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].

51 As of May 2020, no clinically approved vaccine or antiviral agents against coronaviruses had
52 been discovered [5]. The clinical treatment procedure was under trial. This, together with the
53 observation that the highly contagious severe acute respiratory syndrome coronavirus 2
54 (SARS-CoV-2) could spread at unprecedented rates, caused massive psychological effects on
55 the public, and public health agencies struggled to keep their confidence to mentally strengthen
56 people [6]. In this context, public health actions has been crucial in slowing the spread of
57 COVID-19 [7]. Based on earlier research works and practices, the WHO issued frequent
58 washing of hands with soap and water as a precautionary measure to reduce the possible spread
59 of the virus. Furthermore, the use of masks, disinfectants, and alcohol-based hand sanitizers
60 (ABHS) is highly recommended [8,9], and strict maintenance of social distancing and
61 enhanced personal hygiene has been suggested [7,10].

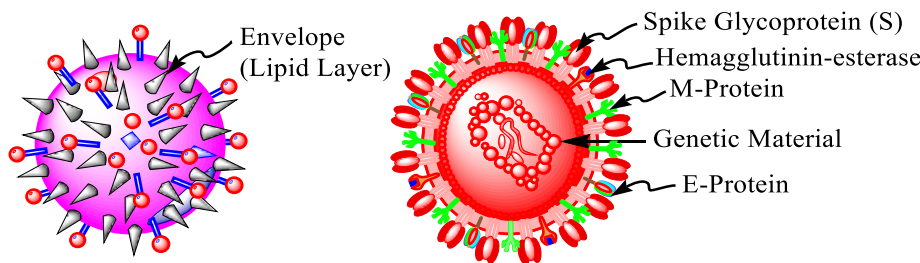
63 Previous research on coronavirus outbreaks has primarily focused on the epidemiology and
64 clinical characteristics of infected patients, the genomic characterization of the virus, and
65 identifying the challenges for global health governance. However, there have been no studies
66 on the effectiveness of handwashing with soap-water against the transmission of coronavirus.
67 In this article, we provide a detailed review of the history, characteristics and emergence of the
68 SARS-CoV-2 virus, the current global COVID-19 situation and control measures, the possible
69 mechanisms of disinfection by soap, and the potential effectiveness of soap in reducing the
70 spread of coronaviruses including SARS-CoV-2. The referenced literature for this study was
71 systematically reviewed and searched in PubMed, Google Scholar, and various academic and
72 research publication websites. We did not set year limit for this search. A manual search was
73 also performed to collect appropriate literature. This search was conducted based on title,
74 author name, and journal scope. Since the COVID-19 outbreak is continuously evolving, the
75 reported information was conducted based on real-time analysis. The compositional aspects of
76 soap and its chemistry for the deactivation of the virus were collected from different journal
77 sources.

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

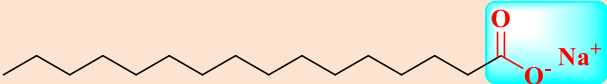
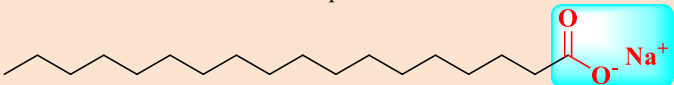
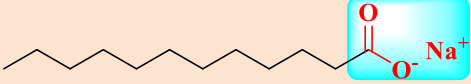
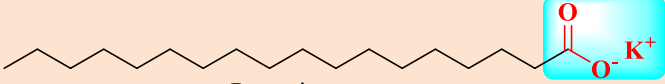
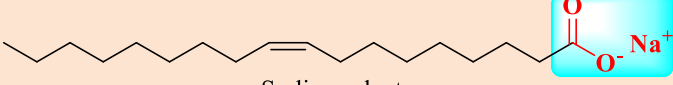
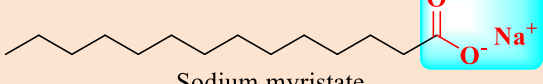
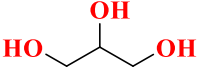
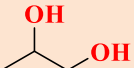
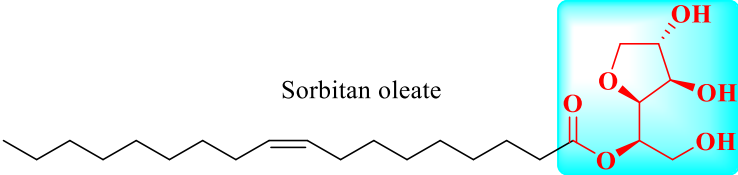
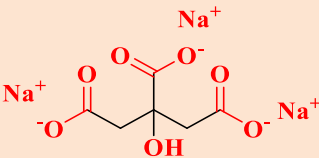
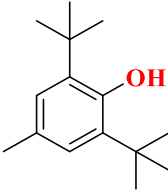
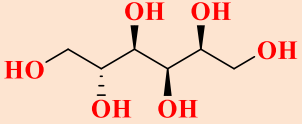
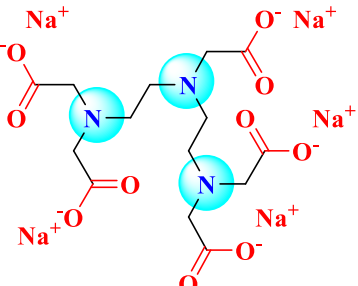
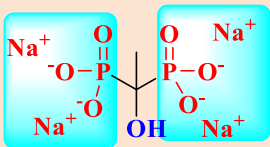
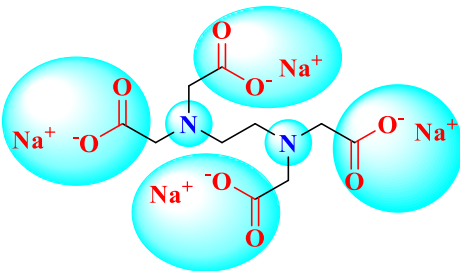
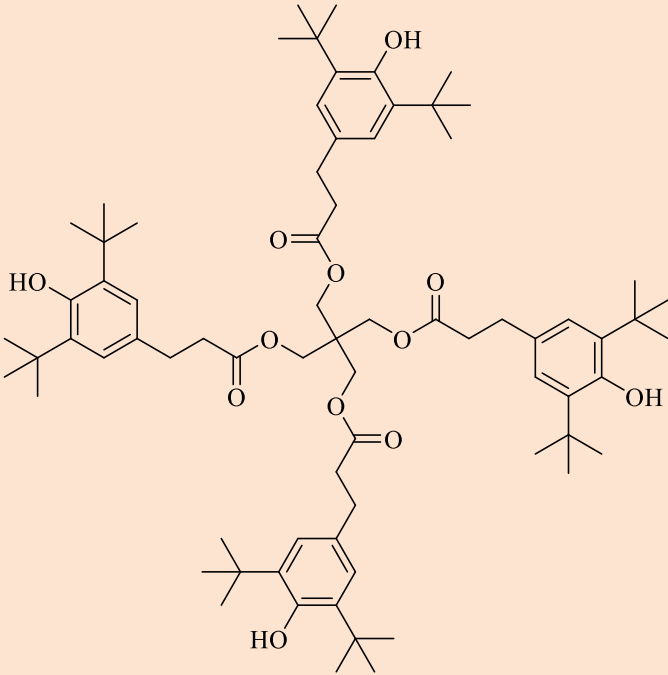
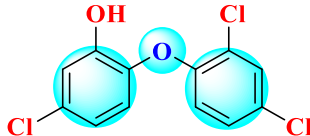
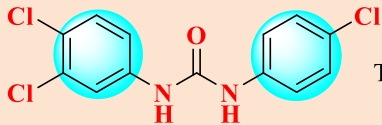
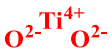
81 **2.1. Taxonomy, structure, and morphology**

83 The name "coronavirus," was coined by Tyrell and co-workers in 1968 [11,12]. It is derived
84 from the Latin word corona (meaning crown) for its crown-like morphology when observed
85 under an electron microscope. The coronavirus (CoV) belongs to the *Coronaviridae* family in
86 the order *Nidovirales,* further sub-classified into four genera: Alpha-CoV, Beta-CoV, Gamma-
87 CoV, and Delta-CoV [10]. Among these, Alpha-CoV and Beta-CoV consist of human
88 pathogenic coronaviruses (HCoV) [1]. In January 2020, the World Health Organization (WHO)
89 temporarily named it a 2019 novel coronavirus [13]. Considering the high (almost 86%)
90 genomic similarity of this virus with the SARS-CoV [14], the International Committee on
91 Taxonomy of Viruses (ICTV) named the novel coronavirusSARS-CoV-2, and the disease
92 caused by this virus as the COVID-19, on 11th February 2020 [3].

