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HIV-AIDS and SAR-COV-2: Importance of HIV-AIDS in SARS-CoV-2 Research and Drug Development

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***Abstract*— The outbreak of Novel Coronavirus (SARS-CoV-2) Disease (COVID-19) has put the world on alert. Experts suggest that almost everyone in the world is susceptible to SARS-CoV-2 infection, and to date, there are no effective treatments. In light of the references published, SARS-CoV-2 has demonstrated more mutations in its genome giving new strains of the virus just like HIV-AIDS. This has made it difficult to developahighly effective vaccine for prevention of the novel COVID-19. There have been some serious side effects of the vaccination thus a number of people are not willing to be vaccinated. The three main vaccines—Pfizer BioNTech, Moderna, and Oxford AstraZeneca—all target the spike protein of the virus, where these variants have mutations therefore the vaccines are not 100% effective. This review aims to analyze the similarities of SARS-CoV-2 and HIV-AIDS and use the HIV-AIDS experience to research more on SARS-COV-2 and find probable drug targets for the virus which will not mutate continuously.**

***Index Terms*— HIV-AIDS, genome, mutations, SARS-CoV-2, vaccine.**

I. Introduction

In December 2019, a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in the city of Wuhan, China. It has resulted in the most catastrophic pandemic in modern history (ECDPC,2020). On 30 January 2020, the Director-General of the World Health Organization (WHO) said that the outbreak of the new virus constitutes a Public Health Emergency of International Concern (Liu *et al.*, 2020). The coronavirus belongs to a family of viruses that causes various symptoms such as pneumonia, fever, breathing difficulty, and lung infection (WMHC, 2020). By 22 July 2020, SARS-CoV-2 had been detected in approximately 216 countries and regions. Epidemiologists and doctors advised that the infection could be effectively controlled if people reduced exposure, blocked transmission and volunteered to isolate themselves while infected. Nevertheless, a number of barriers must be overcome to fight SARS-CoV-2. It is therefore necessary to develop stronger preventive measures, improve the public's awareness of protection, and stop the disease from becoming a pandemic.

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The human immunodeficiency virus (HIV) is a lent virus that causes HIV infection and AIDS. AIDS is a condition in humans in which progressive failure of the immune system allows life-threatening infections and cancers to thrive. Infection with HIV occurs by the transfer of blood, semen, vaginal fluid and breast milk. Within these bodily fluids, HIV is present as both free virus particles and virus within infected immune cells. The symptoms of AIDS are primarily the result of conditions that do not normally develop in individuals with healthy immune system. The Joint United Nations Program (UNAIDS) data from 2018 reported that more than 77 million people had been diagnosed with HIV, 35 million of whom died as a result of severe disease condition, and currently, approximately 40 million people are living with HIV (Schwetz and Fauci, 2018).

HIV is the only virus which makes new copies of itself inside the human cells. This process begins when this virus attaches to the CD4 receptor which is a protein found on the outer surface of the cell. HIV mainly infects immune cells i.e., T-helper cells that forms the body immune system (Kapila *et al.*, 2016). There is no cure of AIDS but there are certain medications which are used to slow down the diseases so one can stay healthy for a long time (Coffin *et al.*, 1999). HIVs are the most studied viruses and are the best models for understanding the interplay between host antiviral defense and viruses (Fung *et al.*, 2020). This contributes to a comprehensive understanding of the viral biology and pathogenesis (Schwetz and Fauci, 2018). HIV-AIDS may provide the basic framework for understanding the pathogenicity and cross-species transmission of SARS-CoV-2.

In general, many similarities are present between SARS-CoV-2 and HIVs in terms of cross-species transmission (Fung *et al.*, 2020). What is learned from HIV is relevant to SARS-CoV-2 because both SARS-CoV-2 and HIV-AIDS are spread from their animal reservoirs to human species, mild symptoms for both SARS-CoV-2 and HIV-AIDS are experienced in the animal reservoirs but severe symptoms develop when they infect humans.

