

CORONAVIRUS OUTBREAK, ITS TREATMENT OPPORTUNITIES USING HYDROXYCHLOROQUINE AND MITIGATING SEVERITY

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Abstract

Coronavirus is a new virus that takes control over the immune system making it lose its ability to differentiate between the healthy and infected cells. After enervating its host's capacity to fight, the virus now replicates and transmits to look for other susceptible hosts. Due to this hollowing out of the immune system there are noticeable effects in the health of the people. Mass transmission of this virus leads the disease caused by it, called COVID-19, to take the form of a pandemic. In this study, we aim to underline the importance of carrying out the studies of other diseases with similar symptoms, of different animals carrying the virus and medications used in preceding pandemics. Certain species have been observed to be immune to the disease. The steroid, Hydroxychloroquine ($C_{18}H_{26}ClN_3O.H_2SO_4$) which is an anti-parasitic drug that has been showing promising results in COVID-19, creates an intriguing fact wherein an antidote for Malaria is proving promising against a Coronavirus. Here, we intend to reflect on the importance of an interdisciplinary study across biochemistry, medical sciences and molecular sciences so that we can stay prepared beforehand for an epidemic.

CORONAVIRUS OUTBREAK, ITS TREATMENT OPPORTUNITIES USING HYDROXYCHLOROQUINE AND MITIGATING SEVERITY

Coronavirus Pandemic and Utilization of Drugs

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Abstract: Coronavirus is a new virus that takes control over the immune system making it lose its ability to differentiate between the healthy and infected cells. After enervating its host's capacity to fight, the virus now replicates and transmits to look for other susceptible hosts. Due to this hollowing out of the immune system there are noticeable effects in the health of the people. Mass transmission of this virus leads the disease caused by it, called COVID-19, to take the form of a pandemic. In this study, we aim to underline the importance of carrying out the studies of other diseases with similar symptoms, of different animals carrying the virus and medications used in preceding pandemics. Certain species have been observed to be immune to the disease. The steroid, Hydroxychloroquine ($C_{18}H_{26}ClN_3O.H_2SO_4$) which is an anti-parasitic drug that has been showing promising results in COVID-19, creates an intriguing fact wherein an antidote for Malaria is proving promising against a Coronavirus. Here, we intend to reflect on the importance of an interdisciplinary study so that we can stay prepared beforehand for an epidemic.

Summary

There are an abundant viruses circulating in the environment and they continuously undergo mutations in an attempt to find a host cell and thereby replicate. The case when a virus finds a host cell and vast mass

spread happens, an epidemic or a pandemic is developed. A similar situation has happened in the spread of COVID-19 in which the virus enters the body through the respiratory tract by spreading through physical contact. The extent to which a virus can cause harm to the human beings is unprecedented. The coronavirus outbreak has affected the whole world, stumbling the economies, killing people etc. As of March 2020, there has been 20,64,815 active cases of COVID-19 and caused the death of 1,97,078 people. The country which is the worst hit is the United States of America where there has been the death of 28,579 people as of 16th April 2020 (15:28 IST). There are various ways of transmission of virus with Zoonotic viruses accounting for around 61% of the total viral diseases. Zoonotic viruses are those that transmit between animal to human species. Apart from COVID-19, the coronavirus is also responsible for the spread of diseases like SARS and MARS. After clinical trials, it has been observed that Hydroxychloroquine, which is an antidote for Malaria has shown promising results in encountering COVID-19, so there is an analysis going on comparing Malaria and COVID-19 and about the mechanism of action of Hydroxychloroquine. While the clinical trials are going on, it is important that we take all the precautionary measures from preventing the disease to spread anymore and preventive measures like regular sanitization and social distancing. Also, it is important to conduct various research studies and equip ourselves with the mechanisms of different viruses in different species in order to be prepared for the future.

