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ASPECTS OF COVID-19**



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EDITORIAL



As we know Covid-19 Corona virus, has already been spreaded almost all the countries of the world within few months. It was first reported from Wuhan, a city in China in December, 2019. Now it is impacting all parts of human society as well as wild life which are the important part of the Biodiversity. The frequency of this virus infection is increasing steadily, millions of people have already been affected and the number of infection is increasing rapidly followed by death. It has both negative and positive impact on environment. The world is now searching for the suitable drugs and vaccine using developed biotechnology against the deadly virus. The situation of world economic is under stress and the condition of India is worst.

(Ashis Kumar Panigrahi)

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ENVIS Resource Partner on Environmental Biotechnology publishes two volumes (4 Nos.) of news letter in a year (ISSN: 0974 2476). The articles in the news letter are related to the thematic area of the ENVIS Resource Partner (see the website: <http://deskuenvis.nic.in>).

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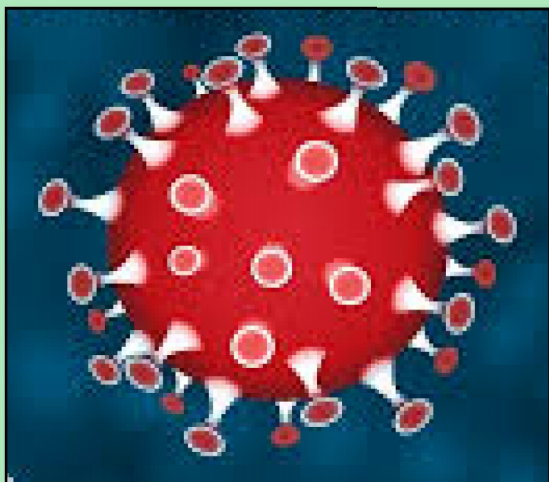
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COVID-19 IN NUTSHELL

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Covid-19 was first outbreak from Wuhan, a city in China in December, 2019 and it spread quickly around the world. Now it is impacting all parts of human society as well as wild life, which are the important part of the Biodiversity. The frequency of this virus infection is increasing steadily, millions of people have already been affected and the number of infection is increasing rapidly followed by death. It has both negative and positive impact on Biodiversity. In negative impact volume of on recyclable waste have arisen several cuts in agricultural and fishery export levels led to generation of huge quantities of organic waste maintenance and monitoring of natural ecosystem have been temporarily halted. Further western countries have seen a significantly higher death rate from Covid-19 than Asian countries. A coronavirus is a kind of common virus that causes an infection in your nose, sinuses, or upper throat. Most coronaviruses aren't dangerous.



As we Covid-19 corona virus, has already been spreaded almost all the countries of the world within few months. It Most of the older people have been affected throughout the world. But as per the report (WHO) age is not the only factor but having different types of genetic diseases, obesity, diabetics, high blood pressure,

heart diseases, acute respiratory problems are also responsible to increase the death rate through this Covid-19 virus infection. It is also reported that this Covid-19 virus may mutated as time passesway. It spread slower in hot and humid weather and spread faster in cooler and dried condition. It can affect upper respiratory tract such as sinuses, nose, and throat or the lower respiratory tract such as windpipe and lungs.

Lockdown helped a lot to check the spreading of this infection as human closeness can increase the infection. Social distancing, stay at home and more immunity power only can check the spreading of this infection.

If we do not maintain all the above, then we have to face a lot of problem as stated below.

The situation of world economic is under stress and the condition of India is worst. As per the report from nearly 1/10th of Indian total population has lost their servive or daily wages. At the same time as per World Bank report nearly 1.5 crores of people will face acute poverty, the number may be increased if the pandemic of corona virus i.e COVID -19 persist for long time. The GDP will even be zero. Due to Covid-19 pandemic followed by lockdown in India. The economic condition is worst and nearly 80% people in rural. India has lost their works. Further, as per report of United Nation University 92 crores people of India will come under below problems like and more people will die in starvation rather than corona infection.