Over the last few months, the world faced a rapid increase in COVID-19 cases termed as the third wave of SARS-CoV-2, leading to enhanced epidemiological and virological investigations. Analysis of viral genome sequence data identified a large proportion of cases belonged to a new single phylogenetic cluster. The new variant is defined by multiple spike protein mutations (deletion 69-70, deletion 144, N501Y,

A570D, D614G, P681H, E484K, T716I, S982A, D1118H) present as well as mutations in other genomic regions (Mahase, 2020). While it is known and expected that viruses constantly change through mutation leading to the emergence of new variants, preliminary analysis in the UK suggests that this variant is significantly more transmissible than previously circulating variants, with an estimated potential to increase the reproductive number (R) by 0.4 or greater with an estimated increased transmissibility of up to 70% (ECDC: Stockholm; 2020). The N501Y mutation, which is also a feature of the English variant (Mahase, 2020) has been linked to increased infectivity and virulence in mouse models (Rambaut*et al.,* 2020). The E484K mutation is thought to be associated with escape from the neutralizing antibodies produced by the body against SARS-CoV-2 (Voloch*et al.,* 2020). This mutation is present in the South African variant as well.

The three main vaccines—Pfizer BioNTech, Moderna, and Oxford AstraZeneca—all target the spike protein of the virus, where these variants have mutations (BMJ, 2021). This therefore poses a threat that the vaccines may not work effectively. This review aims at using HIV-AIDS experience to research more on SARS-COV-2 and find probable drug targets for the virus which will not mutate continuously.

II. METHODS AND MATERIALS.

HIV has frustrated all efforts to develop of an effective vaccine. The first experiment involving the immunization of humans against HIV-I (a strain of HIV) begun in November 1986 involving a sufficient number of HIV healthy volunteers. In this experiment, vaccinia virus recombinant (V25) that expresses gp160 env at the surface of infected cells were applied. gp160 env were the determinants of HTLVIIIB. The results of this experiment showed that the immune response against HIV could be achieved in humans (Zagury D *et al.*, 1988). Following this experiment, more than 256 clinical trials (phase I and phase II), over 44, 000 healthy volunteers have tested candidate vaccines against HIV (Saunders *et al.*, 2012). Among these clinical trials, only six candidate vaccines have achieved very low clinical efficacy. These six vaccines include VAX004, VAX003, Phambali, HVTN505 and RV144 (Lema D *et al.*, 2014).

HIV vaccine efficacy trial					
Trial Name	Trial duration	Phase type	Type of vaccine	Expected immune response	Outcome
VAX004	1998-2003	III	rpg120 (clade B)	Humoral	No efficacy
VAX003	1999-2003	III	rgp120 (clades B+E)	Humoral	No efficacy
Step	2004-2007 (Stopped for possible enhancement in HIV acquisition)	IIb		Cellular	Enhanced HIV infection risk in uncircumcised men and MSM
Phambili	2007	IIb	rAD5 (gag/polnef)	Cellular	No efficacy
RV 144	2003-2009	III	Canarypox (gag/polnef)	Cellular along with humoral	31.2% efficacy
HTVN 505	2009-2015	IIb	DNA plasmid (gag/polneflenv) +rAD5 (gag/pollen)	Humoral as well as cellular	No efficacy

Table 1; Illustrating trials of different HIV vaccines efficacy. (*Extracted from Asif DF, Irshad M (2017) Efficacy Trials and Progress of HIV Vaccines).*

Trials of the Novavax, Janssen/Johnson & Johnson, and AstraZeneca vaccines in South Africa, where the B.1.351 variant of concern represents virtually all of the circulating SARS-CoV-2, seemed to justify the concerns of vaccine infectivity. The South Africa trials found lower vaccine efficacy compared to trials in other countries where B.1.351 was not dominant. Most of the current data on the messenger RNA (mRNA) vaccines' efficacy against SARS-CoV-2 variants has come from laboratory studies in which researchers exposed serum samples from immunized individuals to genetically engineered versions of concerning variants and then measured neutralizing antibody titers. Such studies have repeatedly shown that the vaccines elicit lower levels of neutralizing antibodies against SARS-CoV-2 variants than older, more common isolates (Rita *et al.*, 2021).

Findings from a phase 2 trial of the Oxford-AstraZeneca vaccine in South Africa seemed quite discouraging, the trial found that the vaccine did not protect against mild to moderate COVID-19 caused by the B.1.351 variant (Rita *et al.*, 2021).

