Fighting the SARS CoV-2 (COVID-19) pandemic with soap

Narendra Kumar Chaudhary[1], Nabina Chaudhary[2], Manish Dahal[3], Biswash Guragain[1], Summi Rai[1], Rahul Chaudhary[2], KM Sachin[4], Reena Lamichhane-Khadka[5], & Ajaya Bhattarai[1]

[1]Department of Chemistry
Mahendra Morang Adarsh Multiple Campus, (Tribhuvan University) Biratnagar, Nepal
[2]Dhaka Central International Medical College, Dhaka University, Bangladesh
[3]Department of Microbiology,
Birat Multiple College, (Tribhuvan University) Biratnagar, Nepal
[4]School of Chemical Sciences, Central University of Gujrat, Gandhinagar, India
[5]Department of Biology, Saint Mary's College, Notre Dame, Indiana, USA

Corresponding email: bkajaya@yahoo.com, chem_narendra@yahoo.com

Abstract:

Today, the entire globe is struggling to deal with the greatest pandemic of the century, COVID-19. With no clinically approved treatments available, we are left with no options other than following the preventive measures issued by the World Health Organization (WHO). Among many others, hand washing with soap and water has been emphasized the most because it is cost-effective and easily accessible to the general public. Various studies have reported that soaps offer unique chemical properties that can disinfect the virus as a whole. However, there is still ambiguity in the general public about whether soaps can really shield us from this highly contagious disease. In an attempt to help eliminate the ambiguity, we analyzed the mechanisms underlying the efficacy of soap and its prospect for preventing the spread of COVID-19. In this paper, we provide an overview of the history and characteristics of SARS-CoV-2 (COVID-19), the detailed mechanisms of the deactivation of viruses by soaps, and the potential effectiveness of soap in eliminating coronaviruses including SARS-CoV-2.

Keywords: *COVID-19, SARS-CoV-2, Soap, Hand washing, WHO*

Background:

While the entire world was bidding farewell to 2019 and welcoming the new year 2020, health officials in Wuhan, the capital city of Hubei Province in China, were dealing with unusual cases of severe pneumonia exceeding in number instantaneously; the cases were later known to be caused by a novel coronavirus [1]. The virus continued to spread at an unprecedented rate, crossing all geographical boundaries, and it has continued to spread infecting almost all nations around the world. In approximately three months, it spread over 210 across the globe. Considering the extent of the threat to global public health, the World Health Organization (WHO) officially declared it a pandemic on 11th March 2020 [2, 3].

The novel coronavirus disease "COVID-19" is the ongoing pandemic that the world is confronted with. However, coronaviruses (CoVs) are not new pathogens; they were discovered in the early the 1930s as the causative agent of a severe respiratory infection in domesticated chickens, and are now known as avian infectious bronchitis virus (IBV). The first human coronavirus (HCoV) was discovered in the 1960s, but it remained relatively obscured for years [4, 5], probably because no severe human disease (only mild common cold) was caused by it. In 2003, a new variant of the coronavirus (named SARS-CoV) emerged in Southern China and caused epidemics of severe acute respiratory syndrome (SARS) in multiple countries. Consequently, in 2012, another new variant, the Middle Eastern respiratory syndrome coronavirus (MERS-CoV) appeared in Saudi Arabia and spread across continents [6]. The emergence of SARS-CoV and MERS-CoV and the impact that these viruses posed on human health led the coronaviruses to be recognized as viruses of significant threat to human health [7].

SARS-CoV-2 is a highly contagious virus. As of April 2020, no clinically approved vaccine or antiviral agents against coronaviruses have been discovered [8]. Based on earlier research works and practices, the WHO has issued frequent washing of hands with soap and water as a precautionary measure to reduce the possible spread of the virus. Furthermore, the use of masks, disinfectants, and alcohol-based sanitizers is highly recommended [9, 10], and strict maintenance of social distancing and enhanced personal hygiene have been suggested [11, 12]. Previous research on coronavirus outbreaks has focused mainly on identifying the epidemiology and clinical characteristics of infected patients, the genomic characterization of the virus, and challenges for global health governance. However, there are no studies on the effectiveness of handwashing with soap-water against the transmission of coronavirus. In this article, we provide a review the potential action of soap against coronaviruses.

