Commentary Article

An Overview of Investigational Drugs for the Treatment of Covid-19

Aman Kapoor[1], Amardeep Ankalgi[1], Upasana Thakur[1], M.S. Ashawat[1], Rohit Bhatia[2]*

[1]Department of Pharmaceutical Analysis, Laureate Institute of Pharmacy Kathog, Jawalaji, Himachal Pradesh, India

[2]Department of Pharmaceutical Chemistry, ISF College of Pharmacy, Moga, Punjab-142001, India

ABSTRACT

SARS-CoV-2 has been emerged from Wuhan in China and has now shacked out more than 200 Countries and territories all over the world. World's best scientists are contributing and endeavouring to find drugs, immuno-modulators and vaccines for the treatment of COVID-19. SARS-CoV-2 virus is a betacoronavirus and positive-stranded RNA virus that originates from the *Coronaviridae* family. The most important structural proteins of SARS-CoV-2 are spike trimeric (S) protein, membrane (M) protein, envelop (E) protein and the nucleocapsid (N) protein. The SARS-CoV-2 begins its life cycle, when the S protein binds with the host cells receptor ACE2 (angiotensin-converting enzyme 2). The viral protein(M) and genome (Protein-N) RNA eventually get assembled into virions (with Protein-S and HE), Endoplasmic reticulum and Golgi apparatus. According to the various research reports, there aremore than 50 drugs, immunomodulators and vaccines that may be effective against COVID-19. Some drugs had shown the *in vitro* activity against MERS-CoV, SARS-CoV and SARS-CoV-2. The aim of this review is to highlight the properties,structure, life cycle of SARS-CoV-2 and description of the agents which show potential efficacy against SARS-CoV-2.

Keywords: SARS-CoV-2; Immune-modulator; ACE2; RNA; MERS-CoV

Introduction

COVID-19 is Zoonotic disease [1] which is caused by severe acute respiratory syndrome causing coronavirus-2(SARS-CoV-2) [2,3], and spreads from animals to human [4]. SARS-CoV-2 has been emerged from Wuhan in China and has now shake out 199 Countries and territories all over the world [5]. It was first reported to the WHO on December 31st, 2019 and WHO declared the COVID-19 outbreak a global health emergency on January 30, 2020. As on 9th July 2020, a total of 12,162,626 confirmed cases of COVID-19 and551,974 deaths have been reported all around the world. The Global death rate is 15% and Global recovery rate is 45.33%[6].All over the world, best scientists are contributing and carrying out immense research to find drugs,immuno-modulators or vaccines for the treatment of COVID-19.

The coronavirus belongs to the family of virus that causesrespiratory tract infections including breathing difficulty, tiredness, fever, dry cough and lung infection [7]. The SARS-CoV-2 virus is a beta, positive-stranded RNA virus that originates from the *Coronaviridae* family. Other viruses from the same family include the SARS-CoV and MERS-CoV which appeared in 2002 and 2016 [8].The name coronavirus springs from the Latin word *corona* which means crown or aureole (Figure 1), which refers to the characteristic look resembling a crown or a solar corona around the virus when viewed under TEM, due to the surface covering of virus with club-shaped protein spikes [9].

Structure of SARS-CoV-2

The most important structural proteins of SARS-CoV-2 are spike trimeric (S) protein, membrane (M) protein, envelop (E) protein and the nucleocapsid (N) protein (Figure 2). The family of corona viruses also have hemagglutinin esterase (HE) glycoprotein[10].The RNA genome consists of seven other genes that are maintainedin the order: ORF1a, ORF1b, S, OEF3, E, M, N in 5' to 3' direction. The maximum part of the RNA genome is secured by the ORF1a/b, which generate the two viral replicase proteins that are polyproteins (PP1a and PP1ab) [11]. These two polyproteins are further producing the sixteen mature non-structural proteins (NSPs) which help in the formation of the replicase transcriptase complex. The rest of the genome encodes the mRNA, which helps in the formation of important structural proteins, i.e., spike, envelope, membrane, nucleocapsid and other essential proteins [11]. Some strains of HE protein produces envelop-associated proteinin the corona virus [12]**.** The RNA genome of Corona viruses is first packed in the nucleocapsid protein and then covered with envelope [13].