Manufacturers (vaccine name)	Technology used	Doses	Efficacy against symptomatic disease*	Safety profile (from phase III trials)	Efficacy against variants*		Are updated versions being made to target variants?	Reported effectiveness from mass rollout
					B.1.1.7. (first detected in UK)	B.1.351 (first detected in South Africa)		
Pfizer and BioNTech (Comirnaty)	mRNA	2	95%[1]	Of the covid-19 vaccine group, 27% of participants reported any adverse event, compared with 12% taking a placebo. This was mainly due to transient reactogenicity events, such as injection site pain. Few people in either group had severe or serious adverse events.	Unknown	Unknown	Yes	Reduced symptomatic cases by 94%, hospital admissions by 87%, and severe covid-19 by 92% in Israel[2]
Oxford and AstraZeneca (AZD1222)	Viral vector	2	82.4% (12 weeks between doses)[3]	Serious adverse events occurred in 168 participants: 79 in the vaccine group and 89 in the controls. Two cases of transverse myelitis were originally reported as potentially related to the vaccine but later determined to be unlikely to be related.	74.6%[4]	TBC (unconfirmed reports as low as 10%)[5]	Yes	In Scotland, risk of hospital admission for covid-19 fell by up to 94% four weeks after first doses administered[6]
Moderna and NIH (mRNA-1273)	mRNA	2	94.5%[7]	Solicited adverse events at the injection site occurred much more often in the vaccine than in the placebo group. Serious adverse events were rare, with incidence similar in the two groups.	Unknown (but reports of decrease in neutralising antibodies)[8]	Unknown	Yes[9]	TBC
Gamaleya (Sputnik V)	Viral vector	2	91.6%[10]	Forty five of 16 427 participants in the vaccine group and 23 of 5435 in the placebo group had serious adverse events, but none were considered associated with vaccination.	Unknown	Unknown	Unknown	TBC
CanSinoBio (Convidecia)	Viral vector	1	65.7%[11]	Unknown	Unknown	Unknown	Unknown	TBC

Manufacturers (vaccine name)	Technology used	Doses	Efficacy against symptomatic disease*	Safety profile (from phase III trials)	Efficacy against variants*		Are updated versions being made to target variants?	Reported effectiveness from mass rollout
Novavax (NVX-CoV2373)	Protein	2	95.6%[12]	A preliminary review of the safety database showed that severe, serious, and medically attended adverse events occurred at low levels and were balanced between vaccine and placebo groups.[13]	85.6%	60%	Yes[14]	TBC
Johnson & Johnson (Ad26.COV2.S)	Viral vector	1	72%	More serious adverse events were reported in participants who received placebo than in the vaccine group.[15]	Unknown	57%[16]	Unknown	TBC
Sinopharm (BBIBP-CorV)	Inactivated virus	2	79.34%[17]	Unknown	Unknown	Unknown (but reports of weekend effect)[18]	Unknown	TBC
Sinovac (CoronaVac)	Inactivated virus	2	50.4%[19]	Unknown	Unknown	Unknown	Unknown	TBC
Bharat Biotech (Covaxin)	Inactivated virus	2	Unknown	Unknown	Unknown	Unknown	Unknown	TBC

Table 2; Illustrating different SARS-CoV-2 vaccines efficacy against variants. (*Derived fromthe bmj | BMJ 2021;372: n597 | doi: 10.1136/bmj. n597). Published: 02 March 2021.*

III. DISCUSSION

A few recent studies on the effects of HIV and SARS-CoV-2 indicate that they do have some similarities. Shanghai-based researchers provided evidence that SARS-CoV-2 can infect T lymphocytes, the same cells targeted by HIV. Other researchers have documented that individuals with severe COVID-19 may exhibit lymphopenia, or atypically low number of lymphocytes in the blood (Madhumita*et al.,* 2021). Likewise, HIV infection results in this abnormality, eventually causing the immunosuppression associated with AIDS.

Perhaps the most important lesson is that vaccine development can be tricky. At a very basic level, vaccination replicates a natural process by intentionally exposing the body to something that looks like a pathogen. The vaccine may be an inactivated or weakened form of the pathogen or a protein isolated from it. In response, the body produces antibodies and cytotoxic white blood cells that can effectively combat the real pathogen, should it ever enter the body. The development of a safe and highly effective vaccine against HIV has been a challenge because of the ability of HIV to escape host immune response. HIV thwarts this seemingly simple process in several ways. Firstly, HIV mutates rapidly, constantly changes its appearance and remains a step ahead of any response produced by the body. Secondly, the HIV genome, upon entering a cell, integrates into the host cell's genome, effectively making itself invisible to the host's immune response (Didigu*et al.,* 2014). Thirdly, HIV is not particularly immunogenic, meaning our bodies do not naturally mount an efficient immune response to it (Leopold Kong*et al.,* 2012). Attempts to develop an effective vaccine against SARS-CoV-1 following the 2003 SARS outbreak was not successful (Deborah R. Taylor, 2006). Several candidate vaccines were shown to be relatively effective when tested on animals but the vaccinated animals also exhibited severe immunopathology – the vaccine appeared to have caused the animals' immune systems to become hyperactive and cause greater damage to them (Deborah R. Taylor, 2006).

