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Mini Review

Chemical Understanding and Preventive Measures of Corona virus Infection

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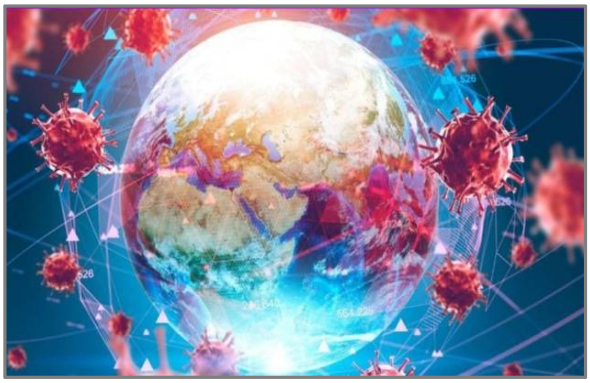
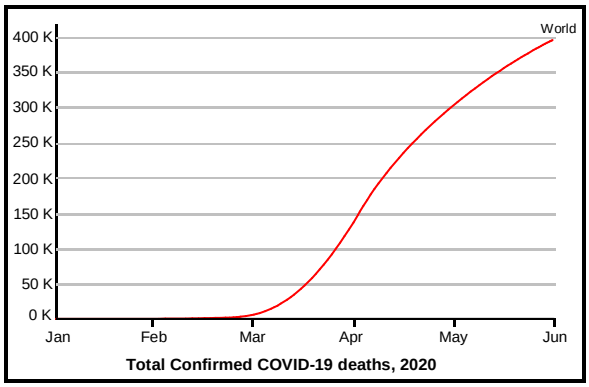
ABSTRACT

World is facing a major health problem due to Corona virus. COVID-19 pandemic as continues to spread globally, killing thousands doctors and health care workers. The governments are on the lookout for safe and effective treatment to help those infected. In this mini review, chemical understanding and biological perspective of Corona virus are described. The posibilistic and pragmatic measures towards better human health conditions are documented.

Graphical Abstract:





Keywords: COVID-19, Chemical Perspective, Medicative measures, Practical hints, Preventive vaccines.

INTRODUCTION

COVID-19 outbreak had endangered over 210 countries and territories by mid April 2020, especially for those areas with high population densities [**1**].

Human beings are now imprisoned in an environment where uncertainty, unknown fear and misbelief pervade. As the COVID-19 pandemic races across the globe, researchers from academic and government laboratories to small biotechnology companies and multinational pharmaceutical laboratories are devoted to develop new techniques to understand the mechanism of infection, virulence, pharmacology and evaluate potential therapeutics and vaccines to combat against corona virus.

The literature reports of a few important antiviral drugs as probable treatments for SARS-CoV-2 But, none of them can be accepted as indisputable remedies for the disease till date. Most of the drugs tested by the doctors so far are totally based on the information for similar kind of infections that occurred in the past.

Corona virus is zoonotic: Corona viruses belong to a family of enveloped viruses with single-stranded, positive-sense RNA genomes infecting animal species [**2-5**] and human. Study reveals that corona viruses are zoonotic i.e. they are almost That means these viruses are mostly present in animals and then transmitted from animals to human beings. In this family of corona virus members, those viruses which are responsible for the common cold are known as severe acute respiratory syndrome corona virus (SARS) and Middle East respiratory syndrome-related corona virus (MERS) [**6**]. However, the one that has recently emerged is the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2, the etiological agent of the Corona Virus Disease 2019. It was provisionally named as 2019-nCoV (new corona virus as was not identified in humans previously). Subsequently, International Committee on Taxonomy of Viruses chose a systemic nomenclature based on an analysis of the new corona virus' evolutionary history and the pathogen that causes severe acute respiratory syndrome (SARS).On 11th of February 2020, they introduced the name as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [**7-10**].

The schematics of COVID-10 is presented in figure 1, while representative structure of electron micrograph of infectious virus [**11, 12**] in figure 2.