94 Coronaviruses are round enveloped viruses, approximately 65-125nm in diameter. They are
95 RNA viruses. Each virus contains a single positive-strand RNA (+ssRNA) that ranges in size
96 from 26-30 kilobases, the largest RNA genome known to date [1]. The genome is complexed
97 with the nucleocapsid (N) protein to form a helical capsid enveloped within the lipid (bilayer)
98 membrane [15]. Embedded into the membrane are at least three viral proteins: the spike (S)
99 glycoprotein that forms the peplomers on the virion surface, giving the virus its crown-like
100 morphology; the membrane (M) protein, the most abundant structural protein, and the envelope

101 (E) protein, the small hydrophobic protein. Some coronaviruses also have an additional
102 membrane protein called hemagglutinin esterase (HE) [16]. The S glycoprotein mediates
103 attachment of the virus to the host cell surface receptors with the subsequent fusion between
104 the virion and host cell membranes, facilitating its entry into the host cell. The M protein and
105 the E protein on the viral surface together define the shape of the viral envelope [17] (Figure
106 1).
107

108
109
110 **Figure1.** A) 3D structure of SARS-CoV-2   B) Internal structure of the virus
111
112 The lipid bilayer enveloped around the virus plays a major role in both infecting the host cell
113 and in inactivating the virus as a whole. It is simply an outer protective layer on the virus made
114 up of fat molecules (phospholipids) that protect the virus when it is outside the host cell. The
115 fat molecules making up the bilayer are amphiphilic with a hydrophilic (phosphate) head
116 covalently bonded to a hydrophobic (lipid) tail. These fatty molecules arrange themselves into
117 a double layer piled on top of each other into a sheet with tails pointing inwards and heads
118 pointing outwards, covering the genome of the virus. The lipid layer also enables the virus to
119 attach to the host cell surfaces, thereby initiating the infection [18].
120
121 **2.2. Transmission and replication**
122
123 Like every other respiratory virus, SARS-CoV-2 spreads to humans when exposed to
124 contaminated respiratory droplets produced by an infected person when they sneeze, cough,
125 and even respire [19]. Inanimate objects and surfaces exposed to such respiratory droplets can
126 become potentially infectious fomites and can easily transfer the virus even after hours of
127 contamination [20]. The deposition of infected droplets or aerosols on the respiratory mucosal
128 epithelium probably initiates viral infection. The most crucial step in viral infection is the
129 fusion between the viral and host cell membranes. The virus binds itself through its spike
130 proteins (S) with the cell surface receptors ACE-2 (Angiotensin Converting Enzyme-2) and
131 TMPRSS-2 (transmembrane protease serine 2) and enters the host cell via endocytosis. Within
132 the host cell, the virus uncoats and releases its +ssRNA. The +ssRNA binds to the cytosolic
133 ribosome or the ribosome on the rough endoplasmic reticulum. Once these +ssRNAs move
134 through the cytosolic ribosome, they are translated into proteins called polyproteins, which are
135 utilized for making spike protein(S), membrane protein (M), an envelope protein (E), and
136 nucleocapsid protein (N). Polyproteins also synthesize an enzyme called RNA-dependent RNA
137 polymerase, which makes more copies of +ssRNA, resulting in the formation of a large number
138 of polyproteins and structural proteins. The +ssRNA molecules combine with the S, M, E, and
139 N proteins and are transported to the Golgi apparatus where they are packed into vesicles and
140 eventually re-assembled into new virus particles surrounded by the lipid bilayer. Finally, the
141 lipid bilayer fuses with the host's cell membrane, and the viruses exit the host cell via
142 exocytosis [21].
143
144 **2.3. Clinical manifestations**

145
146 COVID-19 manifests with a wide range of clinical symptoms, ranging from the mild common
147 cold to severe pneumonia [22]. In general, it is characterized by common symptoms such as
148 high fever, dry cough, tiredness, and other symptoms including aches, nasal congestion,
149 running nose, sore throat, and diarrhea [10]. Some individuals may also experience trouble
150 breathing, persistent pain or pressure in the chest, new confusion or inability to arouse, bluish
151 lips, or face [23].
152
153 **2.4. Emergence and spread of SARS-CoV-2**
154
155 Though the particular coronavirus causing the "COVID-19" pandemic is novel, coronaviruses
156 (CoVs) in general are not new pathogens; they were discovered in the early 1930s as the
157 causative agent of a severe respiratory infection in domesticated chickens, and are now known
158 as avian infectious bronchitis virus (IBV). The first human coronavirus (HCoV) was discovered
159 in the 1960s, but it remained relatively obscured for years [24,25], probably because no severe
160 human disease (only mild common cold) was caused by it. In 2003, a new variant of the
161 coronavirus (named SARS-CoV) emerged in Southern China and caused epidemics of the
162 severe acute respiratory syndrome (SARS) in multiple countries. Consequently, in 2012,
163 another new variant, the Middle Eastern Respiratory Syndrome coronavirus (MERS-CoV)
164 appeared in Saudi Arabia and spread across continents [26]. The emergence of SARS-CoV and
165 MERS-CoV and the impact that these viruses posed on human health led the coronaviruses to
166 be recognized as viruses of significant threat to human health [17].
167
168 Since the onset of the COVID-19 pandemic in late 2019, it has significantly impacted the
169 health, education, and economic sectors on a global scale. The COVID-19 outbreak hit
170 Europe hard, starting in Italy in February 2020, and later made the continent a global
171 epicenter of the disease by late March and April 2020 [27]. During that time, Italy faced the
172 highest COVID-19 fatality rate in the world. A month later, the country faced another wave
173 of uncontrolled COVID-19 outbreak [28]. From the third week of March 2020, the South
174 American countries faced an unprecedented increase in COVID-19 cases causing enormous
175 pressure on their health systems [29]. As of July 5, 2021, a total of 184,573,518 confirmed
176 cases, 3,993,602 deaths, and 168,922,458   recovered cases worldwide have been recorded.
177
178 The United States of America has registered the highest number of confirmed cases
179 (34,275,783 cases) followed by India with 29,274,823 registered cases. Other ten most infected
180 countries include Brazil (17,215,159), France (5,729,967), Turkey (5,313,098) Russia
181 (5,180,454), United Kingdom (4,542,986), Italy (4,239,868), Argentina (4,066,156), Spain
182 (3,729,458), Germany (3,718,617), and Colombia (3,665,137) [30].
183
184 Since the emergence of COVID-19, health intelligence has been trying to analyze the SARS-
185 CoV-2 genome to understand the evolution of this virus. This has been challenging, mainly
186 due to the rapidly changing genome of the virus resulting in new variants [31]. Since SARS-
187 CoV-2 is an RNA virus, it has a high rate of genomic mutation. Several mutations have been
188 identified in the spike proteins, among which the most predominant one is the D614G mutation
189 which efficiently reduces S1 shedding and increases viral infectivity [32,33]. A new variant
190 (B.1.1.7) was first identified in September 2020 in the United Kingdom with an exceptionally
191 large number of mutations, unprecedented spreading ability, and rapidly evolving
192 epidemiologic potential. Over 90 countries, including the United States, have registered cases
193 of the B.1.1.7 variant since December 20, 2020. Another variant (B.1.351) was identified at
194 the beginning of October 2020 in South Africa irrespective of the variant observed in the UK.