Let us look at the infection of T lymphocytes, or white blood cells. SARS-CoV-2 has shown evidence that it can infect certain white blood cells in a laboratory setting (Madhumita*et al.,* 2021). SARS-CoV-2 has not demonstrated any ability to replicate in these cells. It appears that these viruses can enter the cells, but the infection is abortive. HIV, in contrast, replicates aggressively in white blood cells, with infected cells spewing out thousands of new viral particles (Lane, 2010). It has been observed that HIV targets the specific CD4+ immune cells, including T cells, macrophages, and dendritic cells, resulting in a significant reduction in the number of these immune cells in HIV-infected patients (Lane, 2010). These CD4+ T cells (known as helper cells) are the backbone of the immune system where they activate B cells, macrophage, and cytotoxic T cells to secrete antibodies, destroy ingested microbes and kill the infected cells, respectively (Laidlaw, 2016). The HIV membrane contains a transmembrane glycoprotein called glycoprotein-41 (GP41) and surface glycoprotein, namely glycoprotein-120 (GP120), which binds to CD4 receptors on the surface of CD4+ cells (Pancera*et al.,* 2014). There are two other chemokine co-receptors known as C—C chemokine receptor 5 (CCR5) and C—C chemokine receptor 4 (CXCR4), which facilitate HIV binding and infusion into CD4+ cells (Didigu*et al.,* 2014). It has been observed that virus sabotages the CD4+

immune T cells for replication, which leads to increased virus load in the blood and a significant decrease in CD4+ T cells (Goodsell, 2015). Interestingly, some researchers found another mechanism of HIV destruction of CD4+ T cells (Bolton *et al.*, 2002). They observed that depletion of CD4+ T cells by apoptosis pathway because of direct HIV infection was only 5–10% of the total CD4+ T cell pool. It has been found that HIV enzyme (integrase) plays a crucial role in the activation of DNA-PK sensor of host cell, which activates the apoptotic cascade inside the cell. However, another HIV enzyme (protease) activates the caspase-8 that further triggers the apoptosis of infected cells (Yue *et al.*, 2005). The SARS-COV-2 viral envelope is coated by spike (S) glycoprotein, envelope (E), and membrane (M) proteins (Dhama*et al.*, 2020). Host cell binding and entry are mediated by the S protein. The first step in infection is virus binding to a host cell through its target receptor. The S1 sub-unit of the S protein contains the receptor binding domain that binds to the peptidase domain of angiotensin-converting enzyme 2 (ACE 2) (Andersen *et al.*, 2020). In SARS-CoV-2 the S2 sub-unit is highly preserved.

Unlike HIV, the exact mechanism of how COVID-19 induces immune defects is still unknown; however, it could be similar to the previous coronaviruses, including the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV). These viruses induce low level of lymphocytes abnormality in blood, or it is known as lymphopenia related to HIV infection. In addition, T cell lymphopenia has been reported in several SARS-COVID patients, where the total number of CD4+ and CD8+ T cells drastically decreased within two weeks of infection (Cui *et al.*, 2003). The investigation by (Jiang *et al.*, 2019) proves the activation of pyroptosis during MERS-CoV infection. Like HIV infection, MERS-CoV activates caspase-1 in the spleen with high circulating amount of TNF-α, IL-1β, IFN-γ and IL-6, and upward stimulation of macrophages (Jiang *et al.*, 2019). Taken together, the pro-inflammatory molecules released from the immune cells during the onset of COVID-19 infection create an acute inflammatory environment similar to that recorded in HIV exposure, which consecutively activates the pyroptotic cascade of immune cells. Notably, the immune deficiency is more severe in case of coronaviruses because it occurs at the early stage of infection (within a few days), while it takes a longer time for HIV (after ten years).

