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

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Abstract:
The greatest pandemic of the century, COVID-19, is an ongoing global public health problem. With a clinically approved treatment available only for those who are acutely ill and are hospitalized, the control of this disease in the general population is still largely dependent on the preventive measures issued by the World Health Organization. Among the general control measures other than immunization with the COVID-19 vaccines, handwashing with soap and water has been emphasized the most because it is cost-effective and easily accessible to the general public. Studies have reported that soaps offer unique chemical properties that can completely destroy enveloped viruses. However, the general public seems to be still uncertain about whether soaps can shield us from a highly contagious disease such as COVID-19. In an attempt to help eliminate the uncertainty, 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 the SARS-CoV-2 virus, the current global COVID-19 situation, the possible 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; Handwashing; WHO

1. Introduction

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 an unprecedented number of unusual cases of severe pneumonia. Later, the cases were known to be caused by a novel coronavirus [1]. The virus continued to spread at an unprecedented rate, crossing all geographical boundaries, and it continued to spread the infection to almost all nations around the world. In about three months, it spread to 210 nations worldwide. 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]. COVID-19 is now recorded as the deadliest infectious disease of the decade in history [4].
As of May 2020, no clinically approved vaccine or antiviral agents against coronaviruses had been discovered [5]. The clinical treatment procedure was under trial. This, together with the observation that the highly contagious severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) could spread at unprecedented rates, caused massive psychological effects on the public, and public health agencies struggled to keep their confidence to mentally strengthen people [6]. In this context, public health actions have been crucial in slowing the spread of COVID-19 [7]. Based on earlier research works and practices, the WHO 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 hand sanitizers (ABHS) is highly recommended [8,9], and strict maintenance of social distancing and enhanced personal hygiene has been suggested [7,10].

Previous research on coronavirus outbreaks has primarily focused on the epidemiology and clinical characteristics of infected patients, the genomic characterization of the virus, and identifying the challenges for global health governance. However, there have been no studies on the effectiveness of handwashing with soap-water against the transmission of coronavirus.

In this article, we provide a detailed review of the history, characteristics and emergence of the SARS-CoV-2 virus, the current global COVID-19 situation and control measures, the possible mechanisms of disinfection by soap, and the potential effectiveness of soap in reducing the spread of coronaviruses including SARS-CoV-2. The referenced literature for this study was systematically reviewed and searched in PubMed, Google Scholar, and various academic and research publication websites. We did not set year limit for this search. A manual search was also performed to collect appropriate literature. This search was conducted based on title, author name, and journal scope. Since the COVID-19 outbreak is continuously evolving, the reported information was conducted based on real-time analysis. The compositional aspects of soap and its chemistry for the deactivation of the virus were collected from different journal sources.

2. History, characteristics, and evolution of SARS-CoV-2

2.1. Taxonomy, structure, and morphology

The name "coronavirus," was coined by Tyrell and co-workers in 1968 [11,12]. 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 [10]. Among these, Alpha-CoV and Beta-CoV consist of human pathogenic coronaviruses (HCoV) [1]. In January 2020, the World Health Organization (WHO) temporarily named it a 2019 novel coronavirus [13]. Considering the high (almost 86%) genomic similarity of this virus with the SARS-CoV [14], 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 [15]. 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) [16]. The S glycoprotein mediates attachment of the virus to the host cell surface receptors with the 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 [17] (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 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 amphipilic 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].

2.2. Transmission and replication

Like every other respiratory virus, SARS-CoV-2 spreads to humans when exposed to contaminated respiratory droplets produced by an infected person when they sneeze, cough, and even respire [19]. Inanimate objects and surfaces exposed to such respiratory droplets can become potentially infectious fomites and can 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 the fusion between the viral and host cell membranes. The virus binds itself through its spike proteins (S) with the cell surface receptors ACE-2 (Angiotensin Converting Enzyme-2) and TMPRSS-2 (transmembrane protease serine 2) and enters 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), an 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 to the Golgi apparatus where they are packed 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].

2.3. Clinical manifestations
COVID-19 manifests with a wide range of clinical symptoms, ranging from the 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 [10]. 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].

