotech has commercialised 16 vaccines including the one developed against the H1N1 flu that caused the pandemic in 2009.Kawaoksas lab will insert gene sequence from SARS-CoV-2 which cause COVID 19 into M2SR(which is a self- limiting version that induces immunity response against the flu). So that the new vaccine will induce immunity against the coronavirus .[68]Codagenix(CDX-005) from Serum Institute of India manufactures intranasal live attenuated vaccine candidate for SARS-CoV-2 which are expected to be more efficient and patient friendly. As the virus mechanism remains uncertain, it is extremely critical to develop first generation vaccine within short period of time. As prevention is better than cure the immunization programmes is far better for the future perspective. At present there are challenges developing a successful vaccine, but the future may be beneficial enough to tackle the changing strains of coronaviruses. As a matter of moment scientists' tie-up to produce appropriate immune response to terminate the pandemic. There are several concerns, related to the vaccine development which includes reduced small sample size studies, estimation of safety profiles for elderly or minorities and vulnerable groups. Thus, it is difficult to evaluate the efficacy or generalise results as current trials have large gaps in the types of people being enrolled in phase III trials of vaccine development in different countries. It is therefore important to have large scale surveillance trials so that vaccine provides long term safety and prevents infection. Resistance to antivirals are the new emerging challenge in the raising pandemic. The regulatory authority of each country may provide emergency use authorization of vaccines or drugs before the formal approval to just tackle the spread of infection for the moment and monitor their utilization in severely ill patients .[69]Despite of the burst of coronavirus being sudden there are many pharmaceutical companies trying hard for the isolation, identification, and management of the Covid -19 and it might take another 10 years for composing an effective vaccine.[70]
Table 2: Vaccines under phase 3 clinical trial for SARS-CoV-2 infections

CONCLUSION

There have been no effective antiviral therapies or vaccines approved so far for SARS-CoV-2.Vaccines for pandemic infections require rapid development and high production capacity. Many of the vaccine candidates are under developmental phase with a good number in clinical trial phase. An appropriate therapy requires the identification of surface structure of spike glycoproteins for the development of antiviral drug that still has multiple challenges. Clinical

trials have been initiated in different countries to develop effective treatment options, but this may take several years to trace out a reliable treatment therapy for patients. Larger sample size studies are needed to investigate the effects of antiviral therapies for COVID infections leading to a better endpoint. Currently many clinical studies have been reported worldwide and several drugs are repurposed to tackle the new health emergency of COVID-19. But there are no sufficient data to suggest the treatment eradication of COVID -19 as there is lack in comparative studies. Wide population of patients involved RCT opens the era for evaluating and reassuring the efficacy of drug repurposed for COVID-19 .It is early to predict the safety and efficacy of drugs repurposed as they might have an alarming side effect in the future trials. As there is no pre-existing immunity against the new virus the exploration of intranasal delivery techniques with mucosal immunity may be an eye opener. It is also important to acknowledge that there are so far no proven data supporting the standard use of any of these agents for COVID-19.

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Table 1: Table illustrates the mechanism of various drug therapies and reasons for the repurposing of the drug.

Sl. No	Drug name	Mode of action	Drug target on SARS-CoV-2	Factors for the repurposing of the drug(indications)	Plausible adverse effects[62-67]	Reference
1.	Chloroquine/hydroxychloroquine	They create an acidic endosomal pH that inhibits viral fusion with host cell receptors.	Interrupts the endosomal pathway and prevents viral entry and fusion with the host ACE2 receptors.	Antimalarial agent also used for the treatment of autoimmune diseases like rheumatoid arthritis. Their immunomodulatory, anti-inflammatory and anti-viral *in vitro* activities may have a role in viral pneumonia-like symptoms treatment of COVID-19.	Cardiomyopathy, arrhythmias, macular retinopathy	[50,51]
2.	Darunavir/Atazanavir/Cobicistat	Inhibits viral protease	Viral proteins	Anti-HIV agents used in SARS-CoV infections.	Gastrointestnaldisorders,hypersensitivity reactions	[50]

