

# Insights on SARS-CoV-2: Emerging Outbreaks of Viral Infections and the Need for Heightening the Antiviral Research

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## ABSTRACT

**Background:** Today, about 47 life threatening viruses have been notified for their outbreak potentials including SAR-CoV-2. The proximal origin of SARS-CoV-2 and its affinity to human ACE2 receptors ended in COVID-19 disease pandemic. The genome of SARS-CoV-2 is quite complex and unclear, thus the progress on new antiviral drugs and vaccine discovery is hampered. Worldwide, Indian horizon has emerged as potential source for supply of drugs like hydroxychloroquine, remdesvir, ritonavir lopinavir, etc., to several countries. However, the research initiatives undertaken by Indian industries to fight against COVID-19 are relatively lower than the research attempts of developed countries. Furthermore, Indian industry's collaboration with scientists of research institutes or universities is also very limited. Therefore, the need for enhancing antiviral research activities in India is highly recommended to combat COVID-19 like pandemic, if arise in future as well. **Hypothesis:** Being Indian pharma market as one of the top five leading pharma marketer of this globe, the COVID-19 pandemic lessoned us to realize the need for improving the antiviral research among pharmaceutical industries of Indian horizon. It is needed for the hour as measure to sustain the pharma market credibility at globe. **Results and Conclusion:** In this raising era of viral epidemics, it is imperative that Indian pharmaceutical industries should initiate antiviral research through collaborative approach between pharmaceutical industry and scientists across the globe including researchers from academia and non-profit research organization. Thus, this attempt will definitely improve the antiviral and other drug discovery research initiatives among Indian pharmaceutical industries and will save millions of life from viral pandemics like COVID-19 in near future.

**Key words:** Emerging viruses, Antiviral, COVID-19, Pharma industries, Indian Horizon, SARS-CoV-2 genome.

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## INTRODUCTION

Viruses are the most dangerous pathogens having tendency to cause epidemic and pandemic potential. The report of Integrated Disease Surveillance Programme (IDSP) on the total outbreaks during the year 2017 stated that 71% of outbreaks due to viruses whilst only 29% was accounted by other pathogens including bacteria, fungi, parasite etc.<sup>1</sup> In recent years, viral acute respiratory diseases caused about

four million deaths and 8-10 fold millions of infected patients every year especially in developing countries. Till date, about 200 viral pathogens are responsible for causing life threatening illness such as acute respiratory failure, cardiac arrest, kidney failure etc., in humans and these pathogens are belonging to groups *viz.*, *Orthomyxoviridae*, *Paramyxoviridae*, *Picornaviridae*, *Coronaviridae*, *Adenoviridae* and *Herpesviridae* family.<sup>2</sup> In



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addition to above, Influenza, parainfluenza, respiratory syncytial virus (RSV) and adenoviruses are also reported as virulent respiratory pathogens, known for causing human death.<sup>3</sup> The current virulent viruses and mode of transmission are detailed in Table 1. Among the viruses, the human coronavirus exists since about 1960, later in 2003 five more new coronavirus have been reported including severe acute respiratory syndrome coronavirus (Group IV; SARS-CoV), NL63 (Group I), NL (Group I), HCoV-NH (Group I; New Haven coronavirus) and HKU1 (Group II). Among them, SARS viruses are classified under bio-safety risk IV and known for causing contagious disease severely affecting human health and making the entire globe in panic.

### Re-emerging viruses with outbreak potential

Till date, about 47 viruses have been notified as re-emerging viruses and expected to infect humans with outbreak potentials (Table 1). Among them, SARS-CoV-2, SFTS virus, CCHF's virus, KFD virus, H5N1 virus and Nipah virus are categorized under bio-safety risk 4 (Biohazard-4) group and they possess tendency to cause pandemic, accordingly the SARS-CoV-2 infections resulted COVID-19 pandemic (Coronavirus disease – 2019). Some other viruses like quaranf virus, parainfluenza 1-4, LCMV, Bagaza virus, Chitoor virus, Umbre virus, Kaisodi virus, cat que virus, Ganjam virus and Bhanja virus are also suspected to cause epidemics, but adequate data on virulence are not available. The outbreak potentials, biohazard category, symptoms and current treatment option for the emerging viruses are enlisted in Table 1.