2.4. Emergence and spread of SARS-CoV-2

Though the particular coronavirus causing the "COVID-19" pandemic is novel, coronaviruses (CoVs) in general are not new pathogens; they were discovered in the early 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 [24,25], 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 the 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 [26]. 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 [17].

Since the onset of the COVID-19 pandemic in late 2019, it has significantly impacted the health, education, and economic sectors on a global scale. The COVID-19 outbreak hit Europe hard, starting in Italy in February 2020, and later made the continent a global epicenter of the disease by late March and April 2020 [27]. During that time, Italy faced the highest COVID-19 fatality rate in the world. A month later, the country faced another wave of uncontrolled COVID-19 outbreak [28]. From the third week of March 2020, the South American countries faced an unprecedented increase in COVID-19 cases causing enormous pressure on their health systems [29]. As of July 5, 2021, a total of 184,573,518 confirmed cases, 3,993,602 deaths, and 168,922,458 recovered cases worldwide have been recorded.

The United States of America has registered the highest number of confirmed cases (34,275,783 cases) followed by India with 29,274,823 registered cases. Other ten most infected countries include Brazil (17,215,159), France (5,729,967), Turkey (5,313,098) Russia (5,180,454), United Kingdom (4,542,986), Italy (4,239,868), Argentina (4,066,156), Spain (3,729,458), Germany (3,718,617), and Colombia (3,665,137) [30].

Since the emergence of COVID-19, health intelligence has been trying to analyze the SARS-CoV-2 genome to understand the evolution of this virus. This has been challenging, mainly due to the rapidly changing genome of the virus resulting in new variants [31]. Since SARS-CoV-2 is an RNA virus, it has a high rate of genomic mutation. Several mutations have been identified in the spike proteins, among which the most predominant one is the D614G mutation which efficiently reduces S1 shedding and increases viral infectivity [32,33]. A new variant (B.1.1.7) was first identified in September 2020 in the United Kingdom with an exceptionally large number of mutations, unprecedented spreading ability, and rapidly evolving epidemiologic potential. Over 90 countries, including the United States, have registered cases of the B.1.1.7 variant since December 20, 2020. Another variant (B.1.351) was identified at the beginning of October 2020 in South Africa irrespective of the variant observed in the UK.
This new strain shared some mutations with the variant observed in the UK. Recently, Nigeria has also reported the existence of the new variant. However, no evidence leads to cursory disease or an elevated risk of death associated with these new variants [35]. The new variant of SARS-CoV-2 in the UK has created such a harsh situation that the government imposed even stricter restrictions on every sector to control its spread [36]. The P.1 variant stands out as the third major variant of concern. It was identified for the first time in January 2021, when Japan registered four cases of the variant in travelers arriving from Brazil [37]. Recently, the second wave of COVID-19 pandemic which is due to both the old and the new variants of SARS-CoV-2 is hitting the world and we are again under lockdown rules to reduce its spread [38].

The emergence of multiple variants of SARS-CoV-2 has raised concerns in controlling the outbreak of COVID-19 [18, 19]; the recent surge of COVID-19 cases in India, caused by the new SARS-CoV-2 variants B.1.617 and B.1.618, has captured global attention with a record number of new cases reported in a single day (402,110 cases on April 30th, 2021). The hospitals are overcrowded and the health system is unable to cope with the current pandemic situation [40].

3. COVID-19 control measures

In the initial phase of the COVID-19 pandemic, while research for discovery of treatment and vaccine was ongoing, public health leaders recommended non-pharmaceutical interventions such as social distancing, lockdown strategies, and proper sanitization as the means to reduce the transmission of the SARS-CoV-2 virus. However, this strategy alone was insufficient to end COVID-19 pandemic [41]. In March 2020, the U.S. Department of Health and Human Services (HSS) started the “Operation Warp Speed” program to expedite the COVID-19 vaccine [42]. On July 14th and August 12th, 2020, Moderna and Pfizer companies separately published phase I/II clinical trial data on the COVID-19 vaccine. Currently, three vaccines are authorized and recommended in the United States to prevent COVID-19: BNT162b2 vaccine manufactured by Pfizer, Inc., BioNTech; mRNA-1273 vaccine manufactured by Moderna TX, Inc., and JNJ-78436735 vaccine manufactured by Janssen Pharmaceuticals Companies of Johnson & Johnson (CDC, 2021). For therapy, remdesivir (Veklury), has been approved by the FDA for the treatment of COVID-19 in hospitalized patients aged 12 years and older who weigh at least 40 kg (CDC, 2020). Additionally, several novel therapeutics, including monoclonal antibodies, are available under the Emergency Use Authorization for early outpatient treatment, and are being tested to evaluate their effectiveness of these therapeutics in people who are at high risk of disease progression (CDC, 2020).