Keywords: Coronavirus, Hydroxychloroquine, Pandemic, Drug

Chemical Compounds studied in this article

Hydroxychloroquine (PubChem CID:3652)

1. *Viruses and Pandemics*

The recent outbreak of the COVID-19 has rekindled interest in the field of study for the prevention of outbreaks of Pandemics. The most common Pandemic causing microbes all turn out to be classified as viruses (structural examples shown in (fig.1)). Originating from the word poison, a virus is a replicating agent which mostly results in harmful effects to the body. It is still debatable if a virus can be classified as a living creature or not because as long as it is not attached to a host it only has independent particles called virions. Virions have genetic material, a protein coat, and rarely a coat of lipids. There are some viruses known as satellite viruses, these are dependent on other viruses for their existence (la Scola et al. 2008). Generally, the virions are invisible under an optical microscope. The reason viruses are mostly responsible for large scale diseases is their ability to mutate and remain undetectable unless under extreme supervision

There are a number of theories attempting to explain how viruses originated, none of them, however, give a satisfactory unanimously accepted answer to the question. Since the viruses do not form fossils only molecular techniques are used to investigate their genesis. Sometimes the virus integrates into the host organisms to such an extent that they can be passed on to off springs, these are also an important source of information. There is no substantial theory but attempts have still been made to classify them. All the major theories can be watered down to the following three classifications which are:

- Cellular Origin Hypothesis-Jumping Genes i.e. mobile genes might have escaped their parent cells to form Viruses
- Regressive Hypothesis- It assumes that particular parasites may have lost parts not required to become a replicator class
- Co-Evolution Hypothesis-The belief that Viruses began at the same time as life

A detailed study on pandemics is important because it is a deadly phenomenon that shows its occurrence when the mass spread of a particular virus happens, infecting a myriad of people all around the world. These viruses can be seen as a bio-weapon which can arguably be even more dangerous than a nuclear weapon as these viruses have the potential of creating havoc all around the world.

2. *Transmission of Viruses and why are Host-jumps so dangerous?*

Viruses are a type of organic parasite infecting nearly every form of life and they have three stages of survival

and subsequent reproduction, namely- making contact with a susceptible host, infection and replication, and transmission to other individuals. The virus encounters a new host and makes its way into the body through different pathways like human influenza takes the respiratory path. Although this is not a very difficult task the virus has to spread the infection to a significant level to be able to survive and not get broken down by human immunity. To do this the viruses have evolved specific interactions with their host species. For example, human flu matches with proteins adapted to bind with matching receptors on human respiratory cells. Once inside, the virus starts to disturb the host cell's mechanism and starts to replicate (as shown in fig. 2). If the immunity system is unable to counter the replication for some time, the virus will infect more and more cells and at this point, the disease can be passed on to other individuals via any kind of transmission of the infected fluid. In the example of human influenza, a sneeze is the medium of transmission but it also transmits the virus to a large number of different organisms and the virus starts an attempt to infect those organisms. It has been observed that generally the virus from one species fails to infect any other species and that is explained by the large genetic dissimilarity between the two hosts. It has been seen that if two distinct species are closely related, there are higher odds of the virus to find its host in the other one as well. For a virus that infects a mammal, it may take only a few suitable mutations by the virus to infect the human as well. Although most viruses either are unable to find a host in a particular species or are countered by its immunity if they can reach the stage of transmission, it makes it deadly. The diseases that happen due to the transmission of the virus from one to another organism are termed under the category of Zoonoses.

Zoonoses can be transmitted directly, through physical contact with organisms or may even transmit through a medium like air or water, and indirectly through some vector that acts as a carrier of the virus. The Ebola virus or HIV are zoonotic viruses that were transmitted to humans by other organisms. Although the latter after undergoing several mutations has become a separate human-only disease. In the past, diseases like the influenza are the one that has primarily been known to affect humans only while bird flu and swine flu viruses were able to develop certain mutations that could transmit from one species to another.

The Spanish Flu Influenza of 1918 and Swine Flu of 2009 are known to be a few of the most deadly spread of a virus through different species. A range of disease pathogens such as viruses, bacteria, fungi, and parasites are responsible for the spread of zoonoses and as contemporary discoveries say, of 1,400+ pathogens known to infect humans, 61% are zoonotic