3.	Lopinavir/Ritonavir	Viral protease inhibitor	Viral proteins	They are found effective in SARS and MERS-CoV. The combination inhibits viral replication and cleaves new virions in HIV.	Gstrointestinaldisorders,glucoseintolerance,hyperlipidemia,hepatotoxicity,icterus,retinal toxicity	51
4.	Tocilizumab	Inhibits interleukin and cytokine proliferation	IL-6	Monoclonal antibodies effective in rheumatoid arthritis, cytokine release storm.	Hypersensitivity reactions	50
5.	Remdesivir	Nucleotide inhibitors	RNA-dependent RNA-polymerase	Studies showed potential for SARS-CoV,MERS-CoV and Ebola viruses.	Multiple organ dysfunction syndrome,septicshock,hypotension and acute kidney injury	52.53
6.	Umefenovir	Inhibitsmembrane fusion	Viral and host cellular membranes	Approved for influenza, HIV. Currently in phase IV trials for pneumonia associated COVID 19 infections.	Gastrointestinal adverse effects,raised transaminase levels,weightloss,hair loss	50,51
7.	Favipiravir	Inhibits RNA polymerase	RNA dependent RNA polymerase	studies show antiviral activity against the Ebolavirus, Lassa fever, and influenza. Trials conducted on coronavirus associated pneumonia-like fever	Teratogenecity	50,51
8.	Camostatmesylate	They prevent the viral entry and fusion	TMPRSS2 proteins. (protease	They regulate the cytokine expressions and	No reported adverse effects,monitor for common events like elevated peripheral blood eosinophilia,rash	50,54

		with TMPRSS 2 proteins on host cell surfaces.	inhibitors)	inflammatory responses in chronic pancreatic fibrosis. *In vitro* studies show effective blockage of SARS-CoV-2 entry.		
9.	Teicoplanin	Inhibits viral entry	Viral S proteins	Efficient against Ebola virus, HIV,MERS-CoV, and SARS-CoVinfections.	Common adverse effect are rashes,ototoxicity	55,56
10.	Oseltamivir	Inhibits viral replication	Viral polymerase and protease inhibitor	Antiviral agents used in HIV and HCV treatments.	Neuropsychiatric adverse events	56
11.	Statins	Immuno modulatory effects, anti-inflammatory, and lipid-lowering agents	Inflammatory symptoms	They are mostly employed in patients with comorbid conditions. They reduce the host cell lung injury caused by COVID 19 infections.	Muscle related symptoms.	56
12.	Angiotensin receptor blockers+zinc supplements	Reduce the viral multiplication and spread	ACE-2 receptors	Animal studies in mice show improved survival rates and reduce flu-like symptoms.	No reportable effects,commonly include headache,vomiting,diarrhes	45
13.	Sofosbuvir	Inhibits viral polymerase	RNA dependent RNA polymerase	Clinically effective against anti-HCV, Zika viruses.	Pulmonary arterial hypertension	57
14.	Ribavirin	They are nucleotide inhibitors.	Inhibits viral RNA-dependent RNA-	*In vitro* studies showantiviral activity	Haemolytic anemia,teratogenic	57

			polymerase (RdRp)enzymes	against viral RdRp		
15.	Ribavirin+ Interferon α2b	Nucleotide inhibitor+ immune-modulators	Viral genome	This combination therapy shows effectiveness in RSV, HCV, and SARS-CoV. Theyposses s antiviral and immunomodulatory effects that can be repurposed.	Neuropsychiatric effects	58
16.	Telbivudine	Inhibits Viral polymerase	Viral protein-M^{pro}	Nucleoside analogs effective in hepatitis B virus	No reprtedeffects,commonly include headache,liverproblems,allergic reactions	58
17.	Chlorpromazine	Inhibits viral fusion	Spike proteins, inhibition of clathrin-mediated endocytosis	Dopamine and adrenergic antagonists used against SARS, MERS and Ebola entry	No reported data,monitor for hypersensitivity,risk of glaucoma,urinary retention,agranulocytosis,allergy.-NCT04366739	59
18.	Nitazoxanide	Inhibits viral entry	Haemagglutinin (HA)expressions	Useful as anti-helminthic, production of interferons and inhibits in vitro MERS-CoV infections	Pruritis,hairloss,allergic skin reactions	60
19.	Ivermectin	Inhibits nuclear transport of viral and host proteins.	IMPα/β1 transporter of RNA viruses.	The antiparasitic agent is effective against the Zikavirus,pseudorabies virus.	Neurological adverse events	61