So the nature itself will recover gradually us. Till date there was no medicime / vaccine is available in the market to control this Covid -19 infection. So, we have to take care of ourselves by maintain the guidelines issued by WHO as well as our medical council of India.

Thus this new letter will no doubt will help a lot in this present scenario to compact Covid-19 virus.

COVID-19, ENVIRONMENT AND INDIA

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Introduction

Following the announcement of COVID-19 as a pandemic by WHO on 11th March 2020, most countries introduced specific policies to minimise spread of the virus. Partial or full lockdown of non-essential social and economic activities were ensured to achieve social distancing for ‘flattening the curve’. Reduction of travel, industrial production and other economic activities resulted in visible improvement of several environmental parameters. Numerous research papers and news articles have focussed on these positive environmental effects of COVID-19. A literature search in Google Scholar with the keywords ‘COVID+environmental impact’ post 2020 yielded 4000+ results, while SCOPUS search produced about 50 articles. Therefore, this essay will attempt to present some key issues and put them in context of India. Some broader issues related to environment such as economic and policy changes due to COVID-19 will also be briefly discussed.

1. Glimpse of a greener world

1.1. Carbon Emission and air pollution

A study published in Nature Climate Change estimates a 17% decrease in global daily carbon emission by early April compared to the mean 2019 emission level [1]. That study also forecasts an annual emission reduction of 4 to 7%. However, a report from Carbon Brief identifies that this reduction is hardly sufficient to achieve the 1.5°C limit of temperature rise above pre-industrial level – this would take 7.6% emission reduction over a decade [2]. Figure 1 shows the forecasted 2020 emission with respect to the emission trend along with the historical reduction in emission during major economically disruptive events. In Indian context, the

CO₂ emission reduced for the first time in last 40 years, with 15 and 30% reductions in March and April 2020, respectively [3]. According to POSOCO data (Govt. of India), coal burning thermal power plants experienced the entire reduction in energy consumption, thereby reducing the overall emission of India [4].

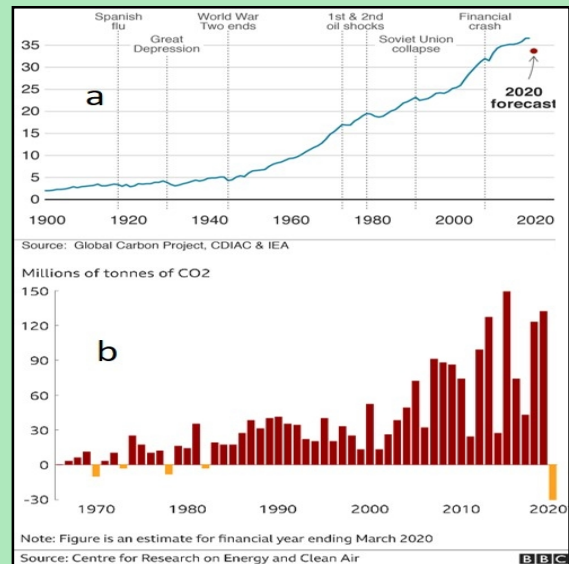


Figure 1: (a) Global carbon dioxide emission (billion tonnes of CO₂ per year) and (b) Indian emission reduction since 1970s [5,6]

Any discussion on carbon emission is inherently linked with energy production. International Energy Agency (IEA) published Global Energy Review, which estimates a 6% reduction in energy demand in 2020 - equivalent to losing the entire energy demand of India [7,8]. Globally, energy generation sector has received largest shock since second world war, resulting in massive reduction in demand from coal, oil and gas fired power stations. On the contrary, electricity from renewables experienced 1.5% growth globally in the 2020 Q1 amidst the pandemic. Solar PV and wind were the primary generators, taking advantage of their preferential dispatch in the supply lines. Notably, bioenergy production experienced slump due to interruption in feedstock supply lines. In Indian context, coal based electricity production decreased by 15% in March and 31% in April, while renewable sources supplied 6.4% more

electricity in March [4]. This is evident from Figure 2. India already has a very aggressive target for renewable energy transition since it aims to produce 175 GW of renewable energy by 2022 without major upgrade of grid, mostly by replacing coal and by introducing EV vehicles. An overall decrease of energy demand due to COVID-19 lockdown by 25% may jeopardise these renewable ambitions over long term, although it looks promising at the moment. This risk comes from cash strapped electricity distribution companies who will now have little money to invest in renewables. With a renewed push for Make in India project, and most of the renewable and EV technology and machinery coming from China, there is a risk that India may prefer domestic coal over short term post-COVID scenario [9]. This is not good.