Life Cycle of Corona Virus

The SARS-CoV-2 begins its life cycle,when the S Protein binds to the host cells receptor ACE2 (angiotensin-converting enzyme 2) [13].After the binding to the receptor, there is conformational change in the S protein which helps in ease of the viral envelope fusion with the host cell membrane, incorporated via an endosomal pathway [14]. Then SARS-CoV-2 releases the viral RNA in the host cell [15, 16]. Then polyprotein gets cleaved into sixteen mature non-structural proteins (NSPs) which help in the formation of the replicase transcriptase complex and then finally translated into suitable viral proteins [17]. The viral

protein(M) and genome(Protein-N) RNA eventually assembled into virions (with Protein-S and HE) in the Endoplasmic reticulum and Golgi apparatus, which are budding into the lumen of the ER-Golgi intermediate compartment.In the finalstep it transportsvia vesicles and released out of the cell [18] (Figure 3).

Treatment of Novel Coronavirus

COVID-19 is a viral infection which spread rapidly.The FDA,WHO,biotech industry, pharmaceutical companies and research organisations such as the National Institutes of Health (NIH) of US,is working together for developing the new vaccines and find the new drugs for the treatment of COVID-19 [19]. According to the scientists, there are 50 drugs, immune-modulators and vaccines that may be effective against COVID-19. Some of these vaccines, immune-modulators or drugs have been under clinical trials and showing better result against COVID-19. Some of investigational Drugs (Table 1), Immuno-modulators (Table 2) and Vaccines (Table 3) are described below which have revealed the *in vitro* activity against MARS-CoV, SARS-CoV, and SARS-CoV-2.

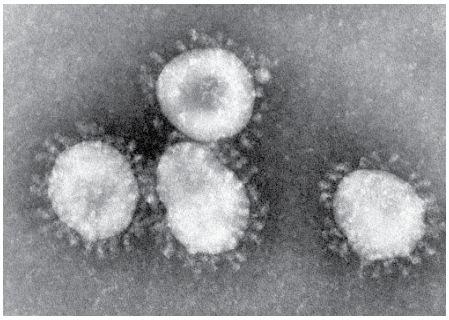

Figure 1: SARS-CoV-2 image under TEM.

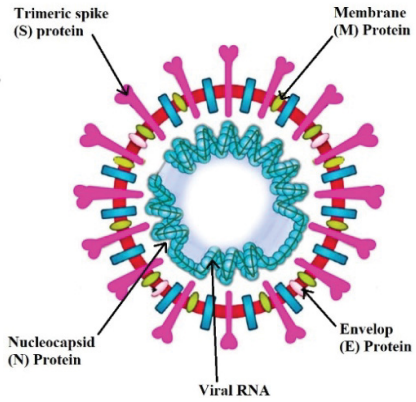

Figure 2: Structure of SARS-CoV-2.

Chloroquine & Hydroxychloroquine

Hydroxychloroquine and chloroquine, both are orally active drugs. Chloroquine has been used for malaria treatment, connective tissue diseases and chemoprophylaxis. Hydroxychloroquine is used for treatment of rheumatoid arthritis, porphyria cutanea tarda and systemic lupus erythematosus. Both drugs have shown *in vitro* activity against MARS-CoV, SARS-CoV, and SARS-CoV-2, where hydroxychloroquine having higher potency against SARS-CoV-2 [20-23]. On 19 March 2020, the President of the United States, Donald Trump, announced that chloroquine and hydroxychloroquine/Plaquenil were approved by the USFDA(Food and Drug Administration) to be tested as a treatment for COVID-19 [24].Chloroquine and hydroxychloroquine is being tested in various clinical trials conducted by academic institutions and government agencies.

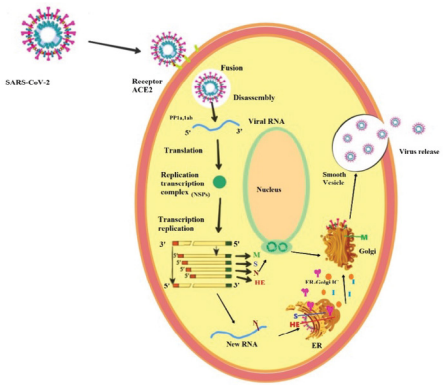

Figure 3: The life cycle of SARS-CoV-2.