Currently, no drugs are approved for treatment of SARS-CoV-2 infection, but some of the HIV protease inhibitors used to treat HIV infection seem to inhibit infection by SARS-CoV-2. The genome of SARS-CoV-2 encodes for two viral cysteine proteases; nsp3 (papain-like protease) and nsp5 (main protease) (Chan *et al.*, 2020). The main protease (M^{pro}) of SARS-CoV-2; also named chymotrypsin-like protease (3CLpr), plays a crucial role in the viral life cycle, cleaving the initial polyproteins translated from the viral RNA at least 11 of its 14 cleavage sites. M^{pro} of SARS-CoV-2 shares 96% sequence identity to that of SARS-CoV. One potential target for the HIV PIs is the M^{pro}. In silico screening identified nelfinavir as its potential inhibitor (Mittal *et al.*, 2020), while lopinavir and ritonavir were found to be potential inhibitors of the viral enzyme by molecular dynamics simulation (Nutho*et al.*, 2020). It is important to note that the HIV protease is a C2-symmetric homodimeric aspartyl protease, composed of two identical subunits that are 99 amino acids each. The active site is located at the interface between the two monomers, and contains the catalytic Asp-Thr-Gly residues (Wlodawer*et al.*, 2020). M^{pro} on the other hand, is a cysteine protease that can also potentially be targeted by peptide mimetics. Given the structural difference between the two proteases, the efficacy of HIV protease inhibitors against SARS-CoV and SARS-CoV-2 is questionable. Studies have reported that a combination of lopinavir/ritonavir and ribavirin was effective against SARS-associated coronavirus, with concentrations of 4 µg/ml and 50 µg/ml, respectively (Chu *et al.*, 2004).

The new class of HIV anti-viral drugs include entry inhibitors, coreceptor antagonists and fusion inhibitor and RNA polymerase inhibitors. Research on the same HIV antiviral drugs can help in determining drugs for the management and treatment of COVID-19.

A. Entry inhibitors

Specifically targeting the viral entry process with inhibitory molecules is considered one of the main preventative therapies as it could interfere with the viral infection at an early point in time. Small molecules can either inhibit viral attachment, priming by the host's proteases or viral fusion. Use of small molecule inhibitors is due to the well-known advantages of small molecules, such as their high stability in biological fluids and their relatively high immunological tolerance. In addition, the use of small molecule drugs is one of the main therapeutic strategies that is continuously under development and implementation in various viral models including HIV-1, Hepatitis B Virus and Ebola Viruses (Litterman *et al.*, 2015). Multiple drugs, such as anti-hypertensive, anticoagulant, antibacterial, antifungal, and some natural flavonoids have strong binding affinities with the spike protein. However, only hesperidin, a bioflavonoid, binds with the RBD of the spike protein that recognizes ACE2, which in turn could interfere with the viral receptor recognition step. The other docking-predicted compounds did not bind the RBD of the spike protein and it is not reported which residues of the spike protein are involved in the drug binding interfaces (Litterman et al., 2015). Another study by Wahedi found that resveratrol, a natural polyphenol, is able to bind with low binding energy to the complex formed by SARS-CoV-2 RBD−ACE2 (Wahedi*et al.*, 2020). Using small molecules to block the interaction of SARS-CoV-2 spike RBD with ACE2 has not yet been experimentally tested. However, since SARS-CoV-2 and SARS-CoV spikes share a high structural similarity, the small molecules that were identified to block the RBD of the SARS-CoV spike can be validated for SARS-CoV-2. Emodin which is an anthraquinone derived from a Chinese medicinal herb, blocked the interaction of spike RBD with ACE2 in a dose-dependent manner (Ho *et al.*, 2007). In addition, oxazole-carboxamide derivative, SSAA09E2, was shown to bind to SARS-CoV RBD and interfere with its recognition of ACE2 (Severson *et al.*, 2013).