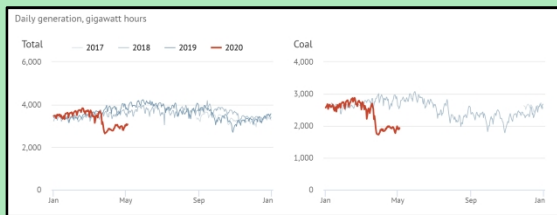


Figure 2: India's energy consumption, with special emphasis on coal [10]

Transport sector accounts for 25% of global carbon emission according to World Bank estimate [11]. Therefore, due to COVID-19 lockdown, when all non-essential travels around the world including road, sea and air travels have been suspended, highly polluted places experienced surprisingly good air quality. Reduction in suspended particulates and aerosols in the city air are the reason for clearer air and higher visibility. NASA satellite image presents a striking image of the aerosol distribution over India during March-April of 2016-2020 (Figure 3) [12]. An article claimed that New Delhi's air pollution to come down by 40-50% within 4 days of lockdown, due to reduction in vehicular traffic [13]. However, there is always the anticipation of increasing transport activities following ease of lockdown restrictions for making up of lost time, supplying the stranded

commodities and to reduce economic impact of the disruptions. This was observed following 2008-2009 recession when emission by transport increased by 6% annually. Additionally, use of public transport to its full capacity following COVID-19 may not be feasible and many people may choose to use personal vehicles for travel. Work from home, if practiced by businesses for prolonged period, may reduce city traffic. In spite of several difficulties following COVID-19, the lockdown produces unique opportunities for the governments to re-strategize their public transport and freight system and choose more sustainable options. An example can be from India where a project is underway to convert a 1360 km stretch of the Ganges river into modern waterway for carrying 65 million tons of cargo a year, cutting down 162,000 tons of GHG emissions annually. Such projects need to be fast-tracked around the world [14].

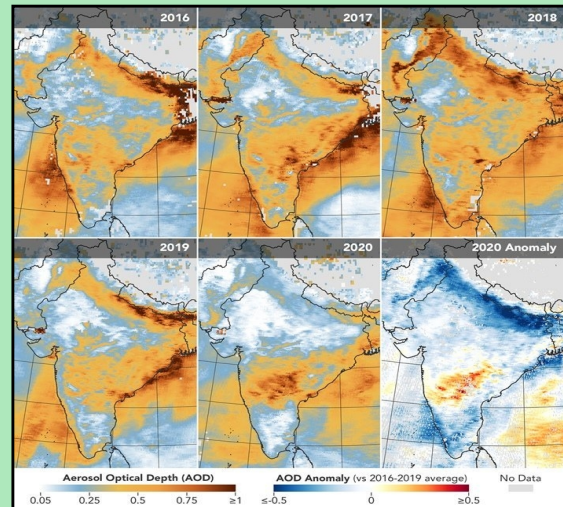


Figure 3: NASA image showing aerosol optical depth measurements (AOD) over India between March 31 and April 5 each year, from 2016 to 2020 [13]