195 [34]. This new strain shared some mutations with the variant observed in the UK. Recently,
196 Nigeria has also reported the existence of the new variant. However, no evidence leads to
197 cursory disease or an elevated risk of death associated with these new variants [35]. The new
198 variant of SARS-CoV-2 in the UK has created such a harsh situation that the government
199 imposed even stricter restrictions on every sector to control its spread [36]. The P.1 variant
200 stands out as the third major variant of concern. It was identified for the first time in January
201 2021, when Japan registered four cases of the variant in travelers arriving from Brazil [37].
202 Recently, the second wave of COVID-19 pandemic which is due to both the old and the new
203 variants of SARS-CoV-2 is hitting the world and we are again under lockdown rules to reduce
204 its spread [38].
205
206 The emergence of multiple variants of SARS-CoV-2 has raised concerns in controlling the
207 outbreak of COVID-19 [18, 19]; the recent surge of COVID-19 cases in India, caused by the
208 new SARS-CoV-2 variants B.1.617 and B.1.618, has captured global attention with a record
209 number of new cases reported in a single day (402,110 cases on April 30th, 2021). The hospitals
210 are overcrowded and the health system is unable to cope with the current pandemic situation
211 [40].
212
213 **3. COVID-19 control measures**
214
215 In the initial phase of the COVID-19 pandemic, while research for discovery of treatment and
216 vaccine was ongoing, public health leaders recommended non-pharmaceutical interventions
217 such as social distancing, lockdown strategies, and proper sanitization as the means to reduce
218 the transmission of the SARS-CoV-2 virus. However, this strategy alone was insufficient to
219 end COVID-19 pandemic [41]. In March 2020, the U.S. Department of Health and Human
220 Services (HSS) started the "Operation Warp Speed" program to expedite the COVID-19
221 vaccine [42]. On July 14th and August 12th, 2020, Moderna and Pfizer companies separately
222 published phase I/II clinical trial data on the COVID-19 vaccine. Currently, three vaccines are
223 authorized and recommended in the United States to prevent COVID-19: BNT162b2vaccine
224 manufactured by Pfizer, Inc., BioNTech; mRNA-1273 vaccine manufactured by Moderna TX,
225 Inc., and JNJ-78436735 vaccine manufactured by Janssen Pharmaceuticals Companies of
226 Johnson & Johnson (CDC, 2021). For therapy, remdesivir (Veklury), has been approved by the
227 FDA for the treatment of COVID-19 in hospitalized patients aged 12 years and older who
228 weigh at least 40 kg (CDC, 2020). Additionally, several novel therapeutics, including
229 monoclonal antibodies, are available under the Emergency Use Authorization for early
230 outpatient treatment, and are being tested to evaluate their effectiveness of these therapeutics
231 in people who are at high risk of disease progression (CDC, 2020).
232
233 **4 Soap as an effective agent against SARS-CoV-2**
234
235 **4.1 Chemistry and cleansing action of soap**
236
237 Soaps are the oldest cleansing agents known to humans. Soaps contain a mixture of surfactants,
238 emulsifying agents, copolymers, coloring agents, perfumes, etc. [43]. Chemically, soaps are
239 sodium or potassium salts of saturated or unsaturated long-chain fatty acids that function as
240 surfactant (surface-active) molecules; the long hydrocarbon chain forms a non-polar
241 hydrophobic tail and the ionic carboxylate group forms a polar hydrophilic head [44] (Figure
242 2). Thus, surfactant molecules are water-soluble amphiphiles; in an aqueous environment, the
243 non-polar hydrophobic tail interacts actively with the hydrophobic ends of oil, grease, dirt, and
244 even virus particles. Therefore, the cleansing action of soap is attributed mainly to the

245   surfactant molecules present in the soap. Surfactants have dynamic surface-active properties
246   that enable them to lower the surface tension of water [45]. The surfactant monomers are
247   adsorbed at the interface, and above a specific threshold, concentration called the critical
248   micelle concentration (CMC), the excess surfactant monomers self-associate to form micellar
249   aggregates [46,47] (Figure 3). The micellar aggregates act as emulsifiers that solubilize
250   molecules such as fat and grease that are otherwise insoluble in aqueous solutions.
251   Micellization is the fundamental characteristic of all surfactants and contributes to their
252   cleansing action against microbial species, including the enveloped viruses. Some important
253   soap ingredients and their useful functions in cleansing and enhancing the antimicrobial
254   property of the soap are reported in table 1.

255   **Table 1:** Structure of Soap ingredients and their useful functions

S.N.	Major soap ingredients	Important Function	Ref.
1.	Sodium palmitate; Sodium stearate; Sodium laurate; Potassium stearate; Sodium oleate; Sodium myristate	Soap molecules functioning as surfactants	[48,49]
2.	Glycerol	Skin conditioner/emollient, texture modifier	[50]
3.	Propylene glycol	Skin conditioner/emollient, texture modifier	[51]
4.	Sorbitan oleate	Emulsifier	[52]
5.	Sodium citrate	Reduces the amount of sticky soap scum.	[53]
6.	Butylated hydroxytoluene	Antioxidant	[54]
7.	Sorbitol	Emollient	[55]

8.	Pentasodium pentetate	Water softener. Lock up Ca/Mg minerals in water to form insoluble soap scum. Foam enhancer.	[56]
9.	Tetrasodium etidronate	Water softener. Lock up Ca/Mg minerals in water to form insoluble soap scum. Foam enhancer.	[56]
10.	Tetrasodium EDTA	Water softener. Lock up Ca/Mg minerals in water to form insoluble soap scum. Foam enhancer.	
11.	Pentaerythritol tetrakis (3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate)	Antioxidant. Prevents soap from rancid.	[57]
12.	Triclosan	Broad-spectrum antimicrobials.	[58]
13.	Triclocarban	Broad-spectrum antimicrobials.	[59]
14.	Titanium dioxide	White pigment and color modifier.	[60]

256
257 All commercially available soaps consist of the same basic chemistry described above, and
258 hence have the potential to disrupt the enveloped viruses. The overall cleansing activity of
259 soaps can be attributed to the following properties of soaps [61]:
260
261 1) Soaps contain ingredients that can moisten the surface to be cleaned,
262 2) Soap monomers adsorb on the dirt and virion particles, thereby charging and stabilizing
263   them.
264 3) Many soaps are alkaline. The basic soap solution (9-10 pH) supports emulsifying and
265   peptizing actions [62,63]. Furthermore, the alkalinity of the soaps (pH approximately 9-10)
266   promotes the dispersal of microbial flora from the skin [64].
267 4) Soap solutions have lower surface tension than most of the aqueous solutions; this allows
268   for the thinning of films, thus enabling the emulsifying action.
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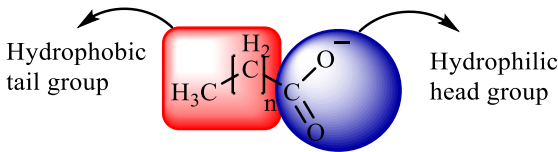
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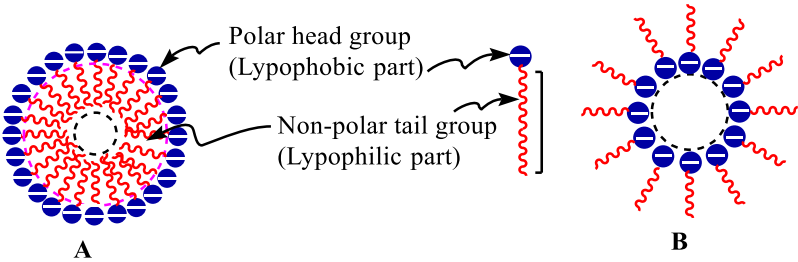
271   **Figure 2.** Molecular structure of soap