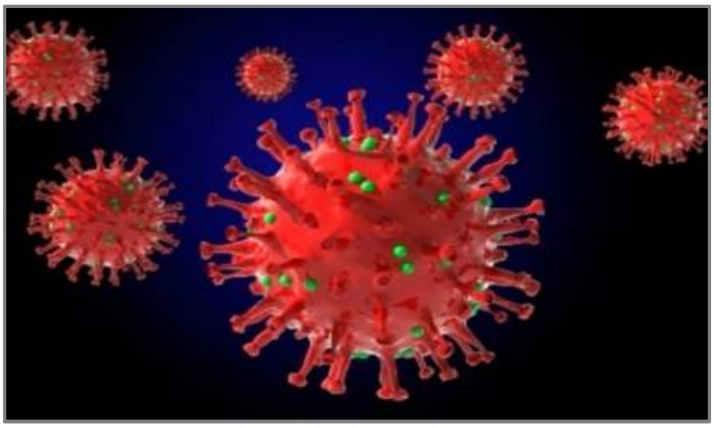


Figure 1. Graphical Illustration schematics of corona virus (SARS-CoV-2).

WHO declared the COVID-19 outbreak as the sixth public health emergency of international concern. Others are H1N1 (2009), Polio (2014), Ebola in West Africa (2014), Zika (2016) and Ebola in the Democratic Republic of Congo (2019).

General symptoms of COVID-19 disease at the onset of illness are general myalgia, fever and cough. Often the symptoms are extended to production of sputum, headache and diarrhea. SARS-CoV-2, like other coronaviruses, mainly infects the respiratory and gastrointestinal tract, pneumocytes, with a cell tropism of nasal epithelial cells and alveolar macrophages in the lung and enterocytes in the bowel [**13, 14**].

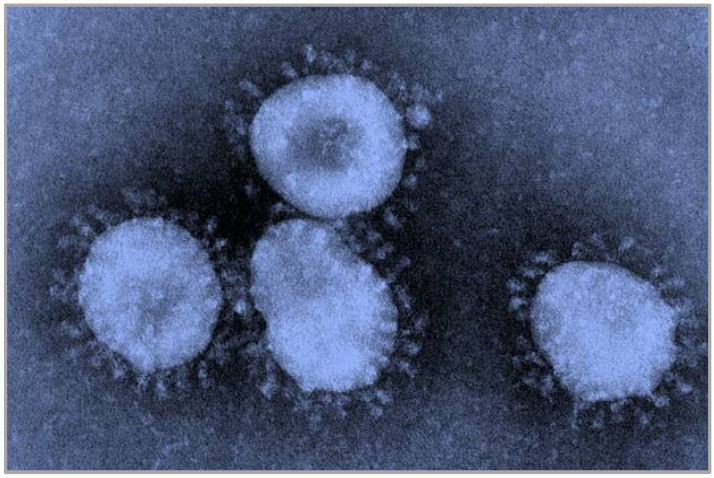


Figure 2. Representative structure of electron micrograph of infectious bronchitis virus.

Recent research indicates that binding of cell through viral S protein to the host receptor angiotensin-converting enzyme 2 (ACE2) is obligatory for the infection to occur [**15,16**]. After entering the cell, gradually the virus complex is translocated to the endosome. Endosomal acid proteases present in endosome then cleaves the S protein. Viral genome is then released and getstranslated into the viral replicase polyproteins PP1a and PP1ab. Viral proteases are responsible for the breaking down of such polyproteins into functional proteins. Through discontinuous transcription, subgenomic templates for mRNA synthesis and translation of the viral structural proteins take place [**17**]. Viral replication complex mediates viral genome replication and it includes an exonucleaseN, RNA-dependent RNA polymerase (RdRp), helicase and other accessory proteins. Viral nucleocapsids from the packaged viral genomes and translated viral structural proteins assemble at the endoplasmic reticulum-Golgi intermediate compartment. Subsequently, there is the release of infectious virions from the cell through exocytosis.

Corona Virus Stability: The corona virus is not a living organism, but a protein molecule (RNA) covered by a protective layer of lipid (fat), which, when absorbed by the cells of the ocular, nasal or buccal mucosa, changes their genetic code (mutation) and convert them into aggressor and multiplier cells [**18**].

Since the virus is not a living organism but a protein molecule, it is not killed, but decays on its own. The disintegration time depends on the temperature, humidity and type of material where it lies.

