

# Therapeutic options for the 2019 novel coronavirus (2019-nCoV)

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Supplementary Table 1 | Summary of antiviral compounds against human coronaviruses

Infectious diseases	Drug targets	Antiviral agents	Reported mechanism of action	Status	Ref.
<b>Virus-based treatment strategies</b>					
2019-nCoV; Influenza	RdRp	Favipiravir	Inhibits RdRp	<ul style="list-style-type: none"> <li>Approved for influenza in Japan</li> <li>Randomized trial for 2019-nCoV (ChiCTR2000029544, ChiCTR2000029600)</li> </ul>	[1,2]
2019-nCoV, MERS-CoV, SARS-CoV, RSV, HCV	RdRp	Ribavirin	Inhibits viral RNA synthesis and mRNA capping	<ul style="list-style-type: none"> <li>Approved for HCV and RSV</li> <li>Randomized trial for 2019-nCoV in combination a pegylated interferon (ChiCTR2000029387).</li> <li>Randomized trial for SARS (NCT00578825)</li> </ul>	[2-8]
2019-nCoV	RdRp	Penciclovir	Inhibits RdRp	Approved for HSV	[2]
2019-nCoV, MERS-CoV, SARS-CoV	RdRp	Remdesivir (GS-5734)	Terminates the non-obligate chain	<ul style="list-style-type: none"> <li>Phase 3 for 2019-nCoV (NCT04252664, NCT04257656)</li> <li>Phase 1 for Ebola (NCT03719586)</li> </ul>	[1,2, 9-11]
Broad-spectrum (e.g. SARS-CoV, MERS-CoV, IAV)	RdRp	Galidesivir (BCX4430)	Inhibits viral RNA polymerase function by terminating non-obligate RNA chain	<ul style="list-style-type: none"> <li>Phase 1 for yellow fever (NCT03891420)</li> <li>Phase 1 for Marburg virus (NCT03800173)</li> </ul>	[12]
Broad-spectrum (e.g. CoV, ZIKV, CHIKV)	RdRp	6'-Fluorinated-aristeromycin analogues (Compound 2c)	Inhibits the activity of RdRp and host cell <i>S</i> -adenosyl-L-homocysteine hydrolase	Preclinical	[13]
HCoV-NL63, MERS-CoV	RdRp	Acyclovir fleximer analogues (Compound 2)	Doubly flexible nucleoside analogues inhibit RdRp	Preclinical	[14]
MERS-CoV, SARS-CoV	PLpro	Disulfiram	Inhibits PLpro	Approved for chronic alcohol dependence	[15]
MERS-CoV, SARS-CoV	PLpro	Thiopurine analogues (6-mercaptopurine and 6-thioguanine)	Inhibits PLpro	Preclinical	[16]
MERS-CoV	PLpro	Compound 6	Inhibits PLpro	Preclinical	[17]
2019-nCoV; MERS-CoV, SARS-CoV; HCoV-229E; HIV, HPV	3CLpro	Lopinavir	Inhibits 3CLpro	<ul style="list-style-type: none"> <li>Approved for HIV</li> <li>Phase 3 for 2019-nCoV (NCT04252274, NCT04251871, NCT04255017, ChiCTR2000029539)</li> <li>Phase 2/3 for MERS (NCT02845843)</li> </ul>	[11, 18-21]
2019-nCoV, MERS-CoV	3CLpro	Ritonavir	Inhibits 3CLpro	<ul style="list-style-type: none"> <li>Approved for HIV</li> <li>Phase 3 for 2019-nCoV (NCT04251871, NCT04255017, NCT04261270)</li> <li>Phase 2/3 for MERS (NCT02845843)</li> </ul>	[11,18, 20,21]
2019-nCoV	3CLpro	Darunavir and cobicistat	Inhibits 3CLpro	<ul style="list-style-type: none"> <li>Approved for HIV</li> <li>Phase 3 for 2019-nCoV (NCT04252274)</li> </ul>	-
2019-nCoV	3CLpro	ASC09F (HIV protease inhibitor)	Inhibits 3CLpro	Phase 3 for 2019-nCoV in combination with oseltamivir (NCT04261270)	-
MERS-CoV, SARS-CoV	3CLpro	GC376	Inhibits 3CLpro	Preclinical	[22]
MERS-CoV	3CLpro	GC813	Inhibits 3CLpro	Preclinical	[23]
SARS-CoV	3CLpro	Phenylisoserine derivatives (SK80)	Inhibits 3CLpro	Preclinical	[24]
MERS-CoV, SARS-CoV	3CLpro	Peptidomimetic inhibitors (Compound 6)	Inhibits 3CLpro	Preclinical	[25]
HCoV-229E	3CLpro	1,2,3-triazoles (Compound 14d)	Inhibits 3CLpro	Preclinical	[26]
SARS-CoV, MERS-CoV	3CLpro	Neuraminidase inhibitor analogues (compound 3k)	Inhibits 3CLpro	Preclinical	[27]
SARS-CoV	3CLpro	Unsymmetrical aromatic disulfides	-	Preclinical	[28]