272
273
274 **Figure 3.** Structure of (**A**) Normal phase micelle (**B**) Reverse phase micelle
275
276 The application of surfactants in the deactivation of viruses is not a new topic. Several targeted
277 studies have reported the deactivation of different viruses by the use of different types of
278 surfactants and products [65–67]. The findings of previous studies on the effectiveness of
279 handwashing using different types of surfactant-based hand hygiene products in reducing
280 different types of viruses are presented in table 2.
281

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 H$_5$N$_1$	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,

306 micellization is completed, i.e., the lipid bilayer is completely solubilized by the surfactants
307 and only the micellar aggregates remain in the solution [79]. Thus, the complete solubilization
308 of the protective lipid bilayer leads to the disintegration of the virus into fragments, making it
309 no longer infective. Further, the fragmented viral components are also completely solubilized
310 by the surfactant molecules in the form of micelles, which can then be easily washed away by
311 water (Figure 4).
312

(a) A single SARS-Cov-2 entity

(b) Enlarged view of lipid bilayer

(c) A soap monomer

(d) Below CMC, the added surfactant monomers inters into the bilayer competing for the phospholipids in the membrane

(e) At CMC, solubilization of lipid bilayer into mixed micelles begins

Rupturing of virus cell wall by soap molecules

(f) Above CMC, complete solubilization of the outer lipid bilayer into mixed micelles, followed by the entraping of the viral fragments within the soap micelles occur.

313
314 **Figure 4**. Diagrammatic representation of membrane ruptures mechanism
315

316 **Simple elution mechanism**
317

318 In general, a minimum of 20 seconds of handwashing with soap and water is shown to be
319 effective in the removal of oily particles [80,81]. However, the complete inactivation of viruses
320 within such a short time of interaction cannot be asserted by the membrane rupture mechanism.
321 Previous studies have reported the inactivation of viruses by soap solutions [39, 42]. However,
322 the interaction time in those studies (5 min) does not mimic common day-to-day conditions.

323   Therefore, there must be a mechanism of virus or dirt removal without necessarily inactivating
324   them. We have proposed a possible mechanism as the 'simple elution' mechanism.
325   The outer lipid layer of SARS-CoV and other enveloped viruses enables their adsorption on
326   the host cell surface [82]. Soap solutions have a very low surface tension because which they
327   can form very thin films [32]. As a result, they can enter into tiny spaces and spread fluently
328   around the dirt particles, including viruses. Also, soap has the potential to moisten the surface
329   and get adsorbed on any foreign particles present, thereby charging and stabilizing them. The
330   amphiphilic nature of soap, in particular the attractive interaction between the hydrophobic
331   ends of soap with hydrophobic lipid membranes, supports the adsorption of soap monomers.
332   The charged viral particles cannot aggregate. Further, their adsorptive property is lost and they
333   are dragged along with water molecules while washing (Figure 5). Within20 seconds of
334   handwashing recommended by the WHO, the viral component cannot be completely
335   inactivated but can be successfully removed from the hand surface. Therefore, there is a
336   substantial rationale for the existence of a 'simple elution' mechanism, especially attributed to
337   general handwashing.
338

(a) SARS-CoV-2

(b) Soap monomers interact with lipid membrane

Coronavirus is enveloped by an amphiphilic lipid bi-layer made up of polar hydrophilic and non polar hydrophobic part. Water molecules being polar are able to interact only with the polar part of the lipid layer via hydrogen bonding. It has to compete with the strong glue like interaction between the skin and virus. So, water alone is not effective against the removal of virus from our skin.

The lipid layer around coronavirus and soap both are of amphiphilic nature and hence interact following a general principle "like dissolves like". As per the rule, non polar part of the soap and lipid layer interact via hydrophobic-hydrophobic interaction. This disrupts the orderly arranged lipid layer thereby destroying it. Following the same rule, polar part of soap then interacts with the polar water molecules via hydrophilic-hydrophilic interaction. This drags away the fragmented virus particles along with the running water.

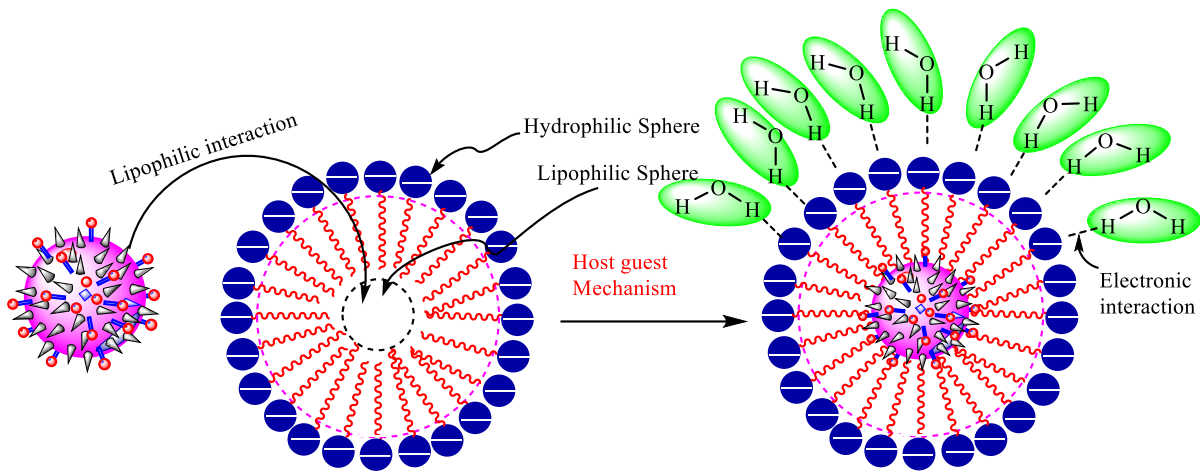
(c) Charged virus suspended in soap solution, which can be easily eluted with water during washing

339

340

341   **Figure 5.** Diagrammatic representation of the simple elution mechanism

342

343 In a study examining the elution of bacteriophages Phi X174 and PRD1 bound to nitrocellulose
344 and charged modified polyether sulfonate membranes, excellent elution of both bacteriophages
345 was achieved using 5mM SDS (Sodium Dodecyl Sulfate) from the BioTrace HP membrane.
346 However, minimum inactivation of PDRI was obtained by 10mM SDS within four min. of
347 exposure, while phiX174 remained unaffected even with 50mM of SDS [83]. These findings
348 support the elution mechanism and that soaps can remove viruses from the adsorbed surfaces
349 even when they are not completely able to inactivate the viruses.
350
351 **Viral entrapment mechanism:**
352
353 As described earlier, SARS-CoV-2 and other enveloped viruses resemble fatty particles of
354 nano-scale diameter. A third probable mechanism involves complete entrapment of the viral
355 particle into the soap micelle. When the surfactant concentration exceeds the CMC value,
356 micellization begins. The soap micelle so formed entraps the viral cell into its nucleus via
357 hydrophobic-hydrophobic interactions. The water molecules then bind with the hydrophilic
358 heads of the micelles, thereby dragging away the entrapped viral cell along with washing
359 (Figure 6). However, since the soap micelles are also of nano-scale diameter, they may not be
360 able to engulf the viral cell as a whole. Further, there is no prior evidence to support this
361 mechanism. Further investigation is required to determine the viability of the proposed
362 mechanism.
363