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

4.1 Chemistry and cleansing action of soap

Soaps are the oldest cleansing agents known to humans. Soaps contain a mixture of surfactants, emulsifying agents, copolymers, coloring agents, perfumes, etc. [43]. 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 [44] (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 [45]. 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 [46,47] (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 the enveloped viruses. Some important soap ingredients and their useful functions in cleansing and enhancing the antimicrobial property of the soap are reported in table 1.
Table 1: Structure of Soap ingredients and their useful functions

| S.N. | Major soap ingredients | Important Function | Ref. |
|------|-----------------------|--------------------|------|
| 1.   | Sodium palmitate      | Soap molecules functioning as surfactants | [48,49] |
| 2.   | Sodium stearate       | Skin conditioner/emollient, texture modifier | [50] |
| 3.   | Sodium laurate        | Skin conditioner/emollient, texture modifier | [51] |
| 4.   | Potassium stearate    | Emulsifier          | [52] |
| 5.   | Sodium oleate         | Reduces the amount of sticky soap scum. | [53] |
| 6.   | Sodium myristate      | Antioxidant         | [54] |
| 7.   | Glycerol              | Skin conditioner/emollient, texture modifier | [50] |
| 8.   | Propylene glycol      | Skin conditioner/emollient, texture modifier | [51] |
| 9.   | Sorbitan oleate       | Emulsifier          | [52] |
| 10.  | Sodium citrate        | Reduces the amount of sticky soap scum. | [53] |
| 11.  | Butylated hydroxytoluene | Antioxidant | [54] |
| 12.  | Sorbitol              | Emollient           | [55] |
8. Water softener.  
   Lock up Ca/Mg minerals in water to form insoluble soap scum.  
   Foam enhancer.  
   \[
   \text{Pentasodium pentetate}
   \]

9. Water softener.  
   Lock up Ca/Mg minerals in water to form insoluble soap scum.  
   Foam enhancer.  
   \[
   \text{Tetrasodium etidronate}
   \]

10. Water softener.  
    Lock up Ca/Mg minerals in water to form insoluble soap scum.  
    Foam enhancer.  
    \[
    \text{Tetrasodium EDTA}
    \]

11. Antioxidant.  
    Prevents soap from rancid.  
    \[
    \text{Pentaerythritol tetrakis}  
    \quad (3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate)
    \]

12. Broad-spectrum antimicrobials.  
    \[
    \text{Triclosan}
    \]

13. Broad-spectrum antimicrobials.  
    \[
    \text{Triclocarban}
    \]

14. White pigment and color modifier.  
    \[
    \text{Titanium dioxide}
    \]
All commercially available soaps consist of the same basic chemistry described above, and hence have the potential to disrupt the enveloped viruses. The overall cleansing activity of soaps can be attributed to the following properties of soaps [61]:

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.
3) Many soaps are alkaline. The basic soap solution (9-10 pH) supports emulsifying and peptizing actions [62,63]. Furthermore, the alkalinity of the soaps (pH approximately 9-10) promotes the dispersal of microbial flora from the skin [64].
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 [65–67]. The findings of previous studies on the effectiveness of handwashing using different types of surfactant-based hand hygiene products in reducing different types of viruses are presented in table 2.
Table 2. Studies on the effectiveness of handwashing 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 | [68] |
| 2     | Norwalk virus | Liquid soap (containing 0.5% triclosan) (Fisher Scientific International) | - | 0.67 ± 0.47 log_{10} | [69] |
| 3     | HIV-1 Strain: SF33 | Ivory: commercial bar soap (Johnson & Johnson) | 2 minutes & 6 minutes: 1:1000 | Infectivity reduced by >1000 fold | [70] |
| 4     | AIV H3N1 | Lifebuoy (Uniliver Pakistan Ltd.) | 5 minutes: 0.1, 0.2 & 0.3% | Complete inactivation | [71] |
| 5     | Human rotavirus | Ivory: Liquid soap (Procter & Gamble) | 1:10 | 86.9 ± 2.42 % | [72] |
| 6     | MS2- Bacteriophage | Foaming hand soap (GOJO Industries, Akron, OH) | - | 2.10 ± 0.57 log_{10} PFU | [73] |
|       |       | Liquid soap (Epare, Staten Island, New York) | - | 2.23 ± 0.51 log_{10} PFU | |
| 7     | Respiratory syncytial virus | Bac-Down (Decon Laboratories) | 5 minutes: 0.045% | 90% Inactivation | [74] |
|       |       | Soft N Sure | 5 minutes: 0.280% | | |
|       |       | Cida-Stat (Ecolab Professional Products) | 5 minutes: 0.333% | | |
|       |       | Alo Guard (Health Link) | 5 minutes: 0.360% | | |
|       |       | Hibiclens (Zeneca Pharmaceuticals) | 5 minutes: 0.390% | | |
|       |       | Kindest Care (Steris) | 5 minutes: 0.390% | | |

4.2 Mechanisms of inactivation of SARS-CoV by soap

The mechanism of cleansing action of soap is based on a general principle of chemistry "like dissolves like". We suggest three possible mechanisms for the deactivation of SARS-CoV by soap.

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 [75]. Upon 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 is 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 [76]. 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 [77,78]. 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 [79]. 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 ruptures mechanism

Simple elution mechanism

In general, a minimum of 20 seconds of handwashing with soap and water is shown to be effective in the removal of oily particles [80,81]. However, the 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 [82]. 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 handwashing 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 handwashing.

**Figure 5.** Diagrammatic representation of the simple elution mechanism
In a study examining the elution of bacteriophages Phi X174 and PRD1 bound to nitrocellulose and charged modified polyether sulfonate membranes, excellent elution of both bacteriophages was achieved using 5mM SDS (Sodium Dodecyl Sulfate) from the BioTrace HP membrane. However, minimum inactivation of PRD1 was obtained by 10mM SDS within four min. of exposure, while phiX174 remained unaffected even with 50mM of SDS [83]. These findings support the elution mechanism and that soaps can 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 handwashing 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 handwashing and final rinsing with clean water is a very effective method for the removal of dirt as well as microbes [84]. 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, handwashing was associated with a greater risk of spread of influenza-like illness compared to hand-washings for 15 seconds or longer [85,86]. Because of the effectiveness of the method, handwashing with soap and water has been tagged as the "gold standard" method for removing dirt and transient flora from the hand [84]. 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].

4.3 Why Soap is better than an alcohol-based sanitizer

The very important message throughout such COVID pandemic has been the need for people to wash their hands regularly and thoroughly. While soap and water are best, hand sanitizer is a good substitute in high populations areas or when suitable hand-washing facilities are not available [87]. As we noticed that people are using hand sanitizer daily, sometimes multiple times a day, so the U.S. Food and Drug Administration (FDA) has decided that the companies making hand sanitizers need to provide proof that those chemicals are safe for that level of exposure, especially for pregnant women and children. Three active ingredients (benzalkonium chloride, ethyl alcohol, and isopropyl alcohol) are still under review. According to a new study, quickly smearing an ethanol-based hand sanitizer onto your hands won’t kill cold and flu bugs. This is because your fingers are still wet with mucus. It is interesting that FDA has treated sanitizers as ‘over-the-counter drugs’ and recommended the use of soap and water over sanitizers. The FDA’s recommendation on sanitizers is very sensitive to impurities or adulterants [88].