The virus is very fragile; the only thing that protects it is a thin outer layer of fat. That is why any soap or detergent is the best remedy, because the foam cuts the fat (that is why you have to rub so much: for 20 seconds or more, to make a lot of foam). By dissolving the fat layer, the protein molecule disperses and breaks down on its own. Heat melts fat; this is why it is so good to use water above 25 degrees Celsius for washing hands, clothes and everything. In addition, hot water makes more foam and that makes it even more useful.

Alcohol or any mixture with alcohol over 65% dissolves any fat, especially the external lipid layer of the virus. Any mix with one part bleach and five parts water directly dissolves the protein, breaks it down from the inside. Respiration droplet containing corona virus is shown in figure 3.

Oxygenated water helps long after soap, alcohol and chlorine. Peroxide dissolves the virus protein, but you have to use it pure and it hurts your skin.

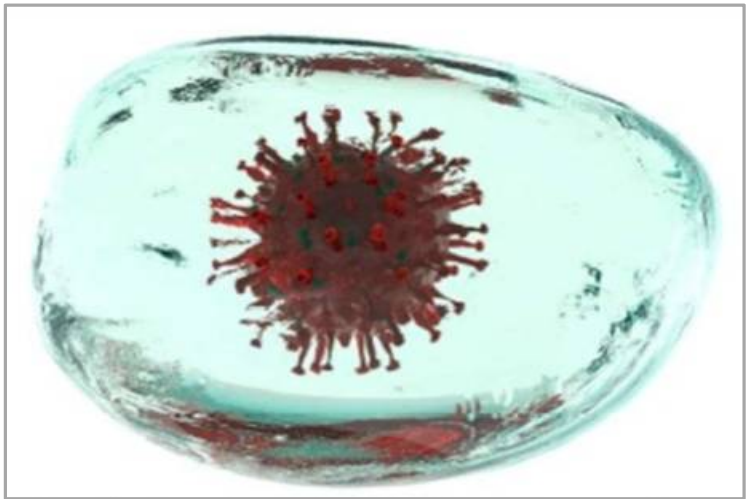


Figure 3. Respiration droplet containing Corona virus.

The virus is not a living organism like bacteria; they cannot kill what is not alive with anthobiotics, but quickly disintegrate its structure with everything said. Never shake used or unused clothing, sheets or cloth. While it is glued to a porous surface, it is very inert and disintegrates only between 3 h (fabric and porous); 4 h (copper, because it is naturally antiseptic and wood, because it removes all the moisture and does not let it peel off and disintegrates); 24 h (cardboard); 42 h (metal) and 72 h (plastic). But if you shake it or use a feather duster, the virus molecules float in the air for up to 3 h and can lodge in your nose.

The virus molecules remain very stable in external cold, or artificial as air conditioners in houses and cars. They also need moisture to stay stable and especially darkness. Therefore, dehumidified, dry, warm and bright environments will degrade it faster.

UV light on any object that may contain it breaks down the virus protein. For example, to disinfect and reuse a mask is perfect. Be careful, it also breaks down collagen (which is protein) in the skin, eventually causing wrinkles and skin cancer. The virus cannot go through healthy skin.

Vinegar is not useful because it does not break down the protective layer of fat. No spirits, Nor Vodka, serve. The strongest vodka is 40% alcohol, and you need 65%. Listerine if it serves! It is 65% alcohol.

The more confined the space, the more concentration of the virus there can be. The more open or naturally ventilated the less. You have to wash your hands before and after touching mucosa, food, locks, knobs, switches, remote control, cell phone, watches, computers, desks, TV, etc. and when using the bathroom.

You have to humidify hands dry from so much washing them, because the molecules can hide in the micro cracks. The thicker the moisturizer, the better is the result. Also keep your nails short so that the virus does not hide there.

Measures of Medication: SARS-CoV-2 being a new disease does not have any clinically proven therapeutics. However, for the treatment of related viruses like SARS and MERS, a substantial preclinical research was reported. It is worthwhile to mention that for the treatment of SARS and MERS, no therapeutic or vaccine designing schedules got completed as these outbreaks did not persist. Consequently, the concepts of drug repositioning and repurposing has received a substantial amount of consideration [19].