Table 1: Investigational drugs for the treatment of covid-19.

S.No.	Drug Name	Drug class	Mechanism	Rationale use	Reference
1	Hydroxychloroquine and chloroquine	Anti-rheumatoid arthritis and Antimalaria Drug	Inhibition of viral enzymes, viral glycosylation, virus assembly transport, and virus release.	*In-vitro* activity against SARS-CoV-2 and may have immune-modulating properties	[21,22,23,24]
2	Favipiravir	Antiviral drug	RNA-dependent RNA polymerase (RdRp) inhibitor	Showing the activity against the SARS-CoV-2	[25,26,27]
3	Remdesivir	Antiviral Drug	Inhibits viral replication through premature termination of RNA transcription	*In vitro* activity against SARS-CoV-2 at low micromolar concentrations and has a high selectivity index.	[28,29,30,31,32]
4	Lopinavir/ritonavir	Anti-HIV Drug	Protease inhibitors	Anti-SARS-CoV activity, *in-vitro* and in clinical studies	[33,34,35]
5	Ribavirin	Antiviral Drug	An adenosine analog that acts as an inhibitor of RNA-dependent RNA polymerases (RdRps)	Reduce the risk of acute respiratory distress syndrome (ARDS) in late-stage patients	[28,34,36,42]
6	IFN-α	Antiviral activity	First-line innate immune defence of the body against having antiviral activity	IFN-α2b spray can adequately reduce the infection rate of respiratory syncytial virus and tnSARS-CoV	[37,38,39]
7	Arbidol	Antiviral drug	Inhibits cell entry of enveloped viruses by blocking viral fusion with host cell membrane.	arbidol can effectively inhibit COVID-19 at a low concentration.	[40,41]

Table 2: Immunomodulators under investigation for the treatment of covid-19.

S.No.	Therapy	Industry Name	Mechanism	Description	Ref.
1.	Remestemcel-L	Mesoblast Ltd	Immunomodulatory, target on MSC.	Allogeneic mesenchymal stem cell (MSC) product candidate being investigated as a treatment for ARDS associated with COVID-19.	[43]
2.	Ifenprodil (NP-120;)	Algernon Pharmaceuticals	N-methyl-d-aspartate(NDMA) receptor glutamate receptor antagonist	NMDA is linked to inflammation and lung injury. An injectable and long-acting oral product are under production to begin clinical trials for COVID-19 and acute lung injury.	[44]
3.	Technosphere, powder Inhaled therapy	MannKind and Immix Ltd	Powders dissolve rapidly with moist lung surface, and release drug quickly to systemic exposure.	Dry powder inhaled formulation with potential to treat ARDS caused by COVID-19.	[45]
4.	Gimsilumab	Roivant Ltd	Monoclonal antibody that targets GM-CSF	A pro-inflammatory cytokine that is up-regulated in patients with COVID-19.	[46]
5.	Brilacidin	Innovation Pharmaceuticals	Defensin- mimetic that mimics the immune system and distort the pathogen membrane and kill the cell.	Still under clinical-stage testing at a US regional biocontainment laboratory.	[47]
6.	TJM2	I-MAB Biopharma	TJM2 is a neutralizing antibody against (GM-CSF),	TJM2 is a neutralizing antibody against human granulocyte-macrophage colony stimulating factor (GM-CSF), an important cytokine that plays a critical role in acute and chronic inflammation.	[48]
7.	(LEAPS) peptide technology	CEL-SCI Corporation	Immunotherapy which stimulates protective cell mediated T cell responses and reduce viral load	Ligand antigen epitope presentation system (LEAPS) peptide technology to reduce COVID-19 viral load and successive lung damage.	[49]
8.	TAK-888	Takeda Pharmaceutical Company	They focus on Concentrated virus-specific antibodies.	Concentrated virus-specific antibodies from plasma collected from people who have already recovered from COVID-19.	[51]
9.	Vascular leakage therapy	Q BioMed Partner Mannin Research	Reduction of endothelial dysfunction	Targets the angiopoietin-Tie2 signaling pathway to reduce endothelial dysfunction.	[53]
10.	Vir and NIH, Antibody-directed therapy	Vir Biotechnology and NIH.	Human monoclonal antibodies	mAbs against coronaviruses	[50]
11.	Antibody-Eli lilly & Abcella	Eli Lilly and AbCellera	Develops antibody which act as immune-modulater	Treatment from more than 500 unique antibodies isolated from one of the first US patients to recover from COVID-19.	[52]

Table 3: Vaccines under investigation for treatment of covid-19.