### COVID-19 outbreak

The infectious disease COVID-19 is caused by SARS-CoV-2 (Severe acute respiratory syndrome coronavirus-2). Initially, the viral infection progress with symptoms like fever, cough, shortness of breath, muscular pain, sputum formation, diarrhoea, sore throat, loss of taste and smell and in later stage it leads to pneumonia, multiple organ failure then followed by death. The mortality rate is relatively high in elders and the death rate is ranging from 0.2 to 15 percent depending on the patient's age and comorbidity history including diabetes, cardiovascular, cancer and immunocompromised diseases.<sup>4</sup> However, the complete pathology of COVID-19 in human and its relation to immunity, age, race etc., are not yet completely understood.

The first COVID-19 patient was identified in December 2019 in Wuhan city of China, but in a span of 60 days, the disease had spread to more than 200 countries

globally and ended in coronavirus pandemic 2019–20. The most affected countries are United States, United Kingdom, Italy, France, China, Spain, Iran and Germany. The COVID-19 is caused by transmission of SARS-CoV-2 through coughing or sneezing but believed that it is neither airborne nor waterborne disease, but yet to be defined scientifically. At room temperature, SARS-CoV-2 virus can spread through contaminated surfaces where viral protein remains active for 48-72 hr on surface at room temperature.<sup>5,6</sup> Unfortunately, the infected people can also spread the virus even though they are asymptomatic, besides the host dependant latency period of this virus ranging from 2 to 14 days.<sup>7</sup> Today, there are no drugs or vaccines or immediate clinical solutions available to treat COVID-19, therefore World Health Organization (WHO) recommended “social distancing” and “lock-down” as chain-breaking strategy to avoid communal spreading of COVID-19.<sup>8</sup> It is unfortunate, Princess Maria Teresa of Spain died because of COVID-19, consequently most of the affected countries have implemented “locked down” as a preventive measure to avoid community spread. For example, India imposed more than 40 days locked down for the first time in the Indian history. Finally, COVID-19 pandemic created panic to entire world and the economy of the world countries become worsen.

Curiously, if any of the ongoing drug repurposing research (Table 2) succeeded, India can lead the global market in manufacturing and supplying of drugs of the need. With respect to the effort in finding diagnostic solutions for COVID-19, researchers were successful in the diagnosis of COVID-19 infection from the nasopharyngeal swab sample of patients by rRT-PCR (reverse transcription-polymerase chain reaction) technique. Nevertheless, globally the quantum of research initiatives undertaken by global pharmaceutical industries to discover new antiviral against and vaccines are quite unsatisfactory. This infers the lack of involvement of research organizations and industries in antiviral research attempts. The current details of ongoing research<sup>9</sup> undertaken in the globe platform against COVID-19 are shown in Table 2.

### Proximal origin of COVID-19

SARS-CoV-2 is notified as the 7<sup>th</sup> coronavirus infecting human very severely like MERS-CoV and SARS-CoV, but other four coronaviruses (HKU1, NL63, OC43 and 229E) are less severe to human. The severity is due to the receptor binding domain (RBD) of spike protein SARS-CoV-2 having high affinity to bind with human ACE2 receptors.<sup>10,11</sup> Despite the existing uncertainty on the origin of SARS-CoV-2, it is implausible that

SARS-CoV-2 can emerge from genomic laboratory manipulation of SARS-CoV like viruses. There is no evidence of genetic manipulation that none of the available reverse-genetic systems of beta-coronaviruses was used.<sup>12</sup> Therefore, the genetic data indisputably claims that genome of SARS-CoV-2 is not derived from any virus backbone.<sup>13</sup> To conclude, Kristian *et al.* of Scripps laboratory of USA have clearly explained two plausible scenarios on the origin of SARS-CoV-2 viz., a) natural selection in animal host before zoonotic transfer; and (b) natural selection in humans following zoonotic transfer.<sup>14</sup> In first scenario, 96 % genomic similarity of SARS-CoV-2 to the genome of bat SARS-CoV was reported,<sup>15</sup> hence it is believed that bats served as reservoir host for its progenitor (Figure 1). In the second scenario, progenitor of SARS-CoV-2 might have been jumped into humans and acquired the genomic features through adaptation via undetected or unknown human-human transmission. So far, all the sequenced genomes of SARS-CoV-2 possess identical genomic features, thus the existing SARS-CoV-2 in COVID pandemic is derived from a common ancestor only.