Taxonomy, structure, and morphology of SARS-CoV-2

The name "coronavirus," was coined in 1968 [13]. It is derived from the Latin word corona (meaning crown) for its crown-like morphology when observed under an electron microscope. The coronavirus (CoV) belongs to *the Coronaviridae* family in the order *Nidovirales*, further sub-classified into four genera: Alpha-CoV, Beta-CoV, Gamma-CoV, and Delta-CoV [12]. Among these, Alpha-CoV and Beta-CoV consist of human pathogenic coronaviruses (HCoV) [1]. The ongoing novel coronavirus outbreak is caused by a highly contagious subtype of Beta-CoV. In January 2020, the World Health Organization (WHO) temporarily named it 2019 novel coronavirus [14]. Considering the high (almost 86%) genomic similarity of this virus with the SARS-CoV [15], the International Committee on Taxonomy of Viruses (ICTV) named the novel coronavirus SARS-CoV-2 and the disease caused by this virus as the COVID-19, on 11th February 2020 [3].

Coronaviruses are round enveloped viruses, approximately 65-125nm in diameter. They are RNA viruses; each virus contains a single positive-strand RNA (+ssRNA) that ranges in size from 26-30 kilobases, the largest RNA genome known to date [1]. The genome is complexed with the nucleocapsid (N) protein to form a helical capsid enveloped within the lipid (bilayer) membrane [16]. Embedded into the membrane are at least three viral proteins: the spike (S) glycoprotein that forms the peplomers on the virion surface, giving the virus its crown-like morphology; the membrane (M) protein, the most abundant structural protein, and the envelope (E) protein, the small hydrophobic protein. Some coronaviruses also have an additional membrane protein called hemagglutinin esterase (HE) [17]. The S glycoprotein mediates attachment of the virus to the host cell surface receptors with subsequent fusion between the virion and host cell membranes, facilitating its entry into the host cell. The M protein and the E protein on the viral surface together define the shape of the viral envelope [7] (*figure 1*).

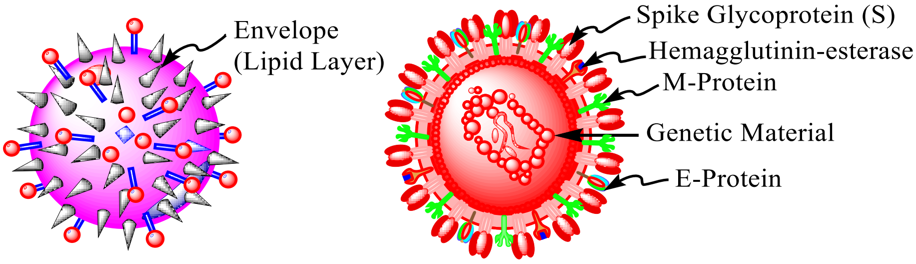

Figure 1. A) 3D structure of SARS-CoV-2 B) Internal structure of the virus

The lipid bilayer enveloped around the virus plays a major role in both infecting the host cell and in inactivating the virus as a whole. It is simply an outer protective layer on the virus made up of fat molecules (phospholipids) that protect the virus when it is outside the host cell. The fat molecules making up the bilayer are amphiphilic with a hydrophilic (phosphate) head covalently bonded to a hydrophobic (lipid) tail. These fatty molecules arrange themselves into a double layer piled on top of each other into a sheet with tails pointing inwards and heads pointing outwards, covering the genome of the virus. The lipid layer also enables the virus to attach to the host cell surfaces, thereby initiating the infection [18].

Transmission and Replication:

Like every other respiratory virus, SARS-CoV-2 is transmitted human to humans via exposure to contaminated respiratory droplets produced by the infected individual when sneezing, coughing, and even respiring [19]. Inanimate objects and surfaces that come in contact with such respiratory droplets can become potentially infectious fomites and easily transfer the virus even after hours of contamination [20]. The deposition of infected droplets or aerosols on the respiratory mucosal epithelium probably initiates viral infection. The most crucial step in viral infection is fusion between the viral and host cell membranes: the virus binds itself with the cell surface receptors ACE-2 (Angiotensin Converting Enzyme-2) and TMPRSS-2 (transmembrane protease serine 2) via its spike proteins (S) and the bound virus then enters into the host cell via endocytosis. Within the host cell, the virus uncoats and releases its +ssRNA. The +ssRNA binds to the cytosolic ribosome or the ribosome on the rough endoplasmic reticulum. Once these +ssRNAs move through the cytosolic ribosome, they are translated into proteins called polyproteins, which are utilized for making spike protein (S), membrane protein (M), envelope protein (E), and nucleocapsid protein (N). Polyproteins also synthesize an enzyme called RNA-dependent RNA polymerase, which makes more copies of +ssRNA, resulting in the formation of a large number of polyproteins and structural proteins. The +ssRNA molecules combine with the S, M, E, and N proteins and are transported into the Golgi apparatus where they are packaged into vesicles and eventually re-assembled into new virus particles surrounded by the lipid bilayer. Finally, the lipid bilayer fuses with the host's cell membrane and the viruses exit the host cell via exocytosis [21].

Clinical manifestations:

COVID-19 manifests with a wide range of clinical symptoms, ranging from mild common cold to severe pneumonia [22]. In general, it is characterized by common symptoms such as high fever, dry cough, tiredness, and other symptoms including aches, nasal congestion, running nose, sore throat, and diarrhea [12]. Some individuals may also experience trouble breathing, persistent pain or pressure in the chest, new confusion or inability to arouse, bluish lips, or face [23].

Soap as an effective agent against SARS-CoV-2:

Chemistry and cleansing action of soap

Soaps are the oldest cleansing agents known to humans. The soaps used for common household purposes are called toilet soaps. Soaps contain a mixture of surfactants, emulsifying agents, copolymers, coloring agents, perfumes, etc. [24]. Chemically, soaps are sodium or potassium salts of saturated or unsaturated long-chain fatty acids that function as surfactant (surface-active) molecules; the long hydrocarbon chain forms a non-polar hydrophobic tail and the ionic carboxylate group forms a polar hydrophilic head [25] (*figure 2*). Thus, surfactant molecules are water-soluble amphiphiles; in an aqueous environment, the non-polar hydrophobic tail interacts actively with the hydrophobic ends of oil, grease, dirt, and even virus particles. Therefore, the cleansing action of soap is attributed mainly to the surfactant molecules present in the soap. Surfactants have dynamic surface-active properties that enable them to lower the surface tension of water [26]. The surfactant monomers are adsorbed at the interface, and above a specific threshold concentration called the critical micelle concentration (CMC), the excess surfactant monomers self-associate to form micellar aggregates [27, 28] (*figure 3*). The micellar aggregates act as emulsifiers that solubilize molecules such as fat and grease that are otherwise insoluble in aqueous solutions. Micellization is the fundamental characteristic of all surfactants and contributes to their cleansing action against microbial species, including viruses.

All soaps available in the market consist of the basic chemistry described above, and hence have the potential to disrupt the virus. The overall cleansing activity of soaps can be attributed to the following properties of soaps [29]: 1) Soaps contain ingredients that can moisten the surface to be cleaned, 2) Soap monomers adsorb on the dirt and virion particles, thereby charging and stabilizing them; and 3) most soaps are basic in nature [30, 31]. The basic soap solution (9-10 pH) supports emulsifying and peptizing actions. Furthermore, the alkalinity of the soaps (pH approximately 9-10) promotes the dispersal of the microbial flora from the skin [32], 4) Soap solutions have lower surface tension than most of the aqueous solutions; this allows for the thinning of films, thus enabling the emulsifying action.

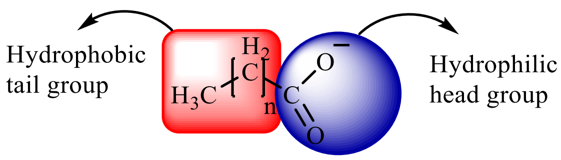

Figure 2. Molecular structure of soap

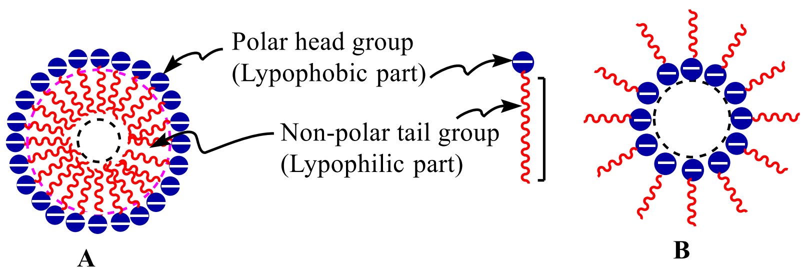

Figure 3. Structure of (**A**) Normal phase micelle (**B**) Reverse phase micelle

The application of surfactants in the deactivation of viruses is not a new topic. Several targeted studies have reported the deactivation of different viruses by the use of different types of surfactants and products [33–35]. Here, we present the findings of previous studies on the effectiveness of hand washing using different types of surfactant-based hand hygiene products in reducing different types of viruses in tabular form (*Table 1*).