364
365
366 **Figure 6.** Diagrammatic representation of the viral entrapment mechanism
367
368 Regarding the effectiveness of handwashing in the control and prevention of SARS-CoV-2 and
369 other viruses, the duration of washing has been shown to have a significant effect on controlling
370 the disease. However, no distinction between the mechanisms is possible, and often they may
371 operate simultaneously. Together, the surfactant action of soaps combined with the friction
372 caused during handwashing and final rinsing with clean water is a very effective method for
373 the removal of dirt as well as microbes [84]. For the mechanisms to function effectively, proper
374 rubbing between hands for an adequate amount of time is important. Using soap and detergent
375 at 0.1, 0.2, and 0.3% concentrations completely inactivated the H5N1 virus within 5 min [39].
376 In a recent study, handwashing was associated with a greater risk of spread of influenza-like
377 illness compared to hand-washings for 15 seconds or longer [85,86]. Because of the
378 effectiveness of the method, handwashing with soap and water has been tagged as the "gold
379 standard" method for removing dirt and transient flora from the hand [84]. Both soap and

380 alcohol-based sanitizers are effective in controlling COVID-19 when applied to hands
381 thoroughly and with scrubbing for at least 20 s [47, 48].
382
383 **4.3 Why Soap is better than an alcohol-based sanitizer**
384
385 The very important message throughout such COVID pandemic has been the need for people
386 to wash their hands regularly and thoroughly. While soap and water are best, hand sanitizer is
387 a good substitute in high populations areas or when suitable hand-washing facilities are not
388 available [87]. As we noticed that people are using hand sanitizer daily, sometimes multiple
389 times a day, so the U.S. Food and Drug Administration (FDA) has decided that the companies
390 making hand sanitizers need to provide proof that those chemicals are safe for that level of
391 exposure, especially for pregnant women and children. Three active ingredients (benzalkonium
392 chloride, ethyl alcohol, and isopropyl alcohol) are still under review. According to a new study,
393 quickly smearing an ethanol-based hand sanitizer onto your hands won't kill cold and flu bugs.
394 This is because your fingers are still wet with mucus. It is interesting that FDA has treated
395 sanitizers as 'over-the-counter drugs' and recommended the use of soap and water over
396 sanitizers. The FDA's recommendation on sanitizers is very sensitive to impurities or
397 adulterants [88].
398
399 If we don't have access to soap and water, then hand sanitizer containing 60% alcohol is a good
400 temporary substitute for neutralizing the coronavirus. Soap provides dual advantage; it
401 neutralizes the coronavirus and also physically knocks it off our hands; soap disrupts the sticky
402 bond between pathogens and our skin, allowing the pathogens to slide right off. Hand sanitizer
403 doesn't do all of that. Besides, hand sanitizers may penetrate deeper into the skin layers and
404 affect the skin cells [89].The use of methanol as an adulterant in hand sanitizers and hand rubs
405 is another concern [90]. Methanol must never be used in hand sanitizers because oral,
406 pulmonary, and/or skin exposures can result in allergic reactions, severe systemic toxicity and
407 even death [91]. Using soap and water is safer and hence recommended.
408
409 **4.4 Role of polyelectrolytes in soaps**
410
411 Many soaps, shampoos, and cosmetics incorporate polyelectrolytes [92,93] and
412 polyelectrolyte builder materials that serve to enhance the cleaning capacity of soaps [94]. The
413 polyelectrolytes have several applications, mostly related to modifying the flow and stability
414 properties of aqueous solutions and gels. For instance, they can be used to destabilize a
415 colloidal suspension and to initiate flocculation (precipitation). When mixed with surfactants,
416 they form polyelectrolyte-surfactant complexes (PESC) spontaneously by self-assembly driven
417 by electrostatic and hydrophobic interactions. PESC containing sodium lauryl ether sulfates
418 (SLES) have found wide application in hair care products such as shampoos and soaps [95].
419 Sodium polyacrylate, an anionic polyelectrolyte retains water molecules and increases the
420 viscosity, hence it is often used in soaps as a thickening agent [96].
421
422 Generally, soap compositions include, by weight, 30% to 60% surfactant, 1% to 35%
423 polysaccharide (strong polyelectrolyte), 1% to 10% fatty acid, and 25% to 50% polymer
424 matrix, of the total weight of the soap composition. The soap compositions may further include
425 a fragrance-generating chemical in an amount of 0.1% to 2% by weight of the soap
426 composition.
427
428
429

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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480
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482
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487
488 **Conflicts of interest:**
489
490 Authors declare no competing interests.
491
492 **References**
493

494 [1] Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P, et al. Coronavirus infections and immune
495   responses. J Med Virol 2020;92(4):424–432. https://doi.org/10.1002/jmv.25685.
496 [2] Sherin A. Coronavirus disease 2019 (COVID-19): A challenge of protecting the general
497   population and health-care workers. Khyber Med Univ J 2020;12:4–5.
498   https://doi.org/10.35845/kmuj.2020.20224.
499 [3] Udwadia ZF, Raju RS. How to protect the protectors: 10 lessons to learn for doctors
500   fighting the COVID-19 Coronavirus. Med J Armed Forces India 2020:1–5.
501   https://doi.org/10.1016/j.mjafi.2020.03.009.
502 [4] Morens DM, Breman JG, Calisher CH, Doherty PC, Hahn BH, Keusch GT, et al. The
503   Origin of COVID-19 and Why It Matters. Am J Trop Med Hyg 2020;103(3):955–959.
504   https://doi.org/10.4269/ajtmh.20-0849.
505 [5] Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Origin,
506   transmission, and characteristics of human coronaviruses. J Adv Res 2020;24:91–98.
507   https://doi.org/10.1016/j.jare.2020.03.005.
508 [6] Kar SK, Yasir Arafat SM, Kabir R, Sharma P, Saxena SK. Coping with mental health
509   challenges during COVID-19. Coronavirus Dis. 2019 (COVID-19), Med. Virol. From
510   Pathog. to Dis. Control, vol. 2019. S. K. Saxe, Springer Nature Singapore Pte Ltd.; 2020;
511   199–213. https://doi.org/10.1007/978-981-15-4814-7_16.
512 [7] Beiu C, Mihai M, Popa L, Cima L, Popescu MN. Frequent hand washing for COVID-
513   19 prevention can cause hand dermatitis: management tips. Cureus 2020;12.
514   https://doi.org/10.7759/cureus.7506.
515 [8] World Health Organization. Recommendations to Member States to improve hand
516   hygiene practices to help prevent the transmission of the COVID-19 virus. 2020.
517   Available online: https://www.who.int/publications/i/item/recommendations-to-
518   member-states-to-improve-hand-hygiene-practices-to-help-prevent-the-transmission-
519   of-the-covid-19-virus (accessed on 1 April 2020)
520 [9] Food and Agriculture Organization of the United Nations, World Health Organization.
521   COVID-19 and food safety : guidance for food businesses. 2020. Available online:
522   https://www.who.int/publications/i/item/covid-19-and-food-safety-guidance-for-food-
523   businesses (accessed on 7 April 2020)
524 [10] Hassan SA, Sheikh FN, Jamal S, Ezeh JK, Akhtar A. Coronavirus (COVID-19): a
525   review of clinical features, diagnosis, and treatment. Cureus 2020;12.
526   https://doi.org/10.7759/cureus.7355.
527 [11] CEBM. Coronaviruses– a general introduction. 2020. Available online:
528   https://www.cebm.net/covid-19/coronaviruses-a-general-introduction/ (Accessed on 25
529   March 2020)