3. *Coronavirus*

Coronavirus disease (COVID-19) is an infectious disease and the newly discovered coronavirus is the root cause behind the mass spread of this disease (fig 3). The coronavirus generally transmits amongst animals but it also has the potential to transmit from animals to humans. The coronavirus preferentially enters the human body through the respiratory pathway and since it is a virus that spreads through interaction amongst species, isolation is advised as a preventive measure. Most people who are attacked by this coronavirus will show mild to moderate respiratory illness as symptoms and may even recover without requiring special treatment because of their immune system. But surprisingly the immune system can be harmful as well. The Coronavirus directs the immune system to an overkill state. The immune system, particularly the killer T-cells and **neutrophils** (see glossary), start killing off healthy body cells as well under the influence. This overkill makes the affected area (lungs in the case of COVID-19) lose their capacity. Also, the immune system loses its own capacity fighting off healthy cells, and thus the organisms become more susceptible to other infections. In the case of COVID-19, the epithelial lining of the lungs is destroyed allowing bacteria in the lung to cause more harm than usual, and an immune system at lower capacity rendered unable to fight off the infection (fig. 5). Older people and people suffering from problems like cardiovascular diseases, diabetes, cancer, etc are the ones who are more likely of encountering the disease as the virus will more easily replicate in such hosts with weaker immunity. There have been numerous ways to prevent and thus slow down the spread of this virus and a few of them are washing hands regularly, wearing masks, and not touching your face. The spread of COVID-19 primarily happens through the droplets of saliva or the sneeze of an infected person and hence as a precautionary measure, we must practice basic respiratory etiquettes.

Although currently the COVID-19 is an incurable disease and we do not have any developed medications or vaccines for this disease, however, researchers all over the world are conducting clinical trials to find a solution.

4. *Corona Family:*

The COVID-19 causing Coronavirus is a part of that family of viruses which is responsible for causing diseases in mammals and birds. In humans, coronaviruses affect the body by infecting the respiratory tract that can lead to symptoms ranging from mild to severely lethal and at times also being the cause of death. Common cold (which has other possible causes, predominantly rhinoviruses) is one of the examples of the mild variety while more lethal varieties have shown their deadly effects in causing diseases like SARS, MERS in the past, and COVID-19 recently. Symptoms in different species vary: like, in chickens, they attack the upper respiratory tract, while in cows and pigs they cause diarrhea. There are no reports of the discovery of any vaccination or drugs for human coronavirus infections as of now. Coronaviridae is the family in which Orthocoronavirinae is a subfamily that is constituted by the coronavirus, order Nidovirales, and realm Riboviria. These viruses are enveloped with a positive-sense single-stranded RNA genome and **nucleocapsid** (see glossary) that shows helical symmetry. 26 kilobases to 32 kilobases is the range of the **genome** (see glossary) size of the coronavirus and that is one of the largest among extant RNA viruses. These viruses have a characteristic club-shaped spike that is projected from their surface. An image reminiscent of the solar corona is created by the electron micrographs.

4.1 *Morphology*

Coronaviruses are large **pleomorphic** (see glossary) spherical particles consisting of bulbous surface projections with an average diameter of around 120 nm (.12 μm). The diameter of the envelope is ~ 80 nm (.08 μm) with the spikes being 20 nm (.02 μm) long. In the electron micrographs, a pair of electron-dense shells appear and these shells are the envelope of the virus (representation of Coronavirus shown in figure 4). Membrane, envelope and spike structural proteins are hosted in a lipid bilayer which is a part of the viral envelope. A few of the coronaviruses which are members of betacoronavirus subgroup A also consist of a shorter spike-like surface protein named hemagglutinin esterase. The nucleocapsid is present inside the envelope and it is generated out of multiple copies of the nucleocapsid protein. They are bound in a continuous confirmation to the positive-sense single-stranded RNA genome. The lipid bilayer envelope, membrane proteins, and nucleocapsid act as shields of the virus when it ventures outside of the host cell.

While looking for solutions to treat Coronavirus, it has been found that Hydroxychloroquine, which had been found as an intensive utility in the treatment of Malaria, also has the potential to fight against Coronavirus and is being put in use. Although Malaria is a disease that happens due to Protozoa but since it has been seen that the medication used in Malaria is also effective in Coronavirus, it may imply that the mechanism with which the immunity system fights both these diseases may be similar. So, we must also discuss the Malaria disease and the mechanism with which Hydroxychloroquine combats this disease.

5. *Malaria*

Malaria is a dreadful and at times lethal disease that is caused by a parasite of the genus plasmodium. These first infect specific kinds of mosquitoes (female Anopheles) which later transfers it to human beings. *Plasmodium vivax*, *P. ovale*, *P. malaria*, and *P. falciparum* are four types of parasites responsible for inducing malaria. Apart from this *P. knowlesi* is a fifth known malaria-causing parasite having long-tailed and pig-tailed macaques as their natural hosts? Reports from Sarawak, Malaysia (2004) indicated the natural acquirement of human infection throughout Southeast Asia confirming the zoonotic nature of the aforementioned parasite. Symptoms to this grievous disease come with a combination of sweats, fever, chills, nausea, vomiting, body ache, and general malaise with physical findings including weakness, liver enlargement, mild jaundice, and proliferated respiratory rates.