Table 2: Vaccines under phase 3 clinical trial for SARS-CoV-2 infections

SL.No	DEVELOPER	VACCINE	TYPE OF VACCINE	PHASE 3 OF CLINICAL TRIAL[71-75]	FUTURE OUTCOMES
1.	ModernaTX,Inc-National Institute of Allergy and Infectious Disease	mRNA-1273	Genetic vaccine (Lipid nanoparticle encapsulated-mRNA based vaccine)mRNA-1273 against SARS-CoV-2 targets the S spike proteins	Began on July 27th 2020 – NCT04470427	Scientists all around the world are in high-pressure to find a potential treatment and vaccine to crack down the COVID -19 pandemic. Vaccines have the capacity to train the immune system to recognize and attack the virus when they encounter the host cells. Vaccines provide permanent cure and rapid targeted drug delivery. The major factors considered are the strength of antigens, vaccine delivery system and route of vaccination. The production of adequate amount of neutralising antibodies and periods of long term protection by vaccines is necessary to block viral pathogens. There can be adverse effects even in case of vaccine administration hence proper clinical phase trials with small animals
2.	CanSino Biologics Inc/Beijing Institute of Biotechnology(approved for limited use in China)	Ad5-nCoV	Recombinant viral vectored vaccine Ad type 5/non replicating viral vaccine	Began on September 15th 2020 - NCT04526990	
3.	Gamaleya Research Institute of Epidemiology and Microbiology(approval for early use in Russia)	Gam-Covid-Vac	Viral vectored vaccine Adenobased Gam-COVID-Vac/non replicating viral vector	Began on September 28th 2020-NCT04564716	
4.	Jhonson&Jhonson(Beth Israel Deaconess Medical Centre in Boston)	Vaccines made with(Ad26.COV2.S) AdVac^{R} technology	Viral vectored vaccine-Ad26(ENSEMBLE trial)	Began on September 7th 2020-NCT04505722	
5.	Novavax/Emergent Biosolutions	NVX-CoV2373	Protein based vaccine(VLP recombinant sub unit,full length S trimer/nanoparticle with matrix M1 (S-glycoprotein helps in binding to ACE-2 receptor and generate antibody against epitopes.	Began onSeptember 28th 2020-NCT04583995	
6.	Sinopharm-Wuhan Institute of Biological Products(approved for limited use in UAE)	Covid-19 vaccine	Inactivated/live attenuated coronavirus vaccine(after passage/inactivation virus lose virulence)	Began on July 16th 2020-NCT04510207	
7.	SinovacBiotech,Butantan Institute(approval for limited use in China)	CoronaVac/Picovac	Inactivated/live attenuated coronavirus vaccine(after passage/inactivation virus lose virulence	Began on July 21st 2020-NCT04456595	
8.	Bharat Biotech International Limited(Indian council of medical research &National Institute of Virology)	Covaxin(BBV152A,B,C)	Inactivated/live attenuated coronavirus vaccine(after passage/inactivation virus lose virulence)	Began on October3rd 2020(Phase1,2-NCT04471519)	

9.	Laboratorio Elea Phoenix S,A.(Beijing institute of biological products)	Covid-19 vaccine	Inactivated SARS-CoV-2 vaccine	Began on September 16th 2020-NCT04560881	and non human primates are mandatory prior to human trials. The use of adjuvants can intercept the side effects to an utmost level. Of this intranasal route stimulates both cellular and humoral immunity and promises a higher level of protection so far in clinical studies. However the safety and efficacy profiles are crucial factors that determines the success of an ideal vaccine development.[76-78]

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