In this regard, Chloroquine, Hydroxychloroquine, Lopinavir, Ritonavir, Remdesivir and Favipiravir, have entered clinical trials to address the current SARS-CoV-2 pandemic. Chemical structures of these drugs are shown in figure 4.

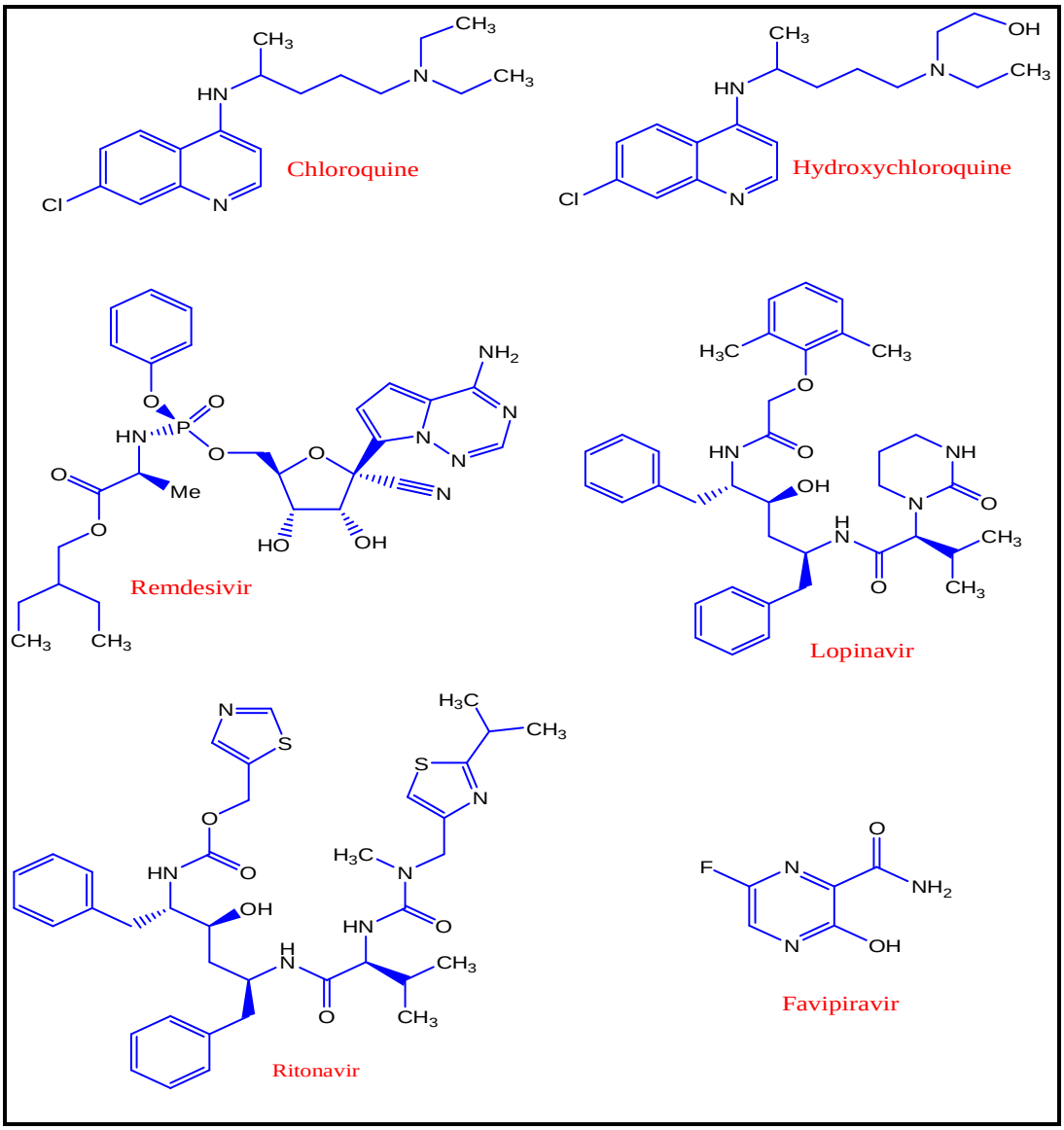


Figure 4. Representative structures of Chloroquine, Hydroxychloroquine, Remdesivir, Lopinavir, Ritonavir and Favipiravir.