### Genome of SARS-CoV-2 for new drug research

The comparison of alpha- and beta-coronaviruses afforded two prominent genomic features of SARS-CoV-2: (a) SARS-CoV-2 is optimized for its binding potential to the human ACE2 receptor; and (b) the spike protein of SARS-CoV-2 possess functional furin (Polybasic) cleavage site at the S1–S2 boundary by the insertion of 12 nucleotides,<sup>16</sup> with three additional O-linked glycans around the furin site (Figure 1).

### Mutations in RBD of SARS-CoV-2

The receptor binding domain (RBD) present in the spike protein of SARS-CoV-2 is the most variable genomic feature of the coronavirus genome.<sup>17</sup> A total of six

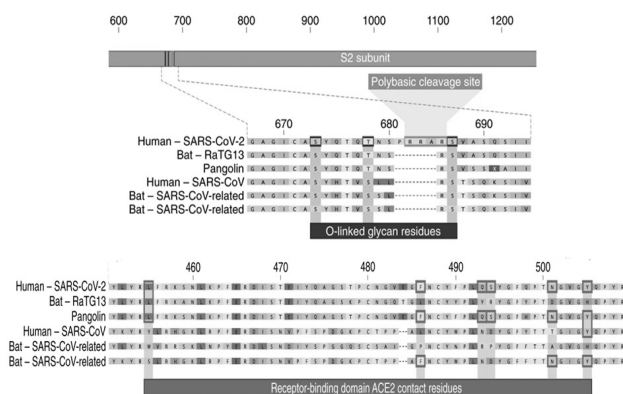
RBD amino acids are critically responsible for binding to human ACE2 receptors and for determining the host range of SARS-CoV like viruses. The coordinate's residues of SARS-CoV are Y442, L472, N479, D480, T487 and Y4911. The corresponding coordinates in SARS-CoV-2 are L455, F486, Q493, S494, N501 and Y505 and the five out of these six residues differed from SARS-CoV. The structural and biochemical experiments revealed that the RBD of SARS-CoV-2 seems to possess high affinity to ACE2 of humans, ferrets, cats and other species with high receptor homology. The computational analyses predicted the RBD sequence of SARS-CoV-2 and showed it is different from SARS-CoV. So, the higher binding ability of SARS-CoV-2 spike protein to human ACE2 receptor is mostly due to the natural selection of the virus on human or human-like ACE2 receptors.<sup>18,19</sup>

### Functional furin cleavage site and O-linked glycans

In SARS-CoV-2, the polybasic cleavage site (furin) present at the junction point of S1 and S2 is accounted for the efficient cleavage by the polybasic furin and other proteases.<sup>20</sup> Especially in SARS-CoV-2, proline is inserted at this furin site (Figure 1) thus, the turn created by the proline insertion might be resulted in the addition of O-linked glycans to S673, T678 and S686, which edge the cleavage site.<sup>14</sup> Notably, this polybasic cleavage site has not been reported in “lineage B” beta coronaviruses but was reported in “lineage A” human beta-coronaviruses (eg. HKU1) with predicted O-linked glycans.<sup>21</sup> However, the functional consequence of the polybasic cleavage site of SARS-CoV-2 is unclear, but unfortunately it is very essential to interpret the pathogenesis in animal models. Similarly, the function of the predicted O-linked glycans is also unknown, but they could form ‘mucin-like domain’, as key residues on the SARS-CoV-2 spike protein.<sup>22</sup>

### Strength of Indian Horizon in fighting COVID-19

Worldwide, being India is the second largest country in population, there is a need for scientific strategies to combat COVID-19. In our perspective, India has proactively launched lockdown in the first stage of COVID-19 itself and has taken many efforts needed for medical emergency in coordination with all state governments. In diagnosis of COVID-19, Indian scientists from Institute of Genomics and Integrative Biology (IGIB) have succeeded in developing cost effective paper strip test for detecting coronavirus within an hour. This test was based on the use of cutting-edge and gene-editing tool (Crispr-Cas9) to detect the



**Figure 1: Genome of SARS-CoV-2 comparison to other Corona Viruses. (Source: Kristian GA *et al.* Nature Medicine. 2020 Mar 24).**