530 [12] Wege H, Siddell S, ter Meulen V. The biology and pathogenesis of coronaviruses. Curr.
531   Top. Microbiol. Immunol., Springer Berlin Heidelberg; 1982, p. 165-200.
532   https://doi.org/10.1007/978-3-642-68528-6_5.
533 [13] WHO. Coronavirus disease (COVID-19) outbreak. 2020. Available online:
534   https://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-
535   19/novel-coronavirus-2019-ncov
536 [14] Wilder-smith A, Chiew CJ, Lee VJ. Can we contain the COVID-19 outbreak with the
537   same measures as for SARS? Lancet Infect Dis 2020, 20(5), p. e102-e107.
538   https://doi.org/10.1016/S1473-3099(20)30129-8.
539 [15] Weiss SR, Navas-martin S. Coronavirus pathogenesis and the emerging pathogen severe
540   acute respiratory syndrome coronavirus. Microbiol Mol Biol Rev 2005;69:635–64.
541   https://doi.org/10.1128/MMBR.69.4.635.
542 [16] Hogue BG, Machamer CE. Coronavirus structural proteins and virus assembly. In:
543   Perlman S, Gallagher T, Snijder EJ, editors. Nidoviruses, ASM Press, Washington, DC;
544   2008, p. 179–200.
545 [17] Schoeman D, Fielding BC. Coronavirus envelope protein : current knowledge. Virol J
546   2019;16. https://doi.org/10.1186/s12985-019-1182-0.
547 [18] Tripet B, Howard MW, Jobling M, Holmes RK, Holmes K V, Hodges RS. Structural
548   characterization of the SARS-Coronavirus spike S fusion protein core. J Biol Chem
549   2004;279(20):20836–20849. https://doi.org/10.1074/jbc.M400759200.
550 [19] Rosa G La, Fratini M, Libera S Della, Iaconelli M, Muscillo M. Viral infections acquired
551   indoors through airborne, droplet or contact transmission. Ann Ist Super Sanità
552   2013;49(02):124–32. https://doi.org/10.4415/ANN_13_02_03.
553 [20] Geller C, Varbanov M, Duval RE. Human coronaviruses: insights into environmental
554   resistance and its influence on the development of new antiseptic strategies. Viruses
555   2012;4(11):3044–3068. https://doi.org/10.3390/v4113044.
556 [21] Sola I, Mateos-Gomez PA, Almazan F, Zuñiga S, Enjuanes L. RNA-RNA and RNA-
557   protein interactions in coronavirus replication and transcription. RNA Biol
558   2011;8(2):237–48. https://doi.org/10.4161/rna.8.2.14991.
559 [22] Daga MK, Kumar N, Aarthi J, Mawari G, Garg S, Rohatgi I. From SARS-CoV to
560   coronavirus disease 2019 (COVID-19) - a brief review. J Adv Res Med 2019;6:1–9.
561   https://doi.org/10.24321/2349.7181.201917.
562 [23] Centers for Disease Control and Prevention. Symptoms of COVID-19. 2021. Available
563   online: https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html
564   (Accessed on 22 February 2021)
565 [24] Pyrc K, Berkhout B, van der Hoek L. Identification of new human coronaviruses. Expert
566   Rev Anti Infect Ther 2007;5:245–53. https://doi.org/10.1586/14787210.5.2.245.
567 [25] Wevers BA, van der Hoek L. Recently discovered human coronaviruses. Clin Lab Med
568   2009;29:715–24. https://doi.org/10.1016/j.cll.2009.07.007.
569 [26] Alsaadi EAJ, Jones IM. Membrane binding proteins of coronaviruses. Future Virol
570   2019;14:275–86.
571 [27] Hiscott J, Alexandridi M, Muscolini M, Tassone E, Palermo E, Soultsioti M, et al. The
572   global impact of the coronavirus pandemic. Cytokine Growth Factor Rev 2020.
573   https://doi.org/10.1016/j.cytogfr.2020.05.010.
574 [28] Bontempi E. The europe second wave of COVID-19 infection and the Italy "strange"
575   situation. Environ Res 2020:110476. https://doi.org/10.1016/j.envres.2020.110476.
576 [29] González-Bustamante B. Evolution and early government responses to COVID-19 in
577   South   America.   World   Dev   2021;137:105180.
578   https://doi.org/10.1016/j.worlddev.2020.105180.
579 [30] Worldometer. COVID live update: 160,416,106 cases and 3,333,785 deaths from the

580   Coronavirus. 2021. Available online: https://www.worldometers.info/coronavirus/
581   (Accessed on 16 May 2021)

582 [31] Wu A, Wang L, Zhou H, Ji C, Xia SZ, Cao Y, et al. One year of SARS-CoV-2 evolution.
583   Cell Host Microbe 2021;29:503–7. https://doi.org/10.1016/j.chom.2021.02.017.

584 [32] Guruprasad L. Human SARS CoV-2 spike protein mutations. Proteins 2021;89:569–76.
585   https://doi.org/10.1002/prot.26042.

586 [33] Zhang L, Jackson CB, Mou H, Ojha A, Rangarajan ES, Izard T, et al. The D614G
587   mutation in the SARS-CoV-2 spike protein reduces S1 shedding and increases
588   infectivity. BioRxiv Prepr 2020. https://doi.org/10.1101/2020.06.12.148726.

589 [34] Hodcroft EB, Zuber, Moira1. Hodcroft EB et al. E and spread of a S-C-2 variant through
590   E in the summer of 2020. medRxiv 2020. 10. 25. 2021906. (2020)., Nadeau S, Comas I,
591   González Candelas F, Consortium S-S, et al. Emergence and spread of a SARS-CoV-2
592   variant through Europe in the summer of 2020. MedRxiv 2020:2020.10.25.20219063.

593 [35] Centers for Disease Control and Prevention (CDC). About variants of the Virus that
594   causes COVID-19. 2021. Available online: https://www.cdc.gov/coronavirus/2019-
595   ncov/transmission/variant.html (Accessed on 2 April 2021).

596 [36] Kirby T. New variant of SARS-CoV-2 in UK causes surge of COVID-19. Lancet Respir
597   Med 2021;9:e20–1. https://doi.org/10.1016/S2213-2600(21)00005-9.

598 [37] The Guardian. Brazilian Covid variant : what do we know about P1? 2021. Available
599   online: https://www.theguardian.com/world/2021/mar/01/brazil-covid-variant-p1-
600   britain (Accessed on 8 April 2021)

601 [38] Korber B, Fischer WM, Gnanakaran S, Yoon H, Theiler J, Abfalterer W, et al. Tracking
602   changes in SARS-CoV-2 spike: evidence that D614G increases infectivity of the
603   COVID-19   virus.   Cell   2020;182:812–827.e19.
604   https://doi.org/10.1016/j.cell.2020.06.043.

605 [39] Edara VV, Norwood C, Floyd K, Ahmed R, Wrammert J, Suthar MS, et al. Infection-
606   and vaccine-induced antibody binding and neutralization of the B . 1 . 351 SARS-CoV-
607   2   variant.   Cell   Host   Microbe   2021;29:516–521.e3.
608   https://doi.org/10.1016/j.chom.2021.03.009.

609 [40] Rozanova L, Temerev A, Flahault A. Comparing the scope and efficacy of COVID-19
610   response strategies in 16 countries : An overview. Int J Environ Res Public Health
611   2020;17:1–17. https://doi.org/10.3390/ijerph17249421.

612 [41] Weintraub RL, Subramanian L, Karlage A, Ahmad I, Rosenberg J. COVID-19 Vaccine
613   To Vaccination: Why Leaders Must Invest In Delivery Strategies Now. Health Aff
614   2021;40:33–41. https://doi.org/10.1377/hlthaff.2020.01523.

