pharmacoepidemiology

MDPI

Review

Use of Hand Sanitizers in COVID-19 Prevention: A Comprehensive Overview

Suneetha Vuppu [1,*], Toshika Mishra [1] and Arjun Chinamgari [2]

1 Department of Biotechnology, School of Bio Sciences and Technology, Vellore Institute of Technology, Vellore 632014, India
2 Department of Industrial Engineering, University of Florida, Gainesville, FL 32611, USA
* Correspondence: vsuneetha@vit.ac.in; Tel.: +91-9994716743

Abstract: The pandemic outbreak of Coronavirus disease 2019 (COVID-19) has drastically changed the picture of global healthcare. With the rapid emergence of novel variants of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) that rendered the currently available therapeutic and diagnostic approaches inefficient in containing the transmission of infection, it becomes important to focus on strategies to break the transmission chain. The major approach to contain the spread of infection is the promotion of adequate hand hygiene practices in public as hands are an important source of pathogenic microbes. Hand hygiene is an important part of everyday life for maintaining a healthy and disease-free lifestyle. With the outbreak of the pandemic, people are now understanding the importance of hand hygiene practices. The global market of hand sanitizers has experienced rapid growth and high demand. This review aims to discuss the use of sanitizers during the period of COVID-19 and their role in controlling the transmission of infection. It also focuses on global market trends, the advancements in the development of sanitizer formulations, and the limitations of commercial sanitizers. Therefore, the formulation of an effective hand disinfectant is crucial for preventing future pandemic outbreaks.

Keywords: COVID-19; SARS-CoV-2; hand sanitizers; alcohol-based; alcohol-free; market trends; advancements; limitations

check for updates

Citation: Vuppu, S.; Mishra, T.; Chinamgari, A. Use of Hand Sanitizers in COVID-19 Prevention: A Comprehensive Overview. *Pharmacoepidemiology* **2023**, 2, 257–271. https://doi.org/10.3390/pharma2030022

Academic Editor: Cristina Bosetti

Received: 21 April 2023
Revised: 17 July 2023
Accepted: 19 July 2023
Published: 1 August 2023

1. Introduction

The COVID-19 pandemic caused by SARS-CoV-2 has taught the human population the importance of hygiene and sanitation practices in the prevention of infections. SARS-CoV-2 is an RNA virus that evolves frequently due to mutations caused by a lack of fidelity of RNA Polymerase and recombination [1,2]. Consequently, it leads to the emergence of numerous novel variants with varied transmission and virulence rates. The emerging variants are further classified into variants of concern, variants of interest, variants of high consequences, and variants being monitored [1]. According to the data from World Health Organization (WHO), there are over 763 million confirmed COVID-19 cases with over 6 million deaths reported till April 2023 [3]. The virus causes complications in multiple organs and organ systems resulting in increased hospitalization and mortality [2]. It also renders the old and immunocompromised people susceptible to various co-infections, the prominent being opportunistic fungal pathogens. These co-infections have reportedly resulted in enhanced severity and increased mortality [4].

Therefore, the most important approach is to break the transmission chain and focus on developing efficient prevention strategies to avoid consequential complications and problems. The SARS-CoV-2 virus gets transmitted primarily through droplets and aerosols released from the respiratory tract of an infected individual. The predominantly used preventive interventions used for the containment of COVID-19 include surface disinfection, hand hygiene, Personal Protective Equipment (PPE), vaccination, physical distancing, and movement restriction [5]. The outbreak of COVID-19 has made the public realize the significance of hand hygiene to contain infection transmission and prevent nosocomial infections [6,7]. Hands are a reservoir of numerous pathogenic microorganisms that can easily enter the body through the eyes, nose, and mouth. The microflora on the hand is categorized into resident and transient flora (including pathogenic microbes) [6]. It is an important aspect of everyday life for the maintenance of a healthy and disease-free lifestyle. Important methods of hand hygiene include handwashing with soap and water, alcohol-based hand sanitizers, and alcohol-free hand sanitizers. Additionally, the use of gloves and skin protectants also facilitates the reduction in the pathogenic contamination of hands [6].

The first commercial alcohol-based disinfectant "Sterillium" was released in 1965. It was made up of 75% alcohol and glycerine. In the year 1988, Gojo released a hand gel called "Purell" which contained 70% ethanol and propylene glycol [8]. It has gradually increased in prominence in the global market during the last decade. However, with the spread of the COVID-19 pandemic, the importance of hand hygiene and the benefits of sanitizers was highly popularized, rapidly increasing the market and consumer demand. More research into new formulations for cost-effective, large-scale production resulted in the development of alcohol-free sanitizer formulations.

This review discusses the types, mechanism, and role of hand sanitizers in controlling the transmission of COVID-19. It focuses on the global market trend of sanitizers, advancements in sanitizer formulation and techniques and limitations of the currently available formulations.