**Table 1: Summary of emerging viral infections in India and new viruses.**

Virus family	Virus	Transmission mode	Outbreak potential	Treatment	Symptoms	Biohazard Category
Coronaviridae	MERS Coronavirus	Human to human	Yes	Lopinavir/ritonavir + Interferon-1 + ribavirin	Fever, cough, SOB	3
	SARS Coronavirus	Human to human	Yes	Lopinavir + Ritonavir	Fever, cough, SOB	3
	SARS-COV-2	Human to human	Yes	Symptomatic treatment; Hydroxychloroquine.	Fever, cough, SOB, diarrhoea	4
Bunyaviridae	Ganjam virus	Tick-borne	Yes*	ribavirin, vaccination Rehydration therapy	Fever, diarrhoea, lethargy	2
	Bhanja virus	Tick-borne	Yes*	Symptomatic treatment Rehydration therapy	Fever, photophobia, vomiting	2
	SFTS virus	Tick-borne	Yes	Favipivir	Fever, thrombocytopenia, GI symptoms	4
	Chobar Gorge virus	Tick-borne	No	Not reported	Not reported	2
	EEV	Arthropod-borne	No	Symptomatic treatment	Stiffened mouth, facial expressions, commissures	2
	Cat Que virus	Arthropod-borne	Yes*	Not available	Not reported	2
	Kaisodi virus	Tick-borne	Yes*	Not available	Not reported	2
	Umbre virus	Arthropod-borne	Yes*	Not available	Not reported	2
	Oyavirus (Ingwavuma virus)	Arthropod-borne	No	Not available	Not reported	2
	Chittoor virus	Tick-borne	Yes*	Not available	Unclear (Febrile illness)	2
Thottapalayam virus	Rodent-borne	No	Not available	Unclear (Febrile illness)	2	
Nairoviridae	CCHFs virus	Tick-borne, human to human	Yes	Ribavirine	Severe acute febrile illness, hemorrhagic fever	4
Flaviviridae	Yellow fever	Arthropod-borne	Yes	Symptomatic treatment, 17D vaccine	Fever, hepatitis, yellowing of skin	4
	Zika virus	Arthropod-borne, mother to child, sexual route	Yes	Symptomatic treatment, Rehydration therapy	Joint pains, fever, headache, conjunctivitis	2
	KFD	Tick-borne	Yes	Symptomatic treatment	GI symptoms, severe muscle pain, bleeding	4
	JE	Arthropod-borne	Yes	Symptomatic treatment Derived JE vaccine.	Sudden headache, high fever, brain swelling	2
	Dengue	Arthropod-borne	Yes	Symptomatic treatment Fluid replacement therapy	Fever, chills, erythematous mottling of skin.	2
	Bagaza virus	Arthropod-borne	Yes*	Not available	Febrile illness, apathy, weakness	2