B. Fusion inhibitors

Fusion inhibitors targeting the S2 subunit may be effective therapeutic agents to treat COVID-19 infections. The spike glycoprotein has attracted considerable attention owing to its critical role in SARS-CoV-2 cell entry mechanism. Disruption of its interactions with the ACE2 receptor is being pursued as a potential intervention strategy targeting the cell entry of the virus. Neutralizing antibodies have been identified and studied in detail. A serine endoprotease, furin, cleaves off S1–S2 and, thus, could be a suitable anti-COVID-19 agent (Millet *et al.,* 2014). A red-alga-derived lectin, griffithsin, binds to SARS-COV spike glycoprotein and HIV glycoprotein 120 (O'Keefe*et al.*, 2010). As a result, griffithsin has been tested for HIV prevention in Phase I studies as a gel or an enema and produced promising effect. However, the delivery systems and potency of S inhibitors in general should be re-evaluated for the prevention or treatment of COVID-19. In addition, nafamostat which is under clinical investigation for COVID-19 treatment inhibits spike-mediated membrane fusion of the virus. Moreover, Yang et al revealed that, in a mouse model, a DNA vaccine encoding the full-length S protein SARS-COV urbani strain could induce both the responses of protective immunity and production of neutralizing antibody by the T cells (Barton *et al.,* 2014). Neutralizing monoclonal antibodies (MAbs) are potential candidates for use against emerging viruses and for prophylactic and therapeutic treatment against the COVID-19 virus (Tian *et al.*, 2020). Neutralizing antibodies have already been found in patients of SARS-CoV and MERS-CoV (Jiang *et al.*, 2014). Thus, screening for neutralizing antibodies that target SARS-CoV-2 S glycoprotein has become a priority. Since COVID-19 was declared a pandemic, epitope characterization on the viral RBDs has been particularly important for the development of peptide drugs and fusion inhibitors. The S protein of SARS-CoV-2 shares 76% of its sequence identity with that of SARS-CoV, leading to initial predictions of epitopes. A set of 206 antibodies was isolated from single B-cells of eight SARS-CoV-2 patients and led to the identification of antibodies that could prevent ACE2 binding to the RBD (Ju 2020). Importantly, the antibodies showed that they were able to bind to the trimeric form of SARS-CoV-2 glycoproteins. The presence of antibodies with neutralizing activities without the need to bind to the RBD could suggest other important mechanisms of SARS-CoV-2 neutralization in addition to the prevention of the virus interactions with the ACE2 receptor.

C. RNA-Dependent RNA Polymerase (RdRp) inactivation.

RdRp also known as Nsp12 is a conserved protein in COVID-19 which is an essential enzyme for RNA transcription and replication of this virus. The RdRp domain of polymerase is located at the C-terminus, and has a conserved Ser-Asp-Asp motif (Subissi*et al.,* 2014). Enzymatic activity and binding of Nsp12 to RNA is increased by the Nsp7–Nsp8 complex (Kirchdoerfer*et al.,* 2019). On the other hand, inhibition of RdRp is one of the antiviral drug development strategies, and clinical drugs as well as new compounds are tested for their effect on it. Drugs like favipiravir, ribavirin, penciclovir, remdesivir, galidesivir, itraconazole, novobiocin, chenodeoxycholic acid, cortisone, idarubicin, silybin, pancuronium bromide, dabigatran etexilate 6′-fluorinated-aristeromycin analogues, acyclovir, and fleximer analogues exhibited RdRp inhibition (Wang *et al.*, 2019). In principle, selective inhibition of RdRp by these agents could not cause significant side effects and toxicity on host cells (Chu *et al.,* 2006). In addition, natural compounds and their derivatives with anti-inflammatory, anti-tumor, and antivirus effects such as gnidicin and gniditrin from *Gnidialamprantha*, and betulonal from *Cassinexylocarpa* showed high binding affinity to RdRp with promising anti-COVID-19 activity, though further investigations are needed (Wu C *et al.,* 2020).

D. Viral spike protein cleavage.

The enzyme transmembrane protease, serine 2 (TMPRSS2), triggers the infection of SARS-COV and MERS-COV by cutting the viral spike protein (Imai et al., 2006). Inhibiting the enzymatic activity of TMPRSS2 can prevent some coronaviruses from entering into host cells. To this effect, pivampicillin, hetacillin, cefoperazone, clindamycin, kouitchenside I, phyllaemblicin G7, and neoandrographolide are predicted to be potential inhibitors of TMPRSS2 (Glowacka*et al.*, 2011).

IV. CONCLUSION AND RECCOMENDATION.

Conclusion; HIV and Sars-Cov-2 share many similarities. HIV has formed a good basis for understanding and researching on COVID-19. HIV has frustrated all efforts to develop an effective vaccine because of continuous mutations. Researchers studied and developed different drugs for HIV management. COVID-19 has mutated giving different variants making it difficult for the vaccines to work effectively. Lessons learnt from HIV should be used to provide a good basis for developing treatment pathways that may reduce COVID-19 mortality.

Recommendations; In the near future, therapeutic antibodies, cytokines, and nucleic acid-based therapies targeting viral structural glycoproteins, papain-like protease, RNA-dependent RNA polymerase (RdRp), 3-chymotrypsin-like protease, helicases, IL-1, IL-6, and JAK/STAT signaling pathways should be developed to treat COVID-19. Despite the current development and recently reported drug repositioning studies, there is no such potent and selective approved drug for COVID-19 treatment. Therefore, more investigations need to be done to get rid of the catastrophic impacts of COVID-19. Indeed, ongoing in silico and preclinical investigations on different compounds are being carried out by research companies but, still rapid clinical trials on these compounds and further investigations of novel compounds are needed unequivocally.

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