If we don’t have access to soap and water, then hand sanitizer containing 60% alcohol is a good temporary substitute for neutralizing the coronavirus. Soap provides dual advantage; it neutralizes the coronavirus and also physically knocks it off our hands; soap disrupts the sticky bond between pathogens and our skin, allowing the pathogens to slide right off. Hand sanitizer doesn’t do all of that. Besides, hand sanitizers may penetrate deeper into the skin layers and affect the skin cells [89]. The use of methanol as an adulterant in hand sanitizers and hand rubs is another concern [90]. Methanol must never be used in hand sanitizers because oral, pulmonary, and/or skin exposures can result in allergic reactions, severe systemic toxicity and even death [91]. Using soap and water is safer and hence recommended.

4.4 Role of polyelectrolytes in soaps

Many soaps, shampoos, and cosmetics incorporate polyelectrolytes [92,93] and polyelectrolyte builder materials that serve to enhance the cleaning capacity of soaps [94]. The polyelectrolytes have several applications, mostly related to modifying the flow and stability properties of aqueous solutions and gels. For instance, they can be used to destabilize a colloidal suspension and to initiate flocculation (precipitation). When mixed with surfactants, they form polyelectrolyte-surfactant complexes (PESC) spontaneously by self-assembly driven by electrostatic and hydrophobic interactions. PESC containing sodium lauryl ether sulfates (SLES) have found wide application in hair care products such as shampoos and soaps [95]. Sodium polyacrylate, an anionic polyelectrolyte retains water molecules and increases the viscosity, hence it is often used in soaps as a thickening agent [96].

Generally, soap compositions include, by weight, 30% to 60% surfactant, 1% to 35% polysaccharide (strong polyelectrolyte), 1% to 10% fatty acid, and 25% to 50% polymer matrix, of the total weight of the soap composition. The soap compositions may further include a fragrance-generating chemical in an amount of 0.1% to 2% by weight of the soap composition.
4.5 Effect of temperature on inactivation of SARS-CoV-2 by soap

Besides using soaps and hand sanitizers, another measure that is being explored as a control measure is the inactivation of coronavirus at high temperatures. Using hot water with soap or detergent has been believed to be more effective for cleaning, mainly because high temperatures increase the thermodynamic activity as well as the penetrating ability of the surfactant molecules [97]. However, an increase in the temperature of detergents such as Sodium-lauryl-sulphate (SLS) increases transcutaneous penetration, which can damage the rough outer layer of the skin [98,99]. Further, an increase in temperature also discourages micellization. Therefore, while the use of hot water is believed to have a greater cleansing action, its disruptive effects on our skin should be carefully considered, especially for applications such as frequent handwashing. The particular effects that should be considered are:

1) The activity of the virus decreases at higher temperatures,
2) The activity and penetration of surfactants increased with an increase in temperature,
3) At higher temperatures, the activation energy increases, as a result, the cleansing activity of the surfactants (soaps and detergents) also increases,
4) The absorption of surfactants through the skin depends on the activation energy [98,100].

At higher temperatures, the activation energy increases. This causes increased dermal penetration of surfactants and chemicals. As a result, high amounts of surfactants will be absorbed by the skin, which will negatively affect the health of the user. For these reasons, utilization of high temperature to control the virus are more suitable for disinfecting clothing and other fomites, than for frequent handwashing.

5. Conclusion:

The SARS-CoV-2 (COVID-19) pandemic necessitated the quick implementation of effective control strategies to stop the spread of the disease. While efforts to discover therapeutics and vaccines were ongoing, countries across the globe adopted measures to reduce transmission of the SARS-CoV-2 virus mainly by social distancing and maintaining hand hygiene via frequent handwashing with soap and water and using alcohol-based hand sanitizers. 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 in 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).

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**Authors’ contributions**

N.K.C. and A.B. conceptualized the purpose of the study. N.K.C., B.G., and S.R. prepared the first draft of the manuscript. K.M.S., N.C., and R.C. designed the manuscript. M.D. reviewed the microbiology, N.K.C., R.L.K., and A.B. critically revised and reviewed the manuscript. All authors have read and agreed to publish this version of the manuscript.

**Conflicts of interest:**

Authors declare no competing interests.

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