1.2 Wildlife, habitat and livestock

Following COVID-19 lockdown, the media has been flooded with reports of wildlife roaming freely in towns, turtles hatching uninterruptedly on deserted beaches and returning of whales in untroubled waters. While many of these occurrences are genuine, e.g. hatching of

millions of Olive Ridley turtles in Gahirmatha and Rushikulya rookery at Orissa, a lot of these sightings and reports are found to be fake news and an overstatement, e.g. elephants in Chinese tea gardens and return of fishes in Venice canals (which were always there, only previously hidden in muddy water) [15]. The link between wildlife trade and COVID-19 need to be investigated and specific actions taken [16]. Wildlife markets can propagate emerging diseases such as SARS from animals to humans. China and Vietnam are high up in the list of the countries where action is lacking. Closure of these markets will disrupt a \$23 billion worth illegal wildlife trafficking and ensure that a jaguar from South America does not get poached because of the high price it can fetch in China. However, it must be noted that a pandemic leading to halt of economic activity leads inevitably to increase in poverty, which is always bad news for wildlife, habitat and environment in general. People will hunt animal, invade habitats and over-exploit resources for survival. Collapse of ecotourism is another issue that will affect wildlife conservation efforts to great extent. Tourism revenue often funds the conservation programs – be it coral reef in Seychelles, Tiger in Sundarbans or Mountain Gorillas in Uganda [17].

Abandoning of pets and culling of farm animals is another consequence of COVID-19 that needs to be considered. As meat processing plants close down due to COVID-19, millions of farm animals are culled and their carcass dumped leading to shortage of meat supply in market and methane emission from the carcass, apart from all the wastage of fodder, grass and water needed to make them grow. For an example, in India, half a million pig farmers are engaged in a lucrative pig farming sector with about 10 million animals. Halt in meat processing will put these farmers in extreme challenge with respect to feed management and transport, leading to overcrowding and spread of disease [18].

Therefore, the lockdown effects of COVID-19, has resulted in a clearer sky, less aerosols, lower energy consumption, and higher wildlife sightings, all of which provide a glimpse to a better world if human beings could live a more sustainable life. But all of these effects are short term gains and highlights the need for long term climate change strategy [19]

2. Environment, Economy & COVID

Poverty is always bad news for environment. Environment is closely linked with society and the economy and as such, cannot be studied in isolation. The first among the seventeen 2030 SDGs of UNGA is to 'End Poverty' and COVID-19 hits it in the nail. World Bank forecasts that COVID-19 will lead to increase in global poverty first time since 1998, pushing 50-60 million people into extreme poverty [20]. In India, an estimated 12 million additional population will experience poverty. Mass movement of workers from cities to villages not only spell financial trouble for the migrants pushing their families into poverty, but this mass repatriation puts strain on village environment through natural resource depletion and further spread of COVID-19 in the countryside. While poor people exploits nature more intensively by overusing land, higher deforestation and inappropriate disposal of waste, they are the one to get impacted most due to environmental degradation. Outbreak of COVID-19 and shutting down of the world's economies has exposed the vulnerability of the market. UNEP's Chief Environmental Economist Pushpam Kumar calls for a trade-off analysis to understand the man-environment interaction that has led to the current COVID-19 crisis. Human beings should understand the extent to which nature can be exploited before the push-back can have tremendous negative effect on human civilization. The production-consumption aspirations need to be bounded in such limits of natural resilience. It is also suggested that experts from economics, natural sciences, zoology and ecology

should come together to assess the loss and gain from the COVID-19 outbreak and how to future-proof our environment and economy from such disasters [21].

3. Policy changes in India

In response to the economic impact of COVID-19, the Indian Finance Minister Nirmala Sitharaman announced five big policy updates regarding migrant workers, rural employment, agricultural reform, MSME sector and State borrowing in May 2020 [22]. All of these are targeted towards alleviating poverty, and hence related to prevention of environmental degradation in the long term. However, the most significant reforms to look forward from environmental perspective are the rural employment and the agricultural reforms. The rural employment scheme is being allotted the highest ever 1 lakh crore INR to be spent through MGNREGA scheme in the rural areas and most of the activities proposed will be targeted towards climate change mitigation, e.g. water conservation and reforestation activities. If properly implemented, this can be a good opportunity for the country to benefit environmentally from presence of a large workforce in the countryside. The next big reform that should be eagerly watched for is in the agricultural sector. While 15% of the GDP comes from agriculture, 42% of Indian population is employed in this sector [23]. Amendment of Essential Commodities Act and deregulation of food crops such as cereals, edible oils, oilseeds, pulses, onions and potatoes will ensure that the agricultural market truly opens up for free trade. Currently, the farmer cannot decide the product, price or buyer and gains no benefit from future's market. The middleman in the mandi acts as a cartelised monopoly and fix the rate for the farmer. Similarly, a buyer cannot directly approach a farmer to buy specific crop in specific quantity, but has to go through the mandi trader appointed by Agricultural Produce Market Committee (APMC). APMC, once established to safeguard farmers has now restricted farmer's access