At present most common antimalarial treatment involves:

1. Artemisinin-based combined therapies (ACT's) which are the most widely used treatment for uncompli-

cated *P.falciparum* malaria, usually with chloroquine resistance. It involves a combination of two drugs like artemether-lumefantrine and artesunate-mefloquine.

2. In the case of *P.falciparum* identified, in areas without chloroquine resistance, a chloroquine or hydroxychloroquine dose has opted for the treatment.

3. For *P. malaria* and *P. knowlesi* cases of chloroquine resistance are still rare thus chloroquine and hydroxychloroquine are used for both of these infections, here ACT remains an alternative.

Chloroquine and hydroxychloroquine also remain an effective option in the case of *P.vivax* and *P. ovale* parasite. However, in parts of Southeast Asia and South America chloroquine-resistant *P.vivax* infections cases are recorded. For the latter case recommended treatment regimes are atovaquone-proguanil, quinine sulfate plus doxycycline, or tetracycline. Thus chloroquine and hydroxychloroquine are widely approved drugs used to treat specific malaria. But these may result in pruritis and exacerbate psoriasis. Overdosages may cause death. Thus these drugs are available on prescription only.

6. *Studies conducted with chloroquine and hydroxychloroquine in human COVID-19:*

In the in vitro studies, there has been the identification of the antiviral activity of chloroquine and HCQ and there has been the growth of many different viruses that have been inhibited in the cell culture line by both the agents which includes the SARS coronavirus. Mice studies have also demonstrated the activity of these agents against human coronavirus OC43, enterovirus EV-A71, Zika virus, and influenza A H5N1 have also been demonstrated in the studies carried out on mice. Chloroquine did not show any convincing results about its effectiveness in preventing influenza and dengue infection in a non-placebo testing analysis. In studying chloroquine the results showed the fact that it had potential in ex vivo studies but it was not the case when it underwent in vivo studies against ebola virus and influenza viruses. Chloroquine did manage to show satisfactory antiviral activity against chikungunya but when chloroquine's effectiveness was tested on humans it proved ineffective against chikungunya acute illness and rather backfired by increasing the chronic **arthralgia** which was observed during the post-illness period. Hence, chloroquine's ability to counter the Human Immunodeficiency Virus was inconclusive. Chronic hepatitis C was the only viral disease where chloroquine was modestly effective. This indicated that there was an increment in virological response to pegylated interferon plus ribavirin and this is the reason why the results of chloroquine and HCQ testing on COVID-19 gives more hope of a positive result than any other viral disease. Apart from this, another advantageous fact with this drug is that it is economically viable, reasonably safe, and can be available in an adequate amount.

7. *Hydroxychloroquine (HCQ) :*

Plaquenil is the generic name for Hydroxychloroquine (HCQ), which is a prescribed drug that is ingested orally and is one of the medications which has been employed for the prevention and cure of malaria in areas where malaria remains sensitive to chloroquine. It also finds its usage in the treatment of rheumatoid arthritis, lupus, and porphyria cutanea tarda. Although, it is not completely explained as to how this drug works against lupus erythematosus or rheumatoid arthritis. However, it is widely believed that the mechanism of this drug is similar to the working of the immunity system. Its potential in the treatment for coronavirus disease 2019 (COVID-19) is currently under study. (The chemical structure of Hydroxychloroquine is shown in Fig. 6)

Apart from its curing potential, it does have some common side effects like vomiting, headache, changes in vision, and muscle weakness. Since all the risk is not feasible to be eliminated, it remains a treatment for rheumatic disease during pregnancy. Hydroxychloroquine is in the antimalarial and a part of 4-aminoquinoline families of medication. Hydroxychloroquine was cleared for medical use in the United States in 1955. It finds its place in the World Health Organization's List of Essential Medicines, the safest and most effective medicines needed in a health system. In 2017, it was one of the most prescribed, 128th-most in the United States, prescribed more than 5 million times.