SARS-CoV	3CLpro	Pyriithiobac derivatives (6-5)	Inhibits SARS-CoV 3CLpro	Preclinical	[29]
SARS-Cov, HCV	Helicase	Bananins and 5-hydroxychromone derivatives	Inhibits ATPase and helicase activities	Preclinical	[30]
SARS-CoV, MERS-CoV, MHV	Helicase	SSYA10-001 and ADKs	Inhibits helicase without affecting ATPase activity	Preclinical	[31,32]
MERS-CoV	Helicase	Triazole derivatives (Compound 16)	Inhibits ATPase and helicase activities	Preclinical	[33]
2019-nCoV, MERS-CoV	Spike glycoprotein	Nafamostat	Inhibits spike-mediated membrane fusion	Approved for anticoagulant therapy in Asian countries	[2,34]
SARS-CoV	Spike glycoprotein	Griffithsin	Griffithsin binds to the SARS-CoV spike glycoprotein, thus inhibiting viral entry	Phase 1 for the prevention of HIV transmission (NCT02875119 and NCT04032717)	[35,36]
Broad-spectrum (SARS-CoV, MERS-CoV, influenza)	Spike glycoprotein	Peptide (P9)	Inhibits spike protein-mediated cell-cell entry or fusion	Preclinical	[37]
MERS-CoV, IAV	Spike glycoprotein	$\alpha$ -Helical lipopeptides (e.g. LLS, FFS, IIS, IIK)	Inhibit spike protein-mediated cell-cell entry or fusion	Preclinical	[38]
MERS-CoV	S2 subunit of the spike glycoprotein	HR1P, HR1M, HR1L, HR2L, HR2P, HR2L	Inhibits MERS-CoV replication and spike protein-mediated cell-cell fusion	Preclinical	[39-41]
MERS-CoV	S2 subunit of the spike glycoprotein	HR2P-M1 HR2P-M2	Inhibits MERS-CoV spike protein-mediated cell-cell fusion and infection	Preclinical	[39,42, 43]
MERS-CoV	Spike glycoprotein	P21S10	Inhibits spike protein-mediated cell-cell fusion	Preclinical	[44]
MERS-CoV	Spike glycoprotein	Dihydroantshinone E-64-C, and E-64-D	Blocks the endosomal entry pathway	Preclinical	[45,46]
HCoV (e.g. MERS, SARS)	Spike glycoprotein	OC43-HR2P (most promising EK1)	Inhibits pan-CoV fusion	Preclinical	[47]
MERS-CoV	Spike glycoprotein	MERS-5HB	Inhibits pseudo typed MERS-CoV entry and S protein-mediated syncytial formation	Preclinical	[48]
HCoV-229E	Spike glycoprotein	229E-HR1P 229E-HR2P	Inhibits spike protein-mediated cell-cell fusion	Preclinical	[49]
MERS-CoV	Nucleocapsid protein (possible)	Resveratrol	-	Clinical stages for several diseases (e.g. heart disease)	[50]
HCoV, influenza virus	Fusion inhibitors	1-thia-4-azaspiro [4.5] decan-3-one derivatives (Compound 8n)	-	Preclinical	[51]
MERS-CoV, SARS-CoV	DNA metabolism inhibitor	Gemcitabine hydrochloride	-	Approved as chemotherapy	[46]
MERS-CoV, SARS-CoV	-	Amodiaquine	-	Approved for malaria	[46]
MERS-CoV, SARS-CoV	-	Mefloquine	-	Approved for malaria	[46]
MERS-CoV, SARS-CoV, HCoV-229E	-	Loperamide	-	Approved as an antidiarrheal agent	[19]
2019-nCoV; Influenza virus;	?	Arbidol (Umifenovir)	?	• Approved for influenza in Russia and China • Phase 4 for 2019-nCoV (NCT04260594, NCT04254874, NCT04255017)	-
2019-nCoV; Influenza virus;	?	Oseltamivir	Oseltamivir is an influenza neuraminidase inhibitor.	• Approved for influenza • Phase 4 for 2019-nCoV (NCT04255017), Phase 3 for 2019-nCoV (NCT04261270)	-
<b>Host-based treatment strategies</b>					
2019-nCoV; SARS-CoV; MERS-CoV	Interferon response	Recombinant interferons (interferon- $\alpha$ , interferon- $\beta$ )	Exogenous interferons	• Approved for metastatic renal cell carcinoma (IFN- $\alpha$ 2a), melanoma (IFN- $\alpha$ 2b), multiple sclerosis (IFN- $\beta$ 1a, 1b), chronic granulomatous disease (IFN- $\gamma$ )	[3-8, 21]