to the free market, which is contrary to WTO principles of free and open market. Once the announced reforms are implemented, the farmer can sell produce at any place in India at any price they want to whomever they want to, elevating their status as entrepreneurs. The significance of the agricultural reform in the context of environmental impact lies in alleviating of poverty, probable increment of organic produce and conservation of local crop species and biodiversity. Environmentally sustainable certified products have now higher acceptability around the world at a premium price (e.g. Fairtrade and Rainforest Alliance). Another series of policy changes can be expected in the energy sector where MNRE (Govt of India) is thinking about introducing support scheme for renewable energy as part of COVID-19 recovery [24]. An auction which secured 2000 MW of solar power at the rate of INR 2.55-2.56/kWh turns out to be cheaper than coal power plant [25]. One can only keep the fingers crossed and hope for a sustainable and poverty free world on the other side of the pandemic.

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VACCINE DEVELOPMENT AND DRUG RE-PURPOSING AGAINST SARS-COV-2 VIRUS: AN INSIGHT

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Introduction

Due to the very swift rise in SAR-CoV-2 infections and the number of affected countries, a significant effort has been devoted to develop an effective SAR-CoV-2 vaccine by various countries. Development of a safe, widely acceptable and effective vaccines for COVID-19 pandemic is a challenging task to execute. The main obstacle in vaccine development lies in the complex nature of the virus itself. Findings indicates that SARS-CoV-2 virus have sequence homology similar to MERS and SARS viruses. An adequate and in-depth information from MERS and SARS vaccines development pathways, various research groups throughout the world have started SAR-CoV-2 vaccine development.

Among the various strategies adopted so far to generate an effective vaccine, (1) Inactivation of whole virus using formaldehyde, (2) Live-attenuation virus (Mutant MERS-CoV and SARS-CoV / recombination with other live attenuated virus), (3) generation of Virus-like particles (where full length S or S1 protein expressed in baculovirus) and (4) Subunit (full length S or S1 protein are merged with various adjuvants) are remain in preclinical phases (Prompetchara et al., 2020).

Keeping in mind about SAR-CoV-2 virulence and it's wide and swift spread among the world population, a simultaneous or parallel trial of preclinical

and clinical studies suggested. Though there is a complexity also exists on behalf of regulatory authorities, so a hybrid model of preclinical and clinical study may be approved, keeping in mind about safety aspects of volunteers first (Thomas et al., 2016).

mRNA-Based Vaccines

The main advantages of developing an mRNA based vaccine are their (1) capability to mimic normal infection in order to stimulate a more effective immune response and the (2) capacity to combine multiple mRNAs using a single vaccine. Moderna, filed a patent application (No.WO2017070626) where they claimed that when mice (New Zealand white rabbits) were vaccinated with mRNAs responsible for coronavirus S protein (full-length) triggered a much greater neutralizing antibody titers, compared to mRNA encoding the S protein S2 subunit alone. According to the reports of Moderna, mRNA-1273 vaccine is designed to target the S protein (in a prefusionstabilized form) of SARS-CoV-2 (Mordena Press Release, 2020).

Protein-Based Vaccines

GSK (Glaxo Smith Kline) another pharma giant, in their filed patent (No. WO2010063685) reveals that a vaccine comprises of emulsion adjuvant (oil-in-water) GSK2 and S protein immunogen can prompted a high level of anti-SARS-CoV antibody (IgG2a or IgG2b) responses and thus neutralizing antibody responses when studied in animal models (GlaxoSmithKline press release, 2020). Antigen Express, Inc., a subsidiary of GenereX in their filed patent application (No. US20060002947) claimed that, a hybrid peptides (Ii-Key/ MHC II SARS hybrids) having three different elements (1) an antigenic epitope with the ability to bind with MHC class II molecule, (2) a chemical entity i.e. structure connecting the Ii or the invariant chain to the antigenic epitope and (3) invariant chain or Ii a key peptide capable of antigen presentation

enhancing activity can effectively neutralize SARS CoV (Generex press release, 2020).