615 [42] Van Norman GA. "Warp Speed" Operations in the COVID-19 Pandemic: Moving Too
616   Quickly?   JACC   Basic   to   Transl   Sci   2020;5:730–4.
617   https://doi.org/10.1016/j.jacbts.2020.06.001.

618 [43] Chaudhary NK, Bhattarai A, Guragain B, Bhattarai A. Conductivity, surface tension,
619   and comparative antibacterial efficacy study of different brands of soaps of Nepal. J
620   Chem 2020;2020. https://doi.org/10.1155/2020/6989312.

621 [44] Hill M, Moaddel T. Soap structure and phase behavior. 2nd ed. Elsevier Ltd.; 2016.
622   https://doi.org/10.1016/B978-1-63067-065-8.50002-5.

623 [45] Wolfrum S, Marcus J, Touraud D, Kunz W. Historical perspective A renaissance of
624   soaps ? — How to make clear and stable solutions at neutral pH and room temperature.
625   Adv Colloid Interface Sci 2016:1–15. https://doi.org/10.1016/j.cis.2016.07.002.

626 [46] Llchtenberg D. Characterization of the solubilization of lipid bilayers by surfactants.
627   Biochim Biophys Acta 1985;821:470–8. https://doi.org/10.1016/0005-2736(85)90052-
628   5.

629 [47] Sehgal P, Doe H, Bakshi MS. Solubilization of phospholipid vesicular structures into

630 mixed micelles of zwitterionic surfactants. J Surfactants Deterg 2003;6:31–7.
631 https://doi.org/10.1007/s11743-003-0245-6.

632 [48] Moldovan M, Nanu A. Influence of cleansing product type on several skin parameters
633 after single use. Farmacia 2010;58:29–37.

634 [49] Willcox M. Soap. Poucher's Perfum. Cosmet. Soaps. 10th ed., Kluwer Academic
635 Publishers; 2000, p. 453–65.

636 [50] Becker LC, Bergfeld WF, Belsito D V., Hill RA, Klaassen CD, Liebler DC, et al. Safety
637 assessment of glycerin as used in cosmetics. Int J Toxicol 2019;38:6S–22S.
638 https://doi.org/10.1177/1091581819883820.

639 [51] Perencevich EN, Wong MT, Harris AD. National and regional assessment of the
640 antibacterial soap market: A step toward determining the impact of prevalent
641 antibacterial soaps. Am J Infect Control 2001;29:281–3.
642 https://doi.org/10.1067/mic.2001.115469.

643 [52] Brandner JD. The composition of NF-defined emulsifiers: Sorbitan monolaurate,
644 monopalmitate, monostearate, monooleate, polysorbate 20, polysorbate 40, polysorbate
645 60, and polysorbate 80. Drug Dev Ind Pharm 1998;24:1049–54.
646 https://doi.org/10.3109/03639049809089948.

647 [53] Mabrouk ST. Making usable, quality opaque or transparent soap. J Chem Educ
648 2005;82:1534–7. https://doi.org/10.1021/ed082p1534.

649 [54] Yehye WA, Rahman NA, Ariffin A, Abd Hamid SB, Alhadi AA, Kadir FA, et al.
650 Understanding the chemistry behind the antioxidant activities of butylated
651 hydroxytoluene (BHT): A review. Eur J Med Chem 2015;101:295–312.
652 https://doi.org/10.1016/j.ejmech.2015.06.026.

653 [55] Hon KL, Kung JSC, Ng WGG, Leung TF. Emollient treatment of atopic dermatitis:
654 latest evidence and clinical considerations. Drugs Context 2018;7:1–14.
655 https://doi.org/10.7573/dic.212530.

656 [56] George ED, Raymond DJ. Formulation of traditional soap cleansing systems. 2nd ed.
657 Elsevier Ltd.; 2016. https://doi.org/10.1016/B978-1-63067-065-8.50003-7.

658 [57] Suzuki A, Ulfiati R, Masuko M. Evaluation of antioxidants in rapeseed oils for railway
659 application. Tribol Int 2009;42:987–94. https://doi.org/10.1016/j.triboint.2009.02.001.

660 [58] Yazdankhah SP, Scheie AA, Høiby EA, Lunestad BT, Heir E, Fotland TØ, et al.
661 Triclosan and antimicrobial resistance in bacteria: An overview. Microb Drug Resist
662 2006;12:83–90. https://doi.org/10.1089/mdr.2006.12.83.

663 [59] Breneman DL, Hanifin JM, Berge CA, Keswick BH, Neumann PB. The effect of
664 antibacterial soap with 1.5% triclocarban on Staphylococcus aureus in patients with
665 atopic dermatitis. Cutis 2000;66:296–300.

666 [60] Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Cogliano V. Carcinogenicity of
667 carbon black, titanium dioxide, and talc. Lancet Oncol 2006;7:295–6.
668 https://doi.org/10.1016/S1470-2045(06)70651-9.

669 [61] Hillyer HW. On the cleansing power of soap. J Am Chem Soc 1903;25:511–24.
670 https://doi.org/10.1021/ja02007a010.

671 [62] Dlova NC, Naicker T, Naidoo P. Soaps and cleansers for atopic eczema, friends or foes?
672 What every South African paediatrician should know about their pH. South African J
673 Child Heal 2017;11:146–8. https://doi.org/10.7196/sajch.2017.v11i3.1325.

674 [63] Boonchai W, Iamtharachai P. The pH of commonly available soaps, liquid cleansers,
675 detergents and alcohol gels. Dermatitis 2010;21:154–6.
676 https://doi.org/10.2310/6620.2010.10003.

677 [64] Lambers H, Piessens S, Bloem A, Pronk H, Finkel P. Natural skin surface pH is on
678 average below 5, which is beneficial for its resident flora. Int J Cosmet Sci 2006;28:359–
679 70. https://doi.org/10.1111/j.1467-2494.2006.00344.x.