Table 1. Studies on the effectiveness of hand washing using different types of surfactant-based hand hygiene products in reducing different types of viruses

S. N.	Virus	Cleanser type/ Hand hygiene product	Inactivation time & Effective concentration	Reduction observed	Reference
1	HIV-1 strain: HTLV-III_{RF}	Derma Cidol (containing 0.5% parachlorometaxylenol in a sodium C_{14-16} olefin sulfonate formula	30 seconds: 1:5 & 1:10 60 seconds: 1:5, 1:10, 1:20& 1:30	More than 99.99% of virus was inactivated	[36]
2	Norwalk virus	Liquid soap (containing 0.5% triclosan) (Fisher Scientific International)	-	0.67 ± 0.47 log_{10}	[37]
3	HIV-1 Strain: SF33	Ivory: commercial bar soap (Johnson & Johnson)	2 minutes & 6 minutes: 1:1000	Infectivity reduced by >1000 fold	[38]
4	AIV H_5N_1	Lifebuoy (Uniliver Pakistan Ltd.)	5 minutes: 0.1, 0.2 & 0.3 %	Complete inactivation	[39]
5	Human rotavirus	Ivory: Liquid soap (Procter & Gamble)	1:10	86.9 ± 2.42 %	[40]
6	MS2-Bacteriophage	Foaming hand soap (GOJO Industries, Akron, OH) Liquid soap (Epare, Staten Island, New York)	- -	2.10 ± 0.57 log_{10}PFU 2.23 ± 0.51 log_{10} PFU	[41]
7	Respiratory syncytial virus	Bac-Down (Decon Laboratories) Soft N Sure Cida-Stat (Ecolab Professional Products) Alo Guard (Health Link) Hibiclens (Zeneca Pharmaceuticals) Kindest Care (Steris)	5 minutes: 0.045 % 5 minutes: 0.280 % 5 minutes: 0.333 % 5 minutes: 0.360 % 5 minutes: 0.390 % 5 minutes: 0.390 %	90 % Inactivation	[42]

Mechanisms of cleansing (inactivation) of SARS-CoV by soap

The mechanism of cleansing action of soap is based on a general principle of chemistry like dissolves like. Three mechanisms have been proposed as the basis for the cleansing or deactivation of the SARS-CoV using soap.

1. Membrane rupture mechanism
2. Simple elution mechanism
3. Viral entrapment mechanism

Membrane rupture mechanism

As described previously, the lipid membrane in SARS-CoV and most other enveloped viruses is a bilayer composed of water-insoluble amphiphiles, particularly phospholipids and membrane proteins [43]. Upon the addition of a surfactant solution, the phospholipid in the bilayer and the surfactant monomers interact via hydrophobic–hydrophobic interactions between the lipid tails and the surfactant tails, and vice versa. At low surfactant concentrations (i.e., below CMC), part of the added surfactants are inserted into the bilayer, competing with the phospholipids, thus disturbing the orderly arranged structure of the membrane while the rest of the surfactant remains as monomers in the aqueous solution [44]. When the surfactant concentration reaches the CMC, the lipid-surfactant mixed bilayers become saturated and no longer accommodate additional surfactants. This induces solubilization of the phospholipids via phase transformation of the mixed bilayer into mixed (lipid-surfactant) micelles. At this stage, the surfactant-saturated bilayer remains in thermodynamic equilibrium with the mixed micelles [45]. Above CMC, when the surfactant-to-lipid concentration ratio increases, micellization is completed, i.e., the lipid bilayer is completely solubilized by the surfactants and only the micellar aggregates remain in the solution [46]. Thus, the complete solubilization of the protective lipid bilayer leads to the disintegration of the virus into fragments, making it no longer infective. Further, the fragmented viral components are also completely solubilized by the surfactant molecules in the form of micelles, which can then be easily washed away by water (*figure 4*).