DNA Based Vaccine

Inovio Pharmaceutical, Inc. announced (on March 3, 2020), they had developed a DNA vaccine (INO-4800) onset for human trials in the United States in April. The consensus spike protein (MERS CoV spike protein) capable of inducing both humoral as well as cellular immune responses (including increased IgG titers and neutralizing antibodies in a significant manner. Thus with the induced cellular immune response comprising elevated levels of CD3+CD8+ CD3+CD4+ along with T cell responses that stimulates the productions of IFN- γ , TNF- α , IL-2, or both IFN- γ and TNF- α (Inovio,2020).

In India, ICMR (The Indian Council of Medical Research) along with BBIL i.e. Bharat Biotech International Limited have tied up for vaccine development against COVID-19. Their main target is to boost up the body's immunity to fight against the virus. Beside these, other organizations or companies like Mylab, Indian Immunologicals Limited Serum Institute are also working to develop vaccines. On May 22 Thailand announced that it has advanced to evaluate its novel vaccine on monkeys after seeing encouraging findings on mice. The authorities hoped to get a positive outcome of its effectiveness by September 2020. According to the sources the vaccine is mRNA based vaccine with the capability to weaken the virus strain. British American Tobacco, a leading Tobacco production company is currently working on an experimental vaccine based on proteins from tobacco leaves, yet to get the clearance from FDA.

BCG (Bacillus Calmette - Guerin) Vaccination and morbidity due to COVID-19 has any relation

Miller et al. (2020) have forwarded an interesting epidemiological observation among COVID-19 mortality and BCG

vaccination. According to their observations, countries like USA, Italy, Netherland etc. which do not have an universal BCG vaccination policies are found to be more brutally affected, when compared with those countries having sound BCG vaccination policy. The authors further citing the example of Iran, where in 1984 they started the BCG vaccination also have greater mortality rate. Whereas, in Japan (with BCG vaccination since 1947) in spite of being the early cases of COVID-19 infection but surprisingly had low morbidity as well as having less stringent social isolation regimes (The Japan Times, 2020).

Drug Repurposing and it's potential against COVID-19

Drug repurposing (sometimes also known as redirecting, repositioning or even re-profiling) can be defined as developing different (new) use of a drug beyond it's actual or original or initial approved indication (s) (Simsek et al., 2018). According to the view of Ashburn and Thor (2004) drug repurposing fetch attention because it provides an alternative arena avoiding costly drug discovery methods. Drug repurposing actually finding new therapies for a health complexion or disease in a significantly shorter time span as well as in comparatively lower cost. Now to develop a novel drug or a therapy from concept i.e. lab to market (using proper channel) generally costs around US\$ 1.2 to 2.7 billion and a tome period of 10-20 years. Beside these, ever increasing regulatory norms that authenticates the claims makes the novel or new drug discovery process lengthy and costlier too (Kaitin, 2012; Pushpakom et al., 2018). Moreover, it is also a fact that approximately 90% of test drugs fails in clinical or pre clinical phases. Here comes the importance of drug repurposing. Speaking of available drugs for a disease is around 500 while 5700+ known human diseases have documented so far (DiMasi et al., 2010; Collins, 2016).