680 [65] Lin Q, Lim JYC, Xue K, Yew PYM, Owh C, Chee PL, et al. Sanitizing agents for virus
681   inactivation and disinfection. View 2020;1. https://doi.org/10.1002/viw2.16.
682 [66] Falk NA. Surfactants as antimicrobials: A brief overview of microbial interfacial
683   chemistry and surfactant antimicrobial activity. J Surfactants Deterg 2019;22:1119–27.
684   https://doi.org/10.1002/jsde.12293.
685 [67] Piret J, Roy S, Gagnon M, Landry S, Désormeaux A, Omar RF, et al. Comparative study
686   of mechanisms of herpes simplex virus inactivation by sodium lauryl sulfate and n-
687   lauroylsarcosine.   Antimicrob   Agents   Chemother   2002;46:2933–42.
688   https://doi.org/10.1128/AAC.46.9.2933-2942.2002.
689 [68] Lavelle GC, Gubbe SL, Neveaux JL, Bowden BJ. Evaluation of an antimicrobial soap
690   formula for virucidal efficacy in vitro against human immunodeficiency virus in a blood-
691   virus   mixture.   Antimicrob   Agents   Chemother   1989;33:2034–6.
692   https://doi.org/10.1128/AAC.33.12.2034.
693 [69] Liu P, Yuen Y, Hsiao HM, Jaykus LA, Moe C. Effectiveness of liquid soap and hand
694   sanitizer against Norwalk virus on contaminated hands. Appl Environ Microbiol
695   2010;76:394–9. https://doi.org/10.1128/AEM.01729-09.
696 [70] Li JZ, Mack EC, Levy JA. Virucidal efficacy of soap and water against human
697   immunodeficiency virus in genital secretions. Antimicrob Agents Chemother
698   2003;47:3321–2. https://doi.org/10.1128/AAC.47.10.3321-3322.2003.
699 [71] Shahid MA, Abubakar M, Hameed S, Hassan S. Avian influenza virus (H5N1); effects
700   of   physico-chemical   factors   on   its   survival.   Virol   J   2009;6.
701   https://doi.org/10.1186/1743-422X-6-38.
702 [72] Ansari SA, Sattar SA, Springthorpe VS, Wells GA, Tostowaryk W. In vivo protocol for
703   testing efficacy of hand-washing agents against viruses and bacteria: Experiments with
704   rotavirus   and   Escherichia   coli.   Appl   Environ   Microbiol   1989;55:3113–8.
705   https://doi.org/10.1128/aem.55.12.3113-3118.1989.
706 [73] Conover DM, Gibson KE. Comparison of two plain soap types for removal of bacteria
707   and viruses from hands with specific focus on food service environments. Food Control
708   2016;69:141–6. https://doi.org/10.1016/j.foodcont.2016.04.047.
709 [74] Contreras PA, Sami IR, Darnell MER, Ottolini MG, Prince GA. Inactivation of
710   respiratory syncytial virus by generic hand dishwashing detergents and antibacterial
711   hand   soaps.   Infect   Control   Hosp   Epidemiol   1999;20:57–8.
712   https://doi.org/10.1086/501550.
713 [75] Lichtenberg D, Ahyayauch H, Alonso A, Gon FM. Detergent solubilization of lipid
714   bilayers : a balance of driving forces. Trends Biochem Sci 2013;38:85–93.
715   https://doi.org/10.1016/j.tibs.2012.11.005.
716 [76] Roth Y, Opatowski E, Lichtenberg D, Kozlov MM. Phase behavior of dilute aqueous
717   solutions of lipid-surfactant mixtures: effects of finite size of micelles. Langmuir
718   2000;16:2052–61.
719 [77] Almgren M. Mixed micelles and other structures in the solubilization of bilayer lipid
720   membranes   by   surfactants.   Biochim   Biophys   Acta   -   2000;1508:146–63.
721   https://doi.org/10.1016/S0005-2736(00)00309-6.
722 [78] Kragh-hansen U, Maire M, Møller J V. The mechanism of detergent solubilization of
723   liposomes   and   protein-containing   membranes.   Biophys   J   1998;75:2932–46.
724   https://doi.org/10.1016/S0006-3495(98)77735-5.
725 [79] Koynova R, Tenchov B. Interactions of surfactants and fatty acids with lipids. Curr Opin
726   Colloid Interface Sci 2001;6:277–86.
727 [80] Tan C. Why washing hands with soap is critical in battling Covid-19. The Straits Times
728   2020:1–2. Available online: https://www.straitstimes.com/singapore/why-washing-
729   hands-with-soap-is-critical-in-battling-covid-19 (Accessed on 15 April 2020)

[81] Unicef. Everything you need to know about washing your hands to protect against coronavirus (COVID-19). 2020. Available online: https://www.unicef.org/coronavirus/everything-you-need-know-about-washing-your-hands-protect-against-coronavirus-covid-19#:~:text=In%20general%2C%20both%20handwashing%20with,them%20with%20soap%20and%20water. (Accessed on 17 September 2020)

[82] Cosset FL, Lavillette D. Cell entry of enveloped viruses. vol. 73. 2011. https://doi.org/10.1016/B978-0-12-380860-8.00004-5.

[83] Fujito BT, Lytle CD. Elution of viruses by ionic and nonionic surfactants. Appl Environ Microbiol 1996;62:3470–3. https://doi.org/10.1128/aem.62.9.3470-3473.1996.

[84] Foddai ACG, Grant IR, Dean M. Efficacy of instant hand sanitizers against foodborne pathogens compared with hand washing with soap and water in food preparation settings: a systematic review. J Food Prot 2016;79:1040–54. https://doi.org/10.4315/0362-028X.JFP-15-492.

[85] Abdulrahman AK Bin, Abdulrahman KA Bin, Almadi MK, Alharbi AM, Mahmoud MA, Almasri MS, et al. Do various personal hygiene habits protect us against influenza-like illness? BMC Public Health 2019;19:1–8. https://doi.org/10.1186/s12889-019-7726-9.

[86] Wesley NO, Talakoub L. Handwashing and hand sanitizer on the skin and COVID-19 infection risk. 2020. Available online: https://www.mdedge.com/dermatology/article/219484/aesthetic-dermatology/hand-washing-and-hand-sanitizer-skin-and-covid-19 (Accessed on 23 March 2020)

[87] Dicken RD, Gallagher T, Perks S. Overcoming the regulatory hurdles for the production of hand sanitizer for public health protection: The UK and US academic perspective. ACS Chem Heal Saf 2020;27:209–13. https://doi.org/10.1021/acs.chas.0c00065.

[88] Center for Drug Evaluation and Research. Temporary policy for preparation of certain alcohol-based hand sanitizer products during the public health emergency (COVID-19) guidance for Industry. Pharm. Qual. Stand. (CGMP)/Over-the-Counter, U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) Pharmaceutical; 2020. Available online: https://www.fda.gov/media/136289/download

[89] Jing JLJ, Yi TP, Bose RJC, Mccarthy JR, Tharmalingam N, Madheswaran T. Hand sanitizers: a review on formulation aspects, adverse effects, and regulations. Int J Environ Res Public Heal Rev 2020;17. https://doi.org/10.3390/ijerph17093326.

[90] Chan APL, Chan TYK. Methanol as an unlisted ingredient in supposedly alcohol-based hand rub can pose serious health risk. Int J Environ Res Public Health 2018;15:6–11. https://doi.org/10.3390/ijerph15071440.

[91] FDA. Safely Using Hand Sanitizer. U.S.: 2021. Available online: https://www.fda.gov/consumers/consumer-updates/safely-using-hand-sanitizer (Accessed on 29 April 2021)

[92] Madhav H, Singh N, Jaiswar G. Thermoset, bioactive, metal-polymer composites for medical applications. Elsevier Inc.; 2019. https://doi.org/10.1016/B978-0-12-816874-5.00004-9.

[93] Schanze KS, Shelton AH. Functional polyelectrolytes. Langmuir 2009;25:13698–702. https://doi.org/10.1021/la903785g.

[94] [101] Heilig ML. Polyelectrolyte builders and detergent compositions. 3308067, 1967. Available online: https://patents.google.com/patent/US3308067A/en.

[95] Vleugels LFW, Pollet J, Tuinier R. Polycation-sodium lauryl ether sulfate-type surfactant complexes: influence of ethylene oxide length. J Phys Chem B 2015;119:6338–47. https://doi.org/10.1021/acs.jpcb.5b02043.

780   [96]   English RJ, Laurer JH, Spontak RJ, Khan SA. Hydrophobically modified associative
781   polymer solutions: Rheology and microstructure in the presence of nonionic surfactants.
782   Ind Eng Chem Res 2002;41:6425–35. https://doi.org/10.1021/ie020409s.
783   [97]   Zdziennicka A, Krawczyk J, Szymczyk K, Jańczuk B. Macroscopic and microscopic
784   properties of some surfactants and biosurfactants. Int J Mol Sci 2018;19.
785   https://doi.org/10.3390/ijms19071934.
786   [98]   Som I, Bhatia K, Yasir M. Status of surfactants as penetration enhancers in transdermal
787   drug delivery. J Pharm Bioallied Sci 2012;4:2–9. https://doi.org/10.4103/0975-
788   7406.92724.
789   [99]   Trabaris M, Laskin JD, Weisel CP. Effects of temperature, surfactants and skin location
790   on the dermal penetration of haloacetonitriles and chloral hydrate. J Expo Sci Environ
791   Epidemiol 2012;22:393–7. https://doi.org/10.1038/jes.2012.19.
792   [100]   Schaefer H, Schalla W, Zesch A, Stüttgen G. Skin Permeability. Springer; 1982.
793
794
795