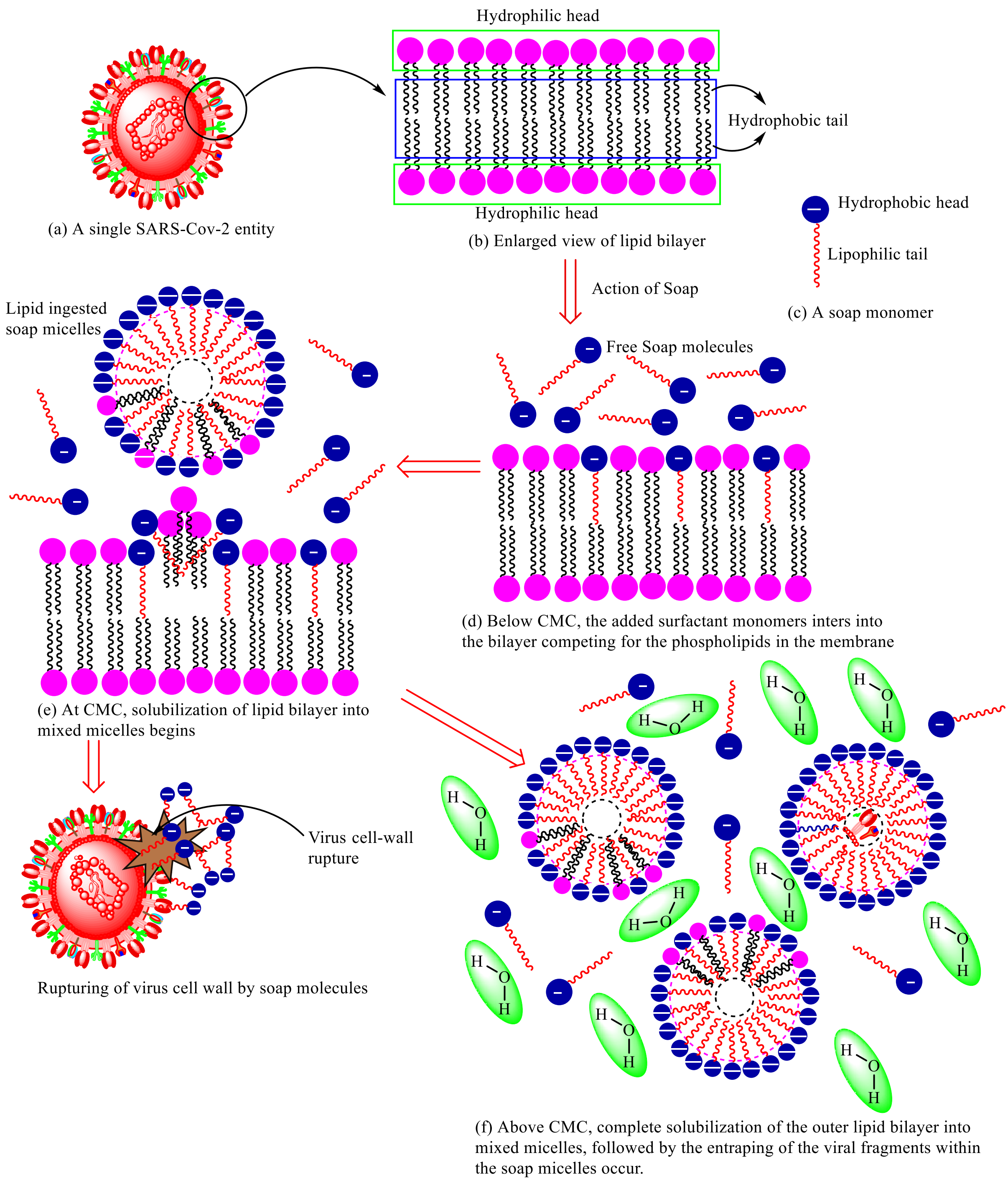

Figure 4. Diagrammatic representation of membrane rupture mechanism

Simple elution mechanism

In general, a minimum of 20 seconds of hand washing with soap and water is shown to be effective in the removal of oily particles [47, 48]. However, complete inactivation of viruses within such a short time of interaction cannot be asserted by the membrane rupture mechanism.