Chloroquine and Hydroxychloroquine as possible remedies: While scientists all over the globe were hell-bent on finding an antidote to the deadly disease caused by this virus, certain experts have zeroed down on Chloroquine and Hydroxychloroquine as possible remedies for this. It is widely used as an anti-malarial drug with immunomodulatory effects, as a potential curative drug in the treatment of malaria and amebiasis. Chloroquine was found to inhibit the growth of SARS-CoV-2 in an in vitro study. Its sister compound, Hydroxychloroquine, however, is a more suitable option for the treatment of malaria and autoimmune conditions because though it shares the same mechanism of action as Chloroquine, the intensity of its toxicity is far lower than that of its sister.

Hydroxychloroquine was reported to have anti-SARS-CoV activity in vitro in the previous SARS outbreak. It can therefore be surmised that Hydroxychloroquine is a reliable pharmacological

agent for the treatment of COVID-19 infection [**20**]. Unfortunately, till date, there is no quantifiable proof to establish the veracity of Chloroquine and Hydroxychloroquine as treatment for SARS-CoV-2 infection. However, according to recent results, both Chloroquine and Hydroxychloroquine have the potential to impede the growth of coronavirus through a series of steps. The changing of the pH at the surface of the cell membrane is the first effect that the drug has on the cell. It can subsequently inhibit viral entry, transport and post-entry events. In addition to this, the compounds have the capacity to control replication of nucleic acid, virus assembly, new virus particle transport, glycosylation of viral proteins, virus release and other processes to achieve their antiviral effects. Inhibition of inflammation and autoimmune reactions can be facilitated with the help of their interactions with cells. They bind to DNA and RNA intercalating between base pairs, thereby stabilizing nucleotides and inhibiting the prepolymerization and transcription necessary for cellular replication and normal protein synthesis. They also accumulate in lysosomes, stabilizing them and thereby interfering with chemotaxis, phagocytosis, autophagy and digestion [**21**].

Treatment with Remdesivir: This is the question which is now plaguing the minds of common people. Remdesivir, one of the initial clinical candidates was developed by Gilead Sciences in a collaborative way with the U.S. Centers for Disease Control and Prevention (CDC) and the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID). The development of Remdesivir was a part of an antiviral development project of Gilead Sciences in 2015 which was initially effective against Ebola virus (EBOV)[11]. Though Remdesivir was not developed for the treatment COVID-19, now it is used to treat COVID-19 as among the candidate therapies. Remdesivir has demonstrated efficacy in both in vitro and in vivo models against corona viruses [**17, 22**].

Remdesivir which is basically a prodrug gets metabolized within cells and then converts into an alanine metabolite. This, on further processing, gets converted into the monophosphate derivative followed by into an active nucleoside triphosphate derivative which can be utilized by the viral RNA-dependent polymerases for genome replication. Now, viral RNA-dependent RNA polymerase (RdRP) enzyme can disintegrate nucleoside triphosphate into viral RNA and the action goes on [**23**].

Working with Lopinavir and Ritonavir: In 2003, after the emergence of SARS, screening of several drugs has been performed. Researchers observed after meticulous screening Lopinavir, a human immunodeficiency virus (HIV) type 1 aspartate protease inhibitor, as having in vitro inhibitory activity against SARS-CoV [**24**]. Lopinavir is formulated in combination with another protease inhibitor, Ritonavir. Ritonavir, when combined with Lopinavir, increases its plasma half-life and this takes place through the inhibition of cytochrome P-450. Research indicated that the addition of Lopinavir–Ritonavir to Ribavirin (an antiviral medication used to treat RSV infection, hepatitis C and some viral hemorrhagic fevers) reduced the risk of acute respiratory distress syndrome [ARDS] [**25**]. This combinatorial medication was also capable of reducing viral load among patients with SARS. Again, Lopinavir found its application both in vitro and in an animal model, against MERS-CoV.