<i>Paramyxoviridae</i>	Influenza - (H3N2) Variant virus	Air-borne	Yes	Oseltamivir, zanamivir, peramivir, baloxavir	Fever, respiratory symptoms	3
	Influenza -Avian (H5N1)	Air-borne	Yes	Neuraminidase inhibitors (zanamivir, oseltamivir)	High fever, lower RTI, diarrhoea	4
	RSV	Air-borne	Yes	Supportive care Ribavirin (inhaled form)	Runny nose, dry cough, headache, SOB	2
	Quaranfil virus	Tick-borne	Yes*	Not available	Mild febrile illness	2
	Parainfluenza 1-4	Air-borne	Yes*	Ribavirin	Sore throat, SOB, fever	2
	Enterovirus-D68	Air-borne	Yes	Human intravenous immunoglobulin (IVIG)	Runny nose, body aches, wheezing, SOB	2
	Nipah virus	Human to human Bat to human	Yes	Supportive care, passive immunization	SOB, encephalitis, fever, headache, sore throat	4
<i>Picornaviridae</i>	Human rhinovirus A, B and C	Air-borne	Yes	Symptomatic therapy (with antihistamines, NSAIDs)	Common cold, chills, head ache, sore throat	2
	Hand, foot and mouth disease	Direct contact, faeco-oral route	Yes	Supportive care (usually clear up in 7 – 10 days)	Malaise, fever, sore throat, red blister on tongue	2
	Coxsackie-A21 virus	Faeco-oral route	Yes	Supportive care	Fever, rashes, joint pain, sore throat	2
	Coxsackie-A10 virus	Faeco-oral route	Yes	Supportive care	Fever, sore throat, pharyngitis, herpangina	2
	Sapoviruses	Faeco-oral route	Yes	Supportive care, nitazoxanide	Vomiting, diarrhea, abdominal cramps	2
	Rota virus	Faeco-oral route	Yes	Rehydration therapy and supportive care	Watery diarrhea, fever, vomiting	2
	Polio flaccid paralysis	Faeco-oral route	Yes	Oral Polio Vaccine (OPV),	Severe acute flaccid paralysis, neck stiffness	3
<i>Caliciviridae</i>	Noroviruses	Faeco-oral route	Yes	Supportive treatment Fluid replacement therapy	Vomiting, diarrhea, stomach cramps, fever	2
<i>Hepadnaviridae</i>	Hepatitis KIs (mutants of HBV)	Blood-borne	Yes	Not available	Not reported	2
<i>Togaviridae</i>	Rubella virus	Ai-borne	Yes	IGIM vaccine	Pink or red rash, fever, swollen lymph nodes.	2
	Chikungunya virus	Arthropod-borne	Yes	Symptomatic treatment NSAIDs and antipyretics	Fever, joint pains, rashes.	2
<i>Poxviridae</i>	Buffalopox virus (orthopoxvirus)	Direct contact	Yes	Symptomatic treatment Antibiotics	Vesicular lesions on hands and forearms	2
<i>Parvoviridae</i>	Human parvovirus-4	Parenteral transmission?	Yes	Not available	Unclear	2
<i>Arenaviridae</i>	LCMV	Rodent-borne	Yes*	Symptomatic treatment, Ribavirin	Retro – orbital headache, myalgia, fever	3
<i>Herpesviridae</i>	CMV	Direct contact	Yes	Gancyclovir, Letemavir	Fever, night sweats, sore throat, joint pains	2
	Chickenpox (varicella) VZV	Air-borne, direct contact	Yes	Acyclovir (for high risk of complications)	Rashes, fluid filled blisters, fever	2
<i>Rhabdoviridae</i>	Chandipura virus	Arthropod-borne	Yes	BPL inactivated vaccine, siRNAs drugs	Fever, convulsions, vomiting	3
<i>Reoviridae</i>	Kammavanpettai virus (orbiviruses)	Tick-borne	No	Not available	Not reported	Unknown

\*May cause epidemic, but no epidemic has been reported. Unknown: No clear information on the risk assessment available. SOB: Shortness of breath