Previous studies have reported the inactivation of viruses by soap solutions [39, 42]. However, the interaction time in those studies (5 min) does not mimic common day-to-day conditions. Therefore, there must be a mechanism of virus or dirt removal without necessarily inactivating them. We have proposed a possible mechanism as the ‘simple elution’ mechanism.

The outer lipid layer of SARS-CoV and other enveloped viruses enables their adsorption on the host cell surface [49]. Soap solutions have a very low surface tension because which they can form very thin films [32]. As a result, they can enter into tiny spaces and spread fluently around the dirt particles, including viruses. Also, soap has the potential to moisten the surface and get adsorbed on any foreign particles present, thereby charging and stabilizing them. The amphiphilic nature of soap, in particular the attractive interaction between the hydrophobic ends of soap with hydrophobic lipid membranes, supports the adsorption of soap monomers. The charged viral particles cannot aggregate. Further, their adsorptive property is lost and they are dragged along with water molecules while washing (*figure 5*). Within 20 seconds of hand washing recommended by the WHO, the viral component cannot be completely inactivated, but can be successfully removed from the hand surface.Therefore, there is a substantial rationale for the existence of a 'simple elution' mechanism, especially attributed to general hand washing.

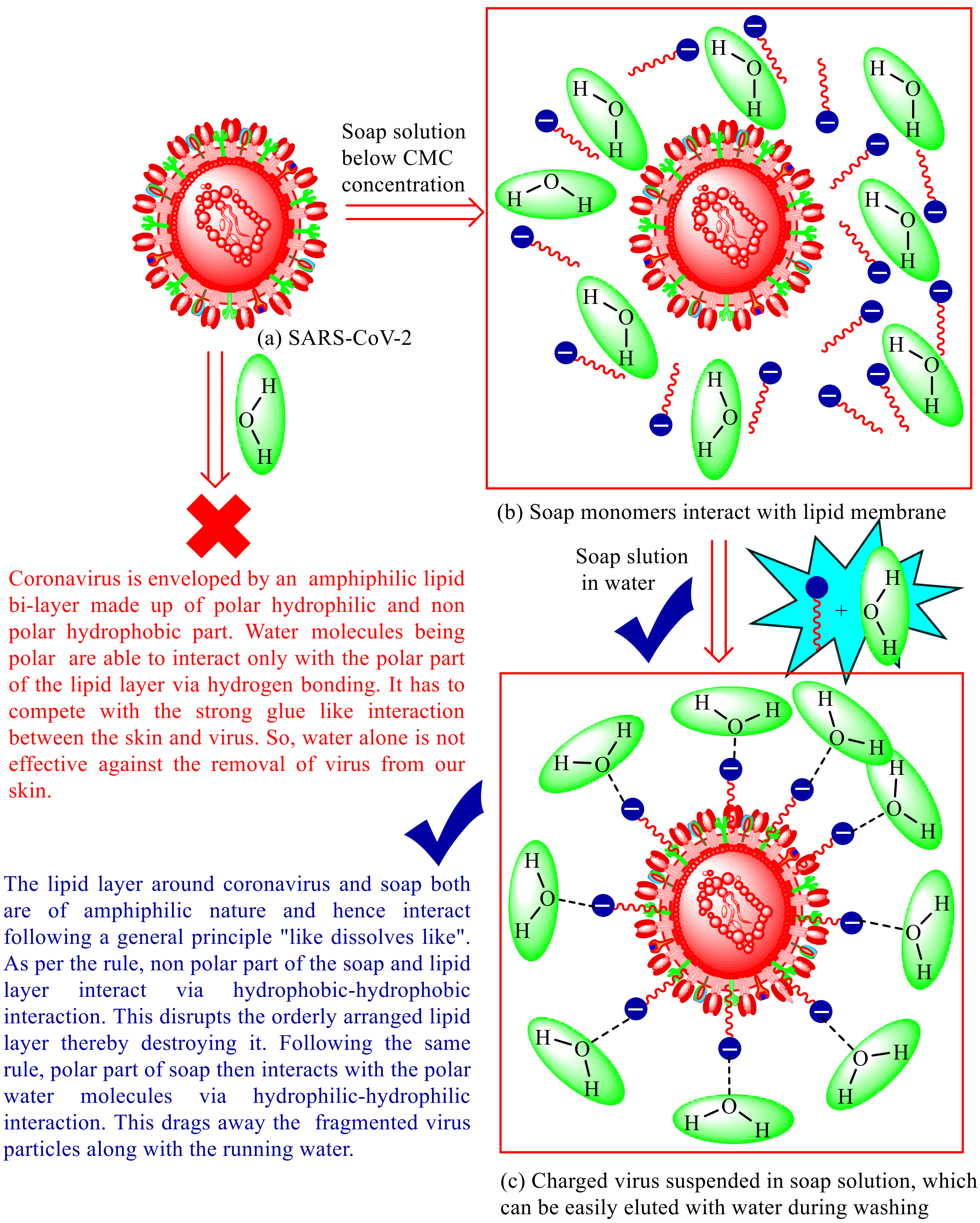