S.No.	Vaccine	PharmaceuticalIndustry	Description	Reference
1.	BNT162mRNA vaccine	BioNTech and Pfizer Ltd.	BioNTech and Pfizer Ltd developed mRNA-based vaccine and start Phase 1 trial.	[54]
2.	S-Trimervaccine	GlaxoSmithKline [GSK] and Clover Biopharmaceuticals	Preclinical trials are underway using GSK's adjuvants and Clover's proprietary proteins, which boost the immune system.	[55]
3.	INO-4800 vaccine	Inovio Pharmaceuticals	Human clinical (Phase 1) trials began in 15 April 2020. In addition, Inovio made smart device (Cellectra 3PSP) for large-scale intradermal vaccine delivery.	[56]
4.	TNX-1800 vaccine	Tonix Pharmaceuticals	The vaccine is a modified horsepox virus.	[57]
5.	Intranasal COVID-19 vaccine	Altimmune, Inc.	Finally developed the vaccine and start the preclinical trial on animal.	[58]
6.	Saponin-based Matrix-M adjuvant vaccine	Novavax, Inc.	Phase I clinical trial expected to initiate in late spring of 2020. Vaccine boosts the immune response.	[59]
7.	Johnson & Johnson. SARS-CoV-2 vaccine	Johnson & Johnson Collaboration with U.S. Department of Health & Human.	BARDA (Biomedical advanced Research and Development Authority) will provide funding accelerated development of a vaccine candidate into Phase 1 clinical studies.	[60]
8.	mRNA-1273 vaccine	Moderna, Inc.	A clinical phase study has been initiated in 45 COVID-19 patients on 16 March 2020 at Kaiser Permanente Washington Health Research Instituted in Seattle.	[61]
9.	Brilacidin adjuvant vaccine	Innovation Pharmaceuticals	Evaluated the potential antiviral properties as a defending adjuvant and activate the primary innate antiviral immune response.	[62]
10.	PCR-based DNA vaccine	Applied DNA Sciences and Takis Biotech Ltd.	Preclinical development of a LinearDNA Covid-19 vaccine	[63]

Favipiravir

Favipiravir is an antiviral drug which is RNA-dependent RNA polymerase (RdRp) inhibitor. It also have anti-influenza virus activity and ability to block the replication of flavi-, noro-, alpha-, bunya-, arena- and other RNA viruses [25].After entering into the cell, Favipiravir gest converted into an active phosphoribosylated form (favipiravir-RTP) which are easily identified as a substrate by viral RNA polymerase,then get attached to the RNA polymerase and inhibits them [26]. The National Medical Products Administration of China has approved the use of Favipiraviras a treatment for COVID-19. According to the clinical report, which was tested on 70 patients, the drug has shown efficacy in treating the disease with minimal side effects. The clinical trial is being conducted in Shenzhen, Guangdong province in china [27].

Remdesivir

Remdesivir is an investigational intravenous drug with a broad-spectrum antiviral action that inhibits viral replication through premature termination of RNA transcription [28]. Remdesivir is having antiviral activity against single stranded RNA viruses such as Junin virus, Nipah virus, respiratory syncytial virus, Lassa fever virus, Hendra virus, and the coronaviruses (including MERS and SARS viruses) [29, 30].*In vivo* testing on mice specified that remdesivir can effectively reduce the viral load in lung tissue of mice infected with MERS-CoV. Remdesivir also helps to improve lung function and diminish pathological damage to lung tissue [31]. Wang *et al*. found that remdesivir is a potent drug having *in vitro* activity against SARS-CoV-2 at low micromolar concentrations and has a high selectivity index (half-maximal effective concentration (EC50), 0.77 μM; half-cytotoxic concentration (CC50) > 100 μM; SI > 129.87) [28]. Holshue *et al*. reported that remdesivir revealed *in vitro* activity against SARS-CoV-2 and related beta-coronaviruses and yielded promising results in the treatment of patients with COVID-19 in the United States [32].