**Table 2: Current ongoing antiviral research against COVID-19 pandemic (Data upto April 2020).**

S. No.	Organization / Industry	Discovery type	Target	Current status	Description
1	National Institute of Health	Drug repurposing	Hydroxychloroquine	Phase IV	Reduces glycosylation of ACE2 and inhibits the production of cytokines
2	Gilead, NIH	Drug repurposing	Remdesvir	Phase III	Inhibition of viral RNA polymerase
3	Sanofi	Drug repurposing	Hydroxy Chloroquine	Preclinical	Reduces glycosylation of ACE2 and inhibits the production of cytokines
4	BioTech and Pfizer	Vaccine	New Vaccine	Phase I	mRNA based Vaccine
5	Johnson and Johnson	Vaccine	Prezcobix	Preclinical	Combination of darunavir (protease inhibitor) and cobicistat (inhibitors of human CYP3A proteins)
6	Abbvie	Drug Combination	Lopinavir + Ritonavir	Phase III	Synergistic effect on viral protease inhibition
7	VacciTech	Drug Combination	Lopinavir + Ritonavir	Phase II	Synergistic effect on viral protease inhibition
8	Regeneron	Antibody	Monoclonal antibodies	Preclinical	Produced from Mouse model, bind to S-Protein of MERS-COV.
9	Ascleptis	Drug Combination	Danoprovir + Ritonavir	Phase I	Synergistic effect on NS3/4A viral protease inhibition
10	Takeda	Antibody	Polyclonal antibody (H-IG)	Preclinical	Plasma derived anti-SARS-CoV-2 hyper-immune globulin therapy
11	Heat Biologics	Vaccine	Gp-96 vaccine	Preclinical	It produce antigen that binds to gp-96 protein.
12	Hoth and Voltron Therapeutics	Vaccine	Self-assembling Vaccine (SAV)	Preclinical	Based on fixed immune adjuvant and one variable immune targeting
13	Moderna	Vaccine	m-RNA-1273	Phase I	Target the spike protein of SARS-CoV-2
14	CanSinoBIO	Vaccine	COVID-19 Vaccine	Phase I	Based fixed immune adjuvant and variable immune targeting
15	Arcturus	Vaccine	COVID-19 Vaccine	Preclinical	Based on nanoparticle non-viral delivery system, to produce proteins inside the human body
16	Abcellera Lilly	Antibody	clonal antibodies	Preclinical	Human functional antibody to neutralize SARS-CoV-2
17	GSK and Clover	Vaccine	COVID-19 Vaccine	Preclinical	Based trimeric S-protein of COVID-19 virus which binds with host cell
18	Inovio	Vaccine	COVID-19 Vaccine INO-4800	Preclinical	DNA Vaccine to fight SAR-CoV
19	Entos	Vaccine	DNA Vaccine	Preclinical	Based on Fusogenix drug delivery platform (proteo-lipid vehicle) that introduce genetic pay load directly into cells.
20	University of Oxford	Vaccine	ChAdOx1 nCoV-19	Preclinical	Based on adenovirus vaccine vector
22	Roivant	Antibody	Gimsilumab	Clinical stage	Human monoclonal antibody targets granulocytes-macrophage colony stimulating factor.
23	Altimune	Vaccine	AdCOVID	Clinical stage	It is a single dose intra-nasal vaccine
24	Mab Biopharma	Antibody	TJM2 Neutralizing antibody	Clinical stage	Treatment for cytokine storm in patients suffering from corona virus acts through granulocytes-macrophage colony stimulating factor

25	Medicago	Drug candidate	Virus like Particle	Preclinical	It mimic the shape and dimension of Corona virus which allows the body to develop immune response in non-infectious ways.
26	Airway Therapeutics	Human recombinant protein	AT100	Preclinical	Human recombinant protein reduce inflammation and infection in lungs
27	Tiziana	Monoclonal antibody	TZLS	Preclinical	Human anti-interleukin-6 receptors which prevent lung damage and elevated levels of IL-6.
28	OyaGen	New Drug	OYA1	Preclinical	Inhibiting replication of SARS-CoV-2 in cell culture similar to chlorpromazine
29	BeyondSpring	Drug candidate	BP002	Preclinical	Small molecules can activate CD4 and helper T cell, CD8+ cytotoxic T-cells
30	Algemon	Drug candidate	Ifenprodil	Clinical	Its NMDA receptor glutamate receptor antagonist.
31	Apeiron	Drug candidate	APN01	Clinical	The molecule interfere with ACE2 receptor
32	Tonix	Vaccine	TNX-1800	Preclinical	Modified horsepox virus
33	Innovation	Drug candidate	Brilacidin	Preclinical	Its antibacterial, anti-inflammatory and immuno modulatory molecules can act as defending mimetic drug candidate to SARS-CoV-2
34	Pfizer	New molecules	New chemical	Under development	-Not disclosed-
35	Codagenix and Serum Institute of India	Vaccine	COVID-19 vaccine	Preclinical	Vaccine strains similar SAR-CoV-2
36	Zydus cedilla	Vaccine	Vaccine	Preclinical	DNA vaccine against viral membrane protein and rMV vectored vaccine
37	Cipla	Drug re-purposing	Lopinavir+ ritonavir	Phase III	Synergetic effect on viral protease inhibition
38	Biocryst	Drug repurposing	Galidesivir	Phase III	Nucleoside RNA polymerase inhibitor

genomic sequences of the SARS-COV-2 in the samples of patients.<sup>23</sup> In addition, Mylab Discovery Solutions in collaboration with Serum Institute of India and AP Globale planned to enhance production of COVID-19 diagnosis kit.<sup>24</sup>

Globally, the Indian pharmaceutical market is ranked as one among the top five pharma marketers and is becoming the largest exporter of pharmaceuticals. The United Nations Children's Fund mentioned about India, as the largest supplier of generic drugs globally and also stated that India is the only country provides life saving medicine at affordable cost to poor patients. It is the credibility of India pharma companies, they manufacture and supply antiviral drugs at very economical rate, thus the cost of antiviral treatment (HIV infections) has declined to 400 dollars from 12,000 dollars, which is the most remarkable contribution made by India to global healthcare.<sup>25</sup> Therefore, if any antiviral drugs discovered

for COVID-19 (Table 2), India can lead the global market in manufacturing and supply of cost effective medicine to treat COVID-19. Being, India as one of the largest manufacturers of antimalarials, agreed to supply hydroxychloroquine and paracetamol to United States and other COVID-19 affected countries.