Figure 5. Diagrammatic representation of the simple elution mechanism

In a study examining the elution of bacteriophages Phi X174 and PRD1 bound to nitrocelular and charged modified polyethersulfonate membranes, excellent elution of both bacteriophages was obtained using 5mM SDS (Sodium dodecyl sulfate) from the BioTrace HP membrane.

However, minimum inactivation of PDRI was obtained by 10mM SDS within four min of exposure, while phiX174 remained unaffected even with 50mM of SDS [50]. These findings support the elution mechanism and that soaps are able to remove viruses from the adsorbed surfaces even when they are not completely able to inactivate the viruses.

Viral entrapment mechanism:

As described earlier, SARS-CoV-2 and other enveloped viruses resemble fatty particles of nano-scale diameter. A third probable mechanism involves complete entrapment of the viral particle into the soap micelle. When the surfactant concentration exceeds the CMC value, micellization begins. The soap micelle so formed entraps the viral cell into its nucleus via hydrophobic-hydrophobic interactions. The water molecules then bind with the hydrophilic heads of the micelles, thereby dragging away the entrapped viral cell along with washing (*figure 6*). However, since the soap micelles are also of nano-scale diameter, they may not be able to engulf the viral cell as a whole. Further, there is no prior evidence to support this mechanism. Further investigation is required to determine the viability of the proposed mechanism.