Lopinavir/Ritonavir

Lopinavir/ritonavir is a protease inhibitor which is used in combination with other medications to treat adults and children over 14 days of age who are infected with HIV-1[33]. Chu *et al*. found that lopinavir/ ritonavir has anti-SARS-CoV activity*in vitro* and in clinical studies[34].Lopinavir-ritonavir did not show promising result for treatment of COVID-19 patients with pneumonia in a recent clinical trial in China[35],but still under investigation in a WHO and USFDA study.

Ribavirin

Ribavirin is a mono-phosphoramidate prodrug of remdesivirtriphosphate (RDV-TP), which is an antiviral drug containingnucleoside analogue that acts as an inhibitor of RNA-dependent RNA polymerases (RdRps) [32].Ribavirinis also used to treat RSV infection, hepatitis C and some viral hemorrhagic fevers[36]. According to the clinical research report, the combined therapy of ribavirin with ritonavir/lopinavir had reduced the risk of acute respiratory distress syndrome (ARDS) in late-stage patients infected with the coronavirus [28,34].

IFN-α

IFN is the first-line innate immune defence of the body against viral activity [37]. IFN-α is a broad-spectrum antiviral candidate that is mainly used in the treatment of hepatitis. Clinical study revealed that recombinant human IFN-α2b spray can adequately reduce the infection rate of respiratory syncytial virus, adenovirus,influenza virus and tnSARS-CoV [37, 38].IFN-α atomization can be utilized as a choice of treatment for COVID-19 [39].

Arbidol

Arbidol is an antiviral that can be used to treat influenza virus [40]. According to the clinical study report arbidol can effectively inhibit COVID-19 at a low concentration [41-64].

Conclusion

COVID-19 outbreak has spread all around the world and matter of great worry is thatthere are presently no drugs and vaccines finally approved by the U.S. food and Drug Administration (FDA) can be used as a therapeutic candidate against COVID-19. Although many approved drugs has been repurposed for the potential treatment of COVID-19 and many are under clinical trials. Many Govt., semi-Govt., private industries, research labs and academicians are working day and night in order to develop the possible treatment of COVID-19.

References

1. Zoonosis (2019)Merriam-Webster Dictionary.
2. Alexander E Gorbalenya, Susan Baker, Ralph Baric, Raoul J de Groot, Christian Drosten, et al. (2020) The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2". Nature Microbiol 5(5): 1-9.
3. Covid-19 (2020)Coronavirus disease named Covid-19.
4. WHO(2015) Zoonoses.
5. https://www.worldometers.info/coronavirus/
6. Covid-19 (2020) Coronavirus: A timeline of how the deadly COVID-19 outbreak is evolving.
7. WMHC (2020) Wuhan Municipal Health and Health Commission's Briefing on the Current Pneumonia Epidemic Situation in Our City.
8. https://www.cdc.gov/coronavirus/types.html
9. Fred Murphy (2017) Photo Credit: Content Providers(s): CDC/ Dr. Fred Murphy - This media comes from the Centers for Disease Control and Prevention's Public Health Image Library (PHIL), with identification number #4814.
10. Hilgenfeld R (2014) From SARS to MERS: Crystallographic studies on coronaviral proteases enable antiviral drug design. Febs J 281:4085-96.
11. McBride R, van Zyl M, Fielding BC (2014)The coronavirus nucleocapsid is a multifunctional protein. Viruses 6:2991-3018.
12. Li F (2016) Structure, function, and evolution of coronavirus spike proteins. Annu Rev Virol 3:237-61.
13. Xing-Yi Ge, Jia-Lu Li, Xing-Lou Yang, Aleksei AChmura, Guangjian Zhu, et al. (2013) Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. Nature 503 (7477): 535-8.
14. Schoeman D, Fielding BC (2019) Coronavirus envelope protein: current knowledge. Virol J 16: 69.

15. Beniac DR, Andonov A, Grudeski E, Booth TF, et al. (2006) Architecture of the SARS coronavirus prefusion spike. Nature structural & molecular biology 13(8): 751-2.

16. Delmas B, Laude H (1990) Assembly of coronavirus spike protein into trimers and its role in epitope expression. J Virol 64(11): 5367-75.