### Need for enhancing antiviral research initiatives in India

To date, in India only few virology institutes including ICMR-National institute of Virology (ICMR-NIV), International Centre for Genetic Engineering and Biotechnology (ICGEB) etc., are prominent in antiviral research. There are other private antiviral research units or laboratories attached with universities are also available, but they do not have adequate fund and infrastructure to handle virus of bio-safety risk group-4 such as SARS-CoV-2, Nipah Virus, CCHF's virus etc. We

are aware that the viral infections and its consequence are continuously evolving since one decade. Despite the preventive measure and control strategies taken on these viral epidemics including SARS, MERS, dengue fever, Chikungunya, COVID-19 etc., the amount of new discovery or new vaccine attempts undertaken by the Indian pharmaceutical industries against COVID-19 is relatively very low while comparing to the developed countries (Table 2). Glance at global research initiatives against COVID-19, several universities such as Tulane University, Columbia University, Biology Institute of Shandong Academy of Sciences, The Hong Kong University of Science and Technology, University of Alabama have initiated collaborated research with industries on discovering vaccine for COVID-19. In contrast, in India few collaborative research initiatives were noted including Tata Consultancy Service and Codegenix have respectively collaborated with Central Scientific and Industrial Research (CSIR) and Serum Institute of India. It was appreciable that Government funding bodies including Indian Council of Medical research (ICMR), Department of Biotechnology (DBT), Department of Science and Technology (DST), Defence research and development organization (DRDO), Central Scientific and Industrial Research organization (CSIR) and renowned central institutes (Indian Institute sciences and Indian institute of technology) are proactive and the respective scientists are working on the discovery of vaccine or new drugs for COVID-19. The DRDO stated that about 50 industries are working in collaboration against COVID-19, still the number is relatively low, despite the number of pharmaceutical industries in Indian horizon. Apart from these governmental research institutions, the anti-COVID-19 drug research initiated by non-governmental research organization and pharmaceutical sectors are very minimal.

### Need to unveil the research potential of Indian Pharmaceutical Industries

At this COVID-19 pandemic, Indian Pharmaceutical industries have emerged as the prime source for remedial drugs like hydroxychloroquine, paracetamol and other antiviral drugs to many developed countries including United States. On the other hand, despite their potential to conduct research with the available finance, intellectual resources and research facilities, the research units of Indian pharmaceutical industries have failed to record adequate research initiatives on COVID-19. Unlike the developed countries, our Indian pharmaceutical industries do not hold sufficient collaborations with scientists from research institute

or universities. Thus there is an absolute lacuna in the collaborative research activities of Indian pharmaceutical industries with Universities and research organization as well. In addition, number of potential researchers on antiviral drug research in India also quite less. But there is wide scope for antiviral drug research in near future for both industries and individuals. Substantially there is an opportunity for unveiling the research potential of Indian Pharmaceutical industries, which can afford appreciable outcome in finding new drugs or vaccine for any life threatening conditions including COVID-19.

## CONCLUSION

In this era of viral epidemic, it is highly essential to improve the antiviral research in India country through collaborative approaches among pharmaceutical industries, scientists across the globe and researchers from academia and non-profit research organization. In near future, the antiviral research initiatives by pharmaceutical industries of Indian horizon will have successful outcome not only in finding remedy to treat COVID-19, but also to other existing life threatening illness.

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## CONFLICT OF INTEREST

Authors have no conflict of interest.

## ABBREVIATIONS

**SARS-CoV-2:** Severe acute respiratory syndrome corona virus – 2; **COVID-19:** Corona virus disease – 2019; **SFTS:** Severe fever thrombocytopenia syndrome; **EEV:** Equine encephalosis virus; **CCHF:** Crimean-Congo hemorrhagic fevers; **KFD:** Kyasanur forest disease; **JE:** Japanese encephalitis; **LCMV:** Lymphocytic choriomeningitis virus; **CMV:** Cytomegalovirus; **VZV:** Varicella-zoster virus; **RSV:** Respiratory syncytial virus; **HBV:** Hepatitis-B virus; **RBD:** Receptor binding domain; **ACE2:** Angiotensin converting enzyme-2.