		interferon- $\beta$		• Randomized trial for 2019-nCoV (NCT04251871, ChiCTR2000029638)	
2019-nCoV SARS-CoV MERS-CoV	Endosomal acidification	Chloroquine	A lysosomotropic base that appears to disrupt intracellular trafficking and viral fusion events	• Approved for malaria and certain amoeba infections • Open-label trial for 2019-nCoV (ChiCTR2000029609)	[2,19,52,53]
Broad-spectrum (e.g. coronaviruses, 2019-nCoV)	Interferon response	Nitazoxanide	Induces the host innate immune response to produce interferons ( $\alpha$ and $\beta$ ) by the host's fibroblasts and protein kinase R (PKR) activation	Approved for diarrhea treatment	[2,54]
SARS-CoV, MERS-CoV, HIV, HCV	Cyclophilins	Cyclosporine A	Cyclophilin inhibitor that could modulate the interaction of cyclophilins with SARS-CoV nsp1 and the calcineurin–NFAT pathway	Approved for immunosuppression during organ transplantation	[55-58]
SARS-CoV, MERS-CoV, HIV, HCV	Cyclophilins	Alisporivir	Modulates the interaction of cyclophilins with SARS-CoV nsp1 and the calcineurin–NFAT pathway	Phase 3 for HCV (e.g. NCT01860326)	[55-57,59]
MERS-CoV SARS-CoV	Abelson kinase	Imatinib mesylate	Blocks events of early viral entry and/or post-entry	Approved for treating cancers	[46,60]
MERS-CoV, SARS-CoV	Abelson kinase	Dasatinib	-	Approved for treating cancers	[46]
MERS-CoV SARS-CoV	Abelson kinase	Selumetinib	Inhibits the ERK/MAPK and PI3K/AKT/mTOR signaling pathways	Clinical trials for cancers (e.g. non-small cell lung cancer, thyroid cancer)	[61]
MERS-CoV, SARS-CoV	Abelson kinase	Trametinib	Inhibits the ERK/MAPK and PI3K/AKT/mTOR signaling pathways	Approved for treating cancers	[61]
MERS-CoV	Kinase signaling pathways	Rapamycin	Inhibits the ERK/MAPK and PI3K/AKT/mTOR pathways significantly inhibited MERS-CoV replication	Approved originally as an antifungal agent	[61]
MERS-CoV	Tyrosine kinases	Saracatinib	-	Approved for treating cancers	[62]
SARS-CoV MERS-CoV	Clathrin-mediated endocytosis	Chlorpromazine, Triflupromazine, Fluphenazine, Thiethylperazine, Promethazine	Antipsychotic that affects the assembly of clathrin-coated pits at the plasma membrane	The former three were approved as antipsychotic agents	[19,46]
Broad-spectrum (HCoV-229E)	Interferon response	Cyclophilin inhibitors (Compound 30)	Inhibiting the activity of PPIase	Preclinical	[63]
SARS-CoV MERS-CoV HCoV-229E	Endosomal protease	K11777, Camostat	Blocks endosomal protease-mediated cleavage and the endosomal entry pathway	Preclinical	[64]
SARS-CoV, MERS-CoV, HCoV-229E	Host cell membrane-bound viral replication complex	K22	Inhibits membrane-bound RNA synthesis and double membrane vesicle formation	Preclinical	[65,66]
Broad-spectrum (influenza virus, HCoV, Ebola, HIV, HCV)	Antibiotics	Teicoplanin derivatives	-	Widely used for treating gram-positive infections in Europe	[67]
Broad-spectrum (e.g. CoV, influenza virus, RSV)	-	Benzo-heterocyclic amine derivative (N30)	Depression of IMPDH activity	Preclinical	[68]
MERS-CoV, HBV, HCV	-	Mycophenolic acid	Inhibits IMPDH and guanine monophosphate synthesis	Approved immunosuppressant during organ transplantation	[16,69]
MERS-CoV, HCoV-229E, EBOV, Picornaviridae	eIF4A	Silvestrol	Inhibits the DEAD-box RNA helicase eIF4A to affect virus translation	Potential anticancer rocaglate derivative	[70]
Broad-spectrum (influenza A and B, RSV, HCoV)	DHODH	Pyrimidine (FA-613)	Inhibits DHODH	Preclinical	[71]
SARS-CoV, MERS-CoV, influenza	-	Convalescent plasma	Inhibits virus entry to the target cells	Phase 2 (NCT02190799 withdrawn)	[72-74]

## Abbreviations

3CLpro: 3C-like protease, CHIKV: Chikungunya virus, DHODH: dihydroorotate dehydrogenase, HBV: hepatitis B virus, HCoV: human coronavirus, HCV: hepatitis C virus, IAV: influenza A virus, IMPDH: inosine-monophosphate dehydrogenase, IMPTH: inosine-5'-monophosphate dehydrogenase, JEV: Japanese encephalitis virus, MERS: Middle East respiratory syndrome, MERS-CoV: Middle East respiratory syndrome coronavirus, PEDV: porcine epidemic diarrhea virus, PLpro: papain-like protease, PPIase: peptidyl-prolyl isomerase, RBD: receptor-binding domain, RdRp: RNA-dependent RNA polymerase, RSV: respiratory syncytial virus, SARS-CoV: severe acute respiratory syndrome coronavirus, ZIKV: Zika virus.

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