17. Sjoerd HE van den Worm, Kèvin Knoops, Jessika C Zevenhoven-Dobbe, Corrine Beugeling, Yvonne van der Meer,et al. (2011) Development and RNA-Synthesizing Activity of Coronavirus Replication Structures in the Absence of Protein Synthesis. J Virol 85(11): 5669-73.

18. Takamasa I, Billy T (2013) How Viruses Use the Endoplasmic Reticulum for Entry, Replication, and Assembly. Cold Spring Harb Perspect Biol 5(1): a013250.

19. Stephen M, Hahn (2020) Coronavirus (COVID-19) Update: FDA Provides More Regulatory Relief During Outbreak, Continues to Help Expedite Availability of Diagnostics.

20. COVID-19 (2020) Coronavirus treatment: Vaccines/drugs in the pipeline for COVID-19.

21. Wang M, Cao R, Zhang L, Yang X, Liu J, et al. (2020) Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res 30(3): 269-71.

22. Colson P, Rolain JM, Lagier JC, Brouqui P, Raoult D (2020) Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. Int J Antimicrob Agents 4:105932.

23. Yao X, Ye F, Zhang M, Cui C, Huang B, et al. (2020) In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Clin Infect Dis.

24. https://www.clinicaltrialsarena.com/analysis/coronavirus-mers-cov-drugs/

25. Delang L, Abdelnabi R, Neyts J (2018) Favipiravir as a potential countermeasure against neglected and emerging RNA viruses. Antiviral Res 153:85-94.

26. Furuta Y, Komeno T, Nakamura T (2017) Favipiravir (T-705), a broad spectrum inhibitor of viral RNA polymerase. Proc Jpn Acad Ser B Phys Biol Sci 93: 449-63.

27. https://www.clinicaltrialsarena.com/analysis/coronavirus-mers-cov-drugs/

28. Wang M, Cao R, Zhang L, Yang X, Liu J, et al.(2020) Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res 30(3): 269-71.

29. Lo MK, Jordan R, Arvey A, Sudhamsu J, Shrivastava-Ranjan P, et al. (2017) GS-5734 and its parent nucleoside analog inhibit Filo-, Pneumo-, and Paramyxoviruses. Scientific Reports 7(1): 43395.

30. Sheahan TP, Sims AC, Graham RL, Menachery VD, Gralinski LE, et al. (2017) Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. Science Translational Medicine 9 (396): eaal3653.

31. Timothy P Sheahan, Amy C Sims, Sarah R Leist, Alexandra Schäfer, John Won, et al. (2020) Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERSCoV. Nat Commun11:222

32. Michelle L Holshue, Chas DeBolt, Scott Lindquist, Kathy H Lofy, et al. (2020) First case of 2019 novel coronavirus in the United States. N Engl J Med 382:929-36.

33. The American Society of Health-System Pharmacists (2015) Ritonavir.

34. Chu CM, Cheng VCC, Hung IFN, Wong MML, Chan KH, et al. (2004) Role of lopinavir/ritonavir in the treatment of SARS: Initial virological and clinical findings. Thorax 59:252-6.

35. Cao B, Wang Y, Wen D, Liu W, Wang J, et al. (2020) A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. N Engl J Med.

36. The American Society of Health-System Pharmacists (2016) Ribavirin.

37. Shen KL, Shang YX, Zhang H (2019) Amulticenter, randomized, controlled clinical study on the efficacy and safety of recombinant human interferon 2b spray (pseudomonas) in the treatment of acute upper respiratory tract infection in children. 34:1010-6.

38. Gao H, Zhang LL, Qin C, Duan ZJ, Tu XM, et al. (2005) Experimental study on the prevention and treatment of SARS-CoV infection in rhesus monkeys with recombinant human interferon 2b nasal spray. Chin J Exp Clin Virol 19: 207-11.

39. National Health Commission of People's Republic of China (2020) Diagnosis and treatment of pneumonia caused by novel coronavirus (trial version 4).

40. Leneva IA, Russell RJ, Boriskin YS, Hay AJ (2009) Characteristics of arbidol-resistant mutants of influenza virus: implications for the mechanism of anti-influenza action of arbidol. Antiviral Research 81 (2): 132-40.