What is the reason that this medication is prescribed so highly? Hydroxychloroquine is a member of the class

of drugs called antimalarials and it is employed in the prevention and treatment of acute malaria attacks. Apart from this, its use is also reported to treat discoid or systemic lupus erythematosus and rheumatoid arthritis in the patients whose symptoms are still present even after other medications and that is the reason behind this medication being prescribed in such volumes.

8. *Pharmacokinetics & Pharmacodynamics Of Hydroxychloroquine (HCQ)*

8.1 *Pharmacokinetics*

Hydroxychloroquine is very similar to chloroquine in regards to pharmacokinetics. There is rapid gastrointestinal absorption and elimination that is done by the kidneys. Cytochrome P450 enzymes (CYP2D6, 2C8, 3A4, and 3A5) are metabolized to N-diethyl hydroxychloroquine from hydroxychloroquine.

8.2 *Pharmacodynamics*

Antimalarials are **lipophilic** weak bases and easily pass plasma membranes. The free base form accumulates in lysosomes (acidic cytoplasmic vesicles) and is then protonated, resulting in concentrations within lysosomes up to 1000 times higher than in culture media. This increases the pH of the lysosome from four to six . Alteration in pH causes inhibition of lysosomal acidic proteases causing a diminished proteolysis effect. Higher pH within lysosomes causes decreased intracellular processing, **glycosylation** (see glossary), and secretion of proteins with many immunologic and nonimmunologic consequences. These effects are believed to be the cause of a decreased immune cell functioning such as **chemotaxis** (see glossary), **phagocytosis** (see glossary), and superoxide production by neutrophils. HCQ is a weak diprotic base that can pass through the lipid cell membrane and preferentially concentrate in acidic cytoplasmic vesicles. The higher pH of these vesicles in macrophages or other antigen-presenting cells limits the association of autoantigenic (any) peptides with class II MHC molecules in the compartment for peptide loading and/or the subsequent processing and transport of the peptide-MHC complex to the cell.

9. *Description of Action*

Hydroxychloroquine enhances the lysosomal pH in the antigen-presenting cells. The toll-like receptors present on the Plasmacytoid Dendritic Cells (PDC's) are blocked when exposed to inflammatory conditions. Production of interferon, the maturity of dendritic cells, and change from present antigen to T cells happen due to toll-like receptor 9 (TLR 9). There is a reduction in the activation of dendritic cells and the inflammatory process because there is a decrease in TLR signaling by Hydroxychloroquine.

Hydroxychloroquine inhibiting stimulation of the toll-like receptor (TLR) 9 family receptors was a novel mechanism whose description dates back to 2003. TLRs are cellular receptors for microbial products that are responsible for inflammatory responses and activation of the innate immune system is the pathway to induce these responses.

Although even now, the determination of the mechanism of action against malaria of other quinolones has not been fully resolved. However, the model focused on Hydroxychloroquinine has been accepted widely and the inhibition of hemozoin biocrystallization is involved in it and the aggregation of cytotoxic heme is also facilitated by this inhibition. Death is caused due to the accumulation of Free cytotoxic heme in the parasites.

10. *Conclusion*

In analyzing Coronaviruses- prevention and cure, we studied the classification of viruses and about the different kinds of viruses that have been so far encountered in different species in order to understand the mechanism of the Coronavirus in a better scale of understanding. There is an essential need to understand the pathway with which the immune systems try to negate the virus's effect and the design of the bodies of different species that help them survive through the virus. Apart from studying the bodily natures of different species, we should also consider studying the effect of a virus on a particular species when a virus from another species is cross-injected. In this way, it would be easier to find antidotes for diseases that originate from Zoonotic viruses. We can also ameliorate the effect of a current pandemic by studying the

vaccines which were used to cure pandemics of the past, analyzing the immune response to different diseases that may show similar symptoms and the medications used to cure these diseases. By knowing in-depth about previously used vaccines (as shown in fig. 7) and historical pandemics may give current researchers a better idea to formulate better preventive measures and medications to mitigate the effects of a deadly pandemic (as shown in table 1). In previous pandemics(as shown in table 2) as well, it was seen that a virus affecting human beings did not affect a few classes of animals at all and thus, a study focused on their body structure and immunity mechanism will lay a better groundwork while we forage for solutions to the current problem. We can conclude by saying that it is important to take lessons from the past and implement them by improvising them on extant problems. Studying a variety of species will also make us interdisciplinary researchers and it would enhance the efficacy with which we work to find a solution to this problem. Being prepared beforehand by having already formulated cures to deadly pandemics like this will cease the spread of this disease and therefore we will be able to save millions of people from getting affected(as shown in fig 8). It is a prudent step to constitute a team of clinical researchers, epidemiologists that are capable enough to be prepared enough for any possible epidemics just like there are Intelligence teams for pre- preparedness against wars.