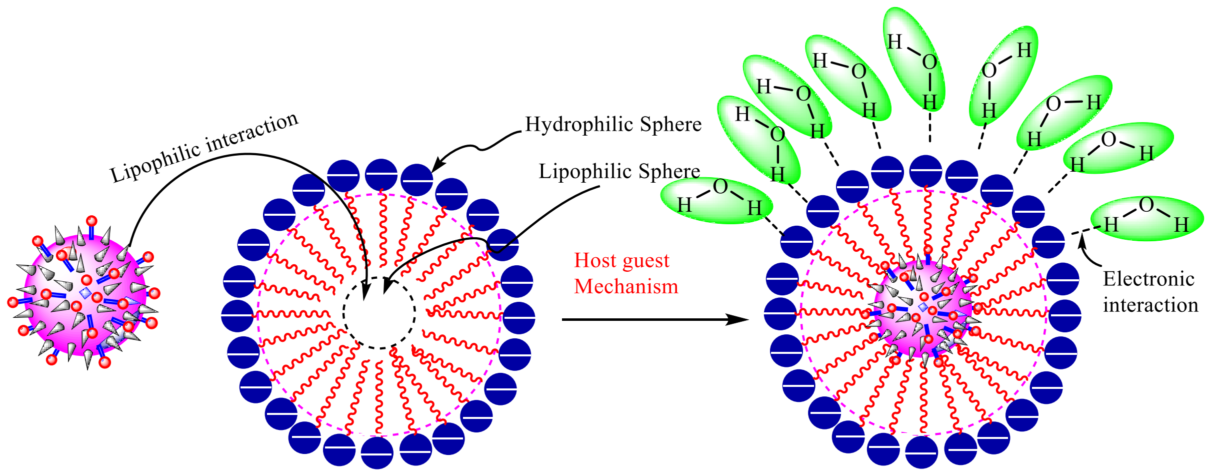

Figure 6. Diagrammatic representation of the viral entrapment mechanism

Regarding the effectiveness of hand washing in the control and prevention of SARS-CoV-2 and other viruses, the duration of washing has been shown to have a significant effect on controlling the disease. However, no distinction between the mechanisms is possible, and often they may operate simultaneously. Together, the surfactant action of soaps combined with the friction caused during hand washing and final rinsing with clean water is a very effective method for the removal of dirt as well as microbes [51]. For the mechanisms to function effectively, proper rubbing between hands for an adequate amount of time is important. Using soap and detergent at 0.1, 0.2, and 0.3% concentrations completely inactivated the H5N1 virus within 5 min [39]. In a recent study, hand washing was associated with a greater risk of spread of influenza-like illness compared to hand-washings for 15 seconds or longer [52, 53]. Because of the effectiveness of the method, hand washing with soap and water has been tagged as the "gold standard" method for removing dirt and transient flora from hand [51]. Both soap and alcohol-based sanitizers are effective in controlling COVID-19 when applied to hands thoroughly and with scrubbing for at least 20 s [47, 48].

Effect of temperature on SARS-CoV-2:

Amidst the increasing crisis of the pandemic, several sources including the media and the Internet are spreading a lot of information about the possible ways to thwart the spread of the virus. Besides using soaps and hand sanitizers, another measure that is being discussed is the inactivation of the coronavirus at higher temperatures. Using hot water for cleansing purposes might be of interest to the public. At high temperatures, the thermodynamic activity as well as the penetrating ability of the surfactant molecule increases [54]. Nevertheless, an increase in the temperature of detergents such as Sodium-lauryl-sulphate (SLS) increases transcutaneous penetration, which can damage the deeper layers of the stratum corneum, the rough outer layer of the skin [55, 56]. Further, an increase in temperature also discourages micellization. Therefore, while the use of warm water is usually preferred and is thought to have more cleansing action, the disrupting effects on our skin should be given carefully considered, especially in frequent hand washing conditions. The particular effects that should be considered are outlined below.

- The activity of the virus decreases at higher temperatures.
- The activity and penetration of surfactants increased with an increase in temperature. At higher temperatures, the activation energy increases. As a result, the cleansing activity of the surfactants (soaps and detergents) will increase.
- The absorption of surfactants through the skin depends on the activation energy [57]. At higher temperatures, the activation energy increases, which causes increased dermal penetration of surfactants and chemicals. As a result, higher amounts of the surfactant will be absorbed by the skin, negatively impacting the health of the user.

For the reasons described above, practices using high temperatures to control the virus are more appropriate for disinfecting clothes and other fomites.

Conclusion:

The SARS-CoV-2 (COVID-19) pandemic has necessitated the implementation of effective control measures to stop the spread of the disease. Unfortunately, an effective medicine for treating COVID-19 has not yet been developed. As of now, the measures adapted by countries across the word are to maintain social distancing, boost immunity, and maintain hand hygiene. It has recommended that Frequent handwashing with soap and water is enough to overcome the challenges associated with the disease. Sanitizers and soaps are recommend by the WHO to reduce the spread. We discussed the cleansing action of soap on SARS-CoV-2 and the mechanisms by which soap potentially eliminates the virus. Soaps are amphiphilic substances capable of interacting with hydrophilic as well as hydrophobic substances. In summary, their effectiveness is attributed to: a) low surface tension of soap solution, b) basic nature, c) amphiphilic orientation and d) capacity to form a micelle. The lipid envelope of SARS-CoV-2 is vulnerable to amphiphilic chemicals like soap. The cleansing mechanisms of surfactants can follow either by i) destroying the lipid membrane of the virus, ii) entrapment of the viral particle within, the soap micelle, or by iii) elution or the viral particles by adsorption of soap monomers on the viral surface, charging and stabilizing them, all of which are then removed by water. Additionally, elimination of the virus using high temperature could also be considered for disinfection of contaminated fomites. Hand washing with soap and water is extensively practiced. Based on the evidence provided by our analysis, we conclude that handwashing with soap and water effectively reduces the risk of viral infections. When practiced following the recommended protocol, it may potentially reduce the spread of SARS-CoV-2 (COVID-19).

Authors' contributions

NKC, BG, and SR wrote the manuscript, KMS, NC, and RC designed the manuscript, MD reviewed the microbiology, RLK and AB critically revised the manuscript.

Conflict of interest statements

Authors declare no competing interests.

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