Table.1. List of exiting drugs and plant products repurposed for COVID-19 treatments

Sl. No	Agent/ Drugs	Traditional Use	Re-purposed for COVID-19	References
1.	Chlorhexidine	Preventing dental plaque, treating yeast infections of the mouth, and to keep urinary catheters from blocking	Possible RdRp inhibitors	Choudhury et al. (2020a)
2.	Remdesivir	Antiviral activity against several RNA viruses including SARS coronavirus and MERS coronavirus. Blocked the Ebola virus in Rhesus monkeys	Possible RdRp inhibitors	do
3.	Novobiocin	Against <i>Staphylococcus epidermidis</i> infection	Possible RdRp inhibitors	do
4.	Ceftibuten	Treat acute bacterial exacerbations of chronic bronchitis, bacterial otitis media, pharyngitis, and tonsillitis etc.	Possible RdRp inhibitors	do
5.	Ribavirin	Treat hepatitis C and viral hemorrhagic fevers and	Possible RdRp inhibitors	do
6.	Stallimycin	Antiviral and antiprotozoal activities	Possible Protease inhibitors	Choudhury et al. (2020b)
7.	Telaprevir	Treatment of hepatitis C	Possible Protease inhibitors	do
8.	Grazoprevir	Treatment of hepatitis C	Possible Protease inhibitors	do
9.	Corylifol A	Plant based product for asthma, diarrhea, and osteoporosis treatments	Possible Protease inhibitors	do
10.	Kazinol J	Plyphenol	Possible Protease inhibitors	do
11.	Ritonavir	Anti HIV drug	Possible Protease inhibitors	Choudhury and Mazumder (2020)

Speaking of the methods applied in drug repurposing, there are two methods. First it is evaluated experimentally and secondly by using computational techniques. Where computational methods are applied for drug repurposing often regarded as “*in silico drug repurposing*” belongs to the computational pharmacology (Shim and Liu, 2014). In “*in silico drug repurposing*” two strategies are followed (1) “*disease-centric approach*” where identification of the effectivity of an existing drug for a particular disease like COVID-19 and (2) “*drug-centric approach*” where focus is diverting towards discovering new signs or indications for an already available drug (Liu et al.,2013).

At this juncture, with the swift increasing in the number of COVID-19 infected person researchers are also focusing towards “*in silico drug repurposing*” beside effective vaccine development. With emphasis being given to drug repurposing for COVID-19 few possible targets were identified. Among the potential targets RNA-dependent RNA polymerase (RdRp) and papain-like protease are focused here. When molecular docking study carried out to screen potential drugs that bind or inhibit. Few drugs emerge out to be effective RdRp and protease inhibitors (Given in Table 1).

At present, beside developing novel vaccines, preclinical and clinical evaluations various other therapeutic interventions like antimalarial drugs (Chloroquine and hydroxychloroquine), identification of anti-IL-6R monoclonal antibodies are going on. Keeping in mind about the success achieved by “*recycling strategy*” (against cancer and other human diseases) based on reuse of clinically approved drugs should also be encouraged.

Conclusion

The “*in silico drug repurposing*” significantly lessens costs for drug development, time by adding new indications for approved drugs. This method permits the combined study of different sources of data (data bases), including pharmaco-

logical, genomic as well as biomedical and chemical data, which enhances drug repositioning effectiveness. With the amplified reputation of precision (accuracy) medicine, personalized medicine, the drug repurposing approaches are likely to be lengthy in nature to find novel indications for individual uses (genomic aspect). Above all drug repurposing approaches can be further refined and polished to address issues like side effects (drug toxicity), inter-patient variability and other associated complexities.

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FORTHCOMING EVENTS		
Events	Date	Place & Correspondence
Webinar on Applied Microbiology and Biotechnology	June 26, 2020	Paris, France https://microbes.annualcongress.com/
Webinar on Recycling and Waste Management	July 09, 2020	Rome, Italy https://www.meetingsint.com/conferences/recycling
25 th World Biotechnology Congress - Webinar	July 15-16, 2020	London https://world.biotechnologycongress.com/
Webinar on Say No to Plastic Pollution	July 18, 2020	DESKU ENVIS, University of Kalyani, India https://forms.gle/SpiS96NYHZFWB4KVA
16 th international expo on recycling and waste management - Webinar	July 24, 2020	https://recycling.enggconferences.com/
3 rd Annual Congress on Environmental Pollution and Health- Webinar	August 03-04, 2020	Hanoi, Vietnam https://pollution.conferenceseries.com/

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