11. Declaration Of Competing Interests

This is to declare that none of the authors had any competing interests

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13. Data Availability

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15. Ethical Statement

The ethical statement is not applicable.

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Glossary

Arthralgia: Arthralgia (from Greek arthro-, joint + -algos, pain) literally means joint pain. Specifically, arthralgia is a symptom of injury, infection, illness (in particular arthritis), or an allergic reaction to medication

Chemotaxis:movement of a motile cell or organism, or part of one, in a direction corresponding to a gradient of increasing or decreasing concentration of a particular substance.

Genome: the haploid set of chromosomes in a gamete or microorganism, or in each cell of a multicellular organism.

Glycosylation : Glycosylation (see also chemical glycosylation) is the reaction in which a carbohydrate, i.e. a glycosyl donor, is attached to a hydroxyl or other functional group of another molecule (a glycosyl acceptor)

Lipophilic:tending to combine with or dissolve in lipids or fats.

Neutrophils:Neutrophils are a type of white blood cell (WBC or granulocyte) that protect us from infections, among other functions.

Nucleocapsid:the capsid of a virus with the enclosed nucleic acid.

Phagocytosis: Phagocytosis is the process where a cell (phagocyte) engulfs a solid particle to form an internal compartment called a phagosome. The membrane of the phagocyte forms a crater shape around the particle that is to be phagocytised. Within the phagosome, the particle can then be degraded

Pleomorphic: Pleomorphism is a term used in histology and cytopathology to describe variability in the size, shape and staining of cells and/or their nuclei. Several key determinants of cell and nuclear size, like ploidy and the regulation of cellular metabolism, are commonly disrupted in tumors.

Tables:

1.	United States	6,44,188	52,629	28,579
2.	Spain	1,80,659	70,853	18,812
3.	Italy	1,65,155	38,092	21,645
4.	Germany	1,34,753	66,169	3,804
5.	France	1,06,206	30,955	17,167
6.	United Kingdom	98,476	-	12,868
7.				

VIRUS	YEAR IDENTIFIED	CASES	DEATHS	NUMBER OF COUNTRIES
Ebola**	1976	33,577	13,562	9

VIRUS	YEAR IDENTIFIED	CASES	DEATHS	NUMBER OF COUNTRIES
Nipah	1998	513	398	2
SARS	2020	8,096	774	29
MARS	2012	2,494	858	28
COVID-19**	2020	20,64,815	1,97,078	180

2020 Novel Coronavirus compared to other viruses[85} The table shows the effects of different viruses mentioned with respect to the year of outbreak, total number of deaths caused, number of countries affected and total number of reported cases *-as of November 2019 *-as of March 2020

Figure Legends:

Figure 1: (a) A view of the SARS-Coronavirus-2 from the family of Coronaviruses, the virus strain responsible for the COVID-19 (b) A view of the Ebola Virus, the causative virus of the viral Haemorrhagic

Figure 2: Figure showing viruses transmitting across the cells

Figure 3: A graph showing the variation in the number of confirmed cases observed per day up till 13 April 2020 in India

Figure 4: Representation of Coronavirus

Figure 5: A graph showing the variation in the number of deaths per day up till 13 April 2020 in India

Figure 6: Skeletal Structure of Hydroxychloroquine in 2D- a drug for Malaria|(C₁₈H₂₆ClN₃O.H₂SO₄) Skeletal Structure of Hydroxychloroquine in 3D- a drug for Malaria|(C₁₈H₂₆ClN₃O.H₂SO₄)

Figure 7: The figure illustrated above shows the pathway of working of vaccines against viruses

Figure 8: For a pandemic, there can be two futures: Fast and Slow. In a fast pandemic a lot of people become infected at the same time resulting in a deficiency of resources to cure it. A slow pandemic has the same number of infected but they are cured because they are not infected at the same time and the healthcare capacity is not exceeded

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