Reports suggested that the combination of Lopinavir/Ritonavir (LPVr) with Ribavirin and interferon alfa resulted in virologic clearance and survival. Researchers nowadays have tried the oral dose of LPVr for SARS-CoV-2 infection. SARS-CoV-2 virus, single-stranded RNA beta-corona virus, enters host cells and replicate, producing strands that contain multiple copies of the viral genetic material (RNA). The strands of genetic material, accumulate at the periphery of the cell, ready to be cleaved, packaged and prepared for release from the host cell. The enzyme 3-chymotrypsin-like protease (3CLpro) plays a crucial role in processing the viral RNA. As LPVr is a protease inhibitor, it may inhibit the action of 3CLpro, thereby disrupting the process of viral replication and release from host cells [**24, 26, 27**].

Clinical trials with Favipiravir: Favipiravir is another drug that has received significant attention as it is undergoing clinic trials in treating COVID-19 patients. It gets converted into an active phosphoribosylated form, Favipiravir-RTP (Favipiravir ribofuranosyl-5'-triphosphate). Consequently,

recognized as a substrate by viral RNA polymerase therefore inhibiting the RNA polymerase activity. Favipiravir, a potential RNA-dependent RNA polymerase (RdRp) inhibitor of RNA viruses which is also capable of inhibiting the replication of a large number of RNA viruses, including influenza A virus, flavi-, alpha, filo-, bunya-, arena-, and noroviruses as well as west nile virus, yellow fever virus, foot-and-mouth-disease virus, ebola virus and lassa virus [**28**]. In this way, SARS-CoV-2 being a RNA virus, experiences the potential antiviral action of Favipiravir. Clinical trials for the treatment of COVID-19 have shown Favipiravir had more potent antiviral action than that of Lopinavir/Ritonavir and adverse effects are also much lesser compared to Lopinavir/Ritonavir [**29**].

Rapid COVID-19 antibody tests: A report and analysis have been put together based on research conducted by teams [**30, 31**], using gold nanoparticles as part of the testing technology. The key advantage to antibody testing is that it requires a finger prick sample that can deliver results within 3-10 min, without the need for laboratory analysis or additional equipment. All the tests should form part of diagnostic supervision and no test can be relied on solely for identifying the status of COVID-19 infection.

There are two key objectives to this rapid testing; (1) to stop the spread of the virus and (2) to get people safely back into work.

Life style tips during COVID-19 era: Global human has to adapt life style and continue activities to escape from covid-19 in the coming few months (Figure 5). A few hints made by Faheem Yourus [**32**] are listed here.

a) Washing hands and maintaining a two-metre physical distance is the best method for protection.
b) If you don't have a COVID-19 patient at home, there's no need to disinfect the surfaces at your house.
c) Packaged cargo, gas pumps, shopping carts and ATMs do not cause infection. But you can heat it all up in the microwave.
d) COVID-19 is not a food infection. There is no demonstrated risk that COVID-19is transmitted by ordering food.
e) You can lose your sense of smell with a lot of allergies and viral infections. This is only a non-specific symptom of COVID-19.
f) The COVID-19 virus doesn't hang in the air. This is a respiratory droplet infection that requires close contact.
g) The air is clean, you can walk through the gardens (just keeping your physical protection distance), through parks.
h) You don't have to worry about your food orders, if you wish.
i) The chance of bringing COVID-19 home with your shoes is like being struck by lightning twice in a day.
j) You can't be protected from the virus by taking vinegar, sugarcane juice and ginger! These are for immunity not a cure.
k) Wearing a mask for long periods interferes with your breathing and oxygen levels. Wear it only in crowds.
l) Wearing gloves is also a bad idea; the virus can accumulate into the glove and be easily transmitted if you touch your face.
m) Immunity is greatly weakened by always staying in a sterile environment. Even if you eat immunity boosting foods, please go out of your house regularly to any park/beach.

Figure 5. Globe need to live around with corona

Corona virus contains protein molecule. Humans also contain protein molecules. Proteins are condensation products of amino acids. About 20 per cent of human body amino acids is glycine and is the basic walling material. It is believed that corona virus has much affinity to amino acids, more specifically to glycine. This is associated with depletion of glycine in virus attacked patients and leads to severe ill health. Even young people with 'A' group blood must be more causes, as they originally have no glycine in their blood.

Future hope: Human kind of whole world is suffering with the corona virus (Figure 5). Tragedy with COVID-19 will continue with no reliable medicine is now available that can cure. Number of corona cases is increasing drastically as shown in Figure 6. Measures of medication suggested on the use of drugs are not foot proof. While living in a community, maintaining about 1.5 meter social distance is a primary requirement.