41. Leneva IA, Russell RJ, Boriskin YS, Hay AJ (2009). Characteristics of arbidol-resistant mutants of influenza virus: implications for the mechanism of anti-influenza action of arbidol". Antivir Res 81(2):132-40.

42. Abidol and darunavir can effectively inhibit coronavirus. (2020).

43. Brown AJ, Won JJ, Graham RL, Dinnon III KH, Sims AC, et al. (2019) Broad spectrum antiviral remdesivir inhibits human endemic and zoonotic delta coronaviruses with a highly divergent RNA dependent RNA polymerase. Antivir Res 169:1-10.

44. COVID-19 (2020) Mesoblast to evaluate anti-inflammatory cell therapy remestemcel-L for treatment of COVID-19.

45. Zhang C, Zhang Y, Qin Y, Zhang Q, Liu Q, et al. (2019) Ifenprodil and flavopiridol identified by Genomewide RNA interference screening as effective drugs to ameliorate murine acute lung injury after influenza A H5N1 virus infection. m Systems 4(6).

46. Investors (2020) MannKind refocuses pipeline resources in response to COVID-19 Pandemic.

47. Cision PR news wire (2020) Roivant announces development of Anti-GM-CSF monoclonal antibody to prevent and treat acute respiratory distress syndrome (ARDS) in patients with COVID-19.

48. Innovation Pharmaceuticals Inc (2020) Innovation Pharmaceuticals Brilacidin Received by U.S. Regional Biocontainment Laboratory; Testing Against Coronavirus (COVID-19).

49. I-MabBiopharma (2020) I-Mabbiopharma announces development of TJM2 to treat cytokine release syndrome associated with severe and critically-Ill patients with coronavirus disease (COVID-19).

50. Gavin de Windt (2020) CEL-SCI initiates development of immunotherapy to treat COVID-19 coronavirus infection.

51. Vir Biotechnology, Inc (2020) Vir biotechnology announces research collaboration with the national institutes of health vaccine research center on antibodies against coronaviruses.

52. Takeda (2020) Rajeev Venkayya, president, global vaccine business unit on the latest on the coronavirus and takeda.

53. Investor Lilly (2020) AbCellera and Lilly to co-develop antibody therapies for the treatment of COVID-19.

54. BioMed (2020) Q BioMed partner mannin research developing potential treatment for patients infected with coronavirus and other infectious diseases.

55. Investorsbiontech (2020) Pfizer and BioNTech to Co-develop Potential COVID-19 Vaccine.

56. Liang J (2020) Clover and GSK announce research collaboration to evaluate coronavirus (COVID-19) vaccine candidate with pandemic adjuvant system. Clover Biopharmaceuticals.

57. INOVIO Receives New $5 Million Grant to Accelerate Scale Up of Smart Delivery Device for Its COVID-19 Vaccine.

58. Saenger B, Kruse T, Vozzo P (2020) Tonix pharmaceuticals announces research collaboration with southern research to develop a potential vaccine to protect against new coronavirus disease 2019 (COVID-19) based on horsepox virus (TNX-1800).

59. Jurchison S, Robinson A (2020) Altimmune completes first development milestone toward a single-dose intranasal COVID-19 vaccine.

60. Novavax (2020) Novavax Awarded Funding from CEPI for COVID-19 Vaccine Development.

61. Johnson & Johnson (2020) Johnson & Johnson announces collaboration with U.S. Department of health & human services to accelerate development of a potential novel coronavirus vaccine.

62. https://www.nih.gov/news-events/news-releases/nih-clinical-trial-investigational-vaccine-covid-19-begins

63. Brilacidin (2020) Innovation pharmaceuticals Brilacidin to be researched as possible novel coronavirus (COVID-19) vaccine; Brilacidin now being tested as drug and vaccine at different institutions.

64. Pharmaceutical Technology (2020) Applied DNA, Takis biotech design four Covid-19 vaccine candidates.

Address of Correspondence: Rohit Bhatia, Assistant Professor, Department of Pharmaceutical Chemistry, ISF College of Pharmacy, Moga, India, Tel:+8628885561; Email Id: bhatiarohit5678@gmail.com

Submitted: July 13, 2020; Accepted: January 20, 2021; Published: January 27, 2021