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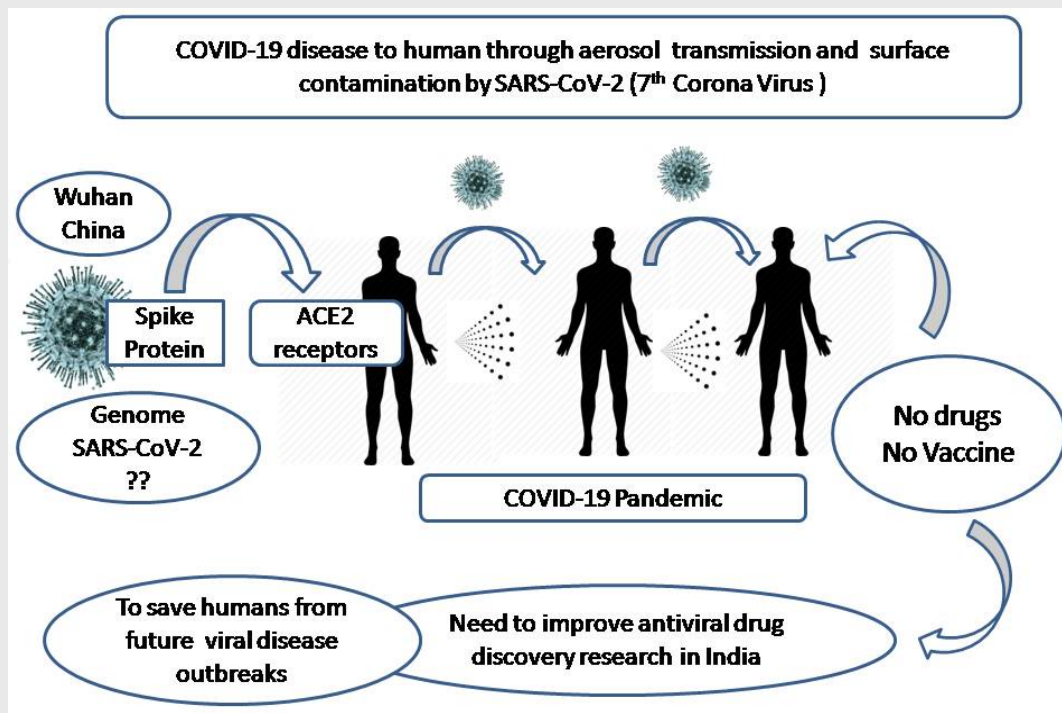


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## SUMMARY

The birth of SARS-CoV-2 at Wuhan city of China in 2019, unfortunately ended in COVID-19 pandemic. The SARS-CoV-2 genome is quite complex and unclear, but it was postulated that it is not derived from laboratory manipulation of other viruses. The existing knowledge on SARS-CoV-2 genome revealed that receptor binding domain (RBD) of spike protein is responsible for its high affinity to human ACE2 receptors. Today, as there is no drug or vaccine for COVID-19, few drugs like hydroxychloroquine, remdesvir, ritonavir and lopinavir are provisionally recommended as suppressive agents. In this global emergency, Indian horizon has emerged as potential supplier for these drugs to several countries including United States. In view of drug discovery initiatives on new antiviral drug or COVID-19 vaccine undertaken by Indian horizon is relatively less as compared to the developed countries. Keeping in view of Corona like other viruses and their expected outbreak potentials, there is an absolute need for immediate collaborative drug discovery initiatives among researchers from industries, research institutions and academia. The need for enhancing antiviral research among Indian pharmaceutical industries is highly appreciable now and this research initiative will enlighten our Indian horizon in the global pharmaceutical market as kingdom. To conclude, in this raising viral epidemic, it is highly essential to improve the antiviral research in our country through collaborative approach between pharmaceutical industry and scientists across the world including researchers from academia and non-profit research organization.

### PICTORIAL ABSTRACT



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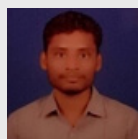
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