Making use of sanitation is a requirement after moving to places and using public items and instruments. However, soap washing is indoubtly recommended the best, as it can form emulsion with germs, bacteria and virus, which can be washed and drained.

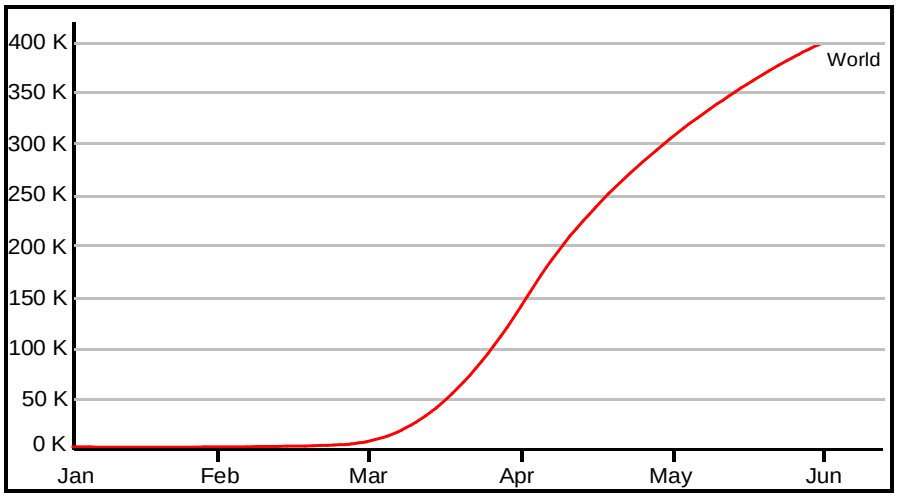


Figure 6. Total confirmed COVID-19 deaths our world in data (Year 2020).

Use of mask covering nose, mouth and eyes is a must during moving, working and talking. N-95 mask, though the best, it is recommended for a single use and a single day. Reusable and recyclable graphene masks are developed [33-35] as shown in figure 7. However, they are not reachable to common human. Use of fabric masks made from cotton and nylon will help everyone to certain extent of simple protection. Moreover these fabric masks are reusable after washing.

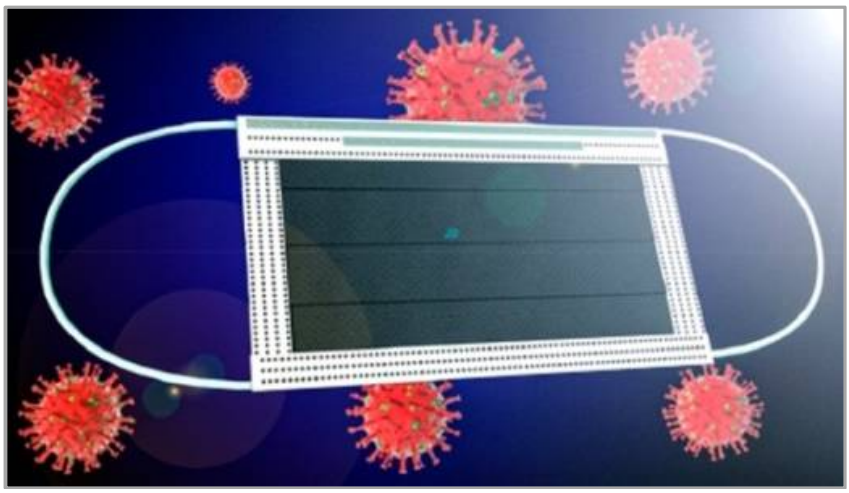


Figure 7. Reusable and recyclable graphine mask.

Preventive vaccines: It is a fact that virus can be destroyed using appropriate chemicals and also by using radiation. However, preventive vaccines are always safer [36].

The big news is that high level research is going on in seven world class laboratories in USA, China, Germany and UK on the preparation of vaccines. Scientists and doctors are working with positive goals. A report was given by Shawn [37], recently on here exactly where we are with vaccines and treatment for COVID-19.

Governments are providing facilities and spending lot of money in serving effected people. Hope that the results will help every citizen of the World, positively by early 2021.

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