2. Types of Sanitizers

According to the Centers for Disease Control and Prevention, if water and soap are not readily available, the use of sanitizer can be favored. Hand sanitizers are categorized into two types, namely, alcohol-based and alcohol-free sanitizers, based on the presence of alcohol in the formulation as the key antimicrobial agent [9], as shown in Figure 1. Alcohol-based sanitizers have alcohols like isopropyl alcohol, ethanol, and n-propanol as the main component, whereas non-alcoholic sanitizers are made of antimicrobials like benzalkonium chloride, triclosan, povidone-iodine, and chlorhexidine gluconate [6].

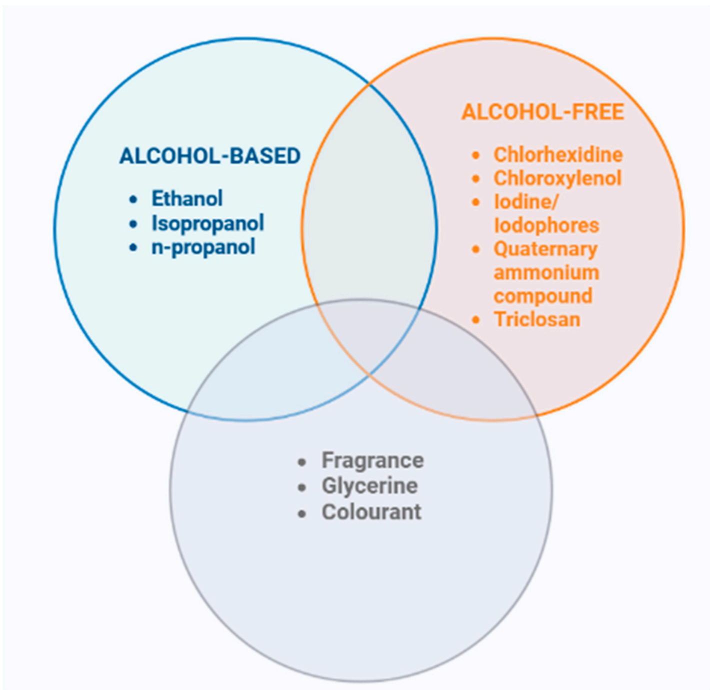

Figure 1. Types of Sanitizers (created by Vuppu et al. using biorender.com).

Alcohol-based sanitizers contain 60% to 95% ethanol, isopropanol, or n-propanol [6,10], which is mixed with water and emollients like propylene glycol and glycerine to prevent drying out skin, thus neutralizing various types of microorganisms [11]. Alcohol-free (aqueous) sanitizers are generally based on disinfectants, such as benzalkonium chloride (BAC), and antimicrobial agents such as triclosan, chlorhexidine, chloroxylenol, and iodine or iodophores [6,12]. These substances effectively eliminate a wide array of microorganisms, and unlike alcohol, are less affected by organic residues. Quaternary ammonium compounds (quats) are formed from benzalkonium chloride and related compounds which are non-corrosive and effective against many microorganisms [12].

Alcohol-based sanitizers reportedly are efficacious against a wide array of microorganisms such as viruses, bacteria, and fungi. However, they are also associated with numerous adverse events like contact dermatitis, redness, and itching [13]. To surmount the limitations of alcohol-based sanitizers, alcohol-free sanitizers containing compounds with antimicrobial activity and a cost-effective production method were developed. This was also with the aim to fulfill the growing demand for sanitizers in the market.

3. Mechanism of Action of Sanitizers

The different types of hand sanitizers have distinct modes of action for the elimination of pathogens. These are explained below.

3.1. Alcohol-Based Sanitizer

Alcohol-based sanitizers are the most widely used hand sanitizers with ethanol and isopropanol as the most commonly used alcoholic components in sanitizers. Alcohol is most effective at concentrations of 60–80% concentrations. Concentrations of alcohol higher than 80% alcohol are less potent as the proteins are not easily denatured in the absence of water [12,14]. Alcohol causes the coagulation/denaturation of proteins, leading to damage to the protective coating of microbes, thus resulting in their elimination. The alcohol n-propanol has high utility in biocides. However, its mode of action is not well understood but is assumed to be related to membrane damage or inhibition of transcription and protein synthesis by affecting ribosomes and RNA Polymerase [15]. The alcohol n-propanol is not accepted by FDA for hand sanitizer formulation as it can exhibit potentially toxic implications on human health. It is generally used to prepare industrial solvents (e.g., cleaner). Accidental or intended exposure by ingestion can result in symptoms like reduced breathing and heart rate, leading to death. Exposure to the skin or eyes can cause irritation and allergies [16].

Alcohols have good in vitro germicidal activity against gram-positive and gram-negative vegetative bacteria in addition to mycobacterium and fungi. Alcohol also shows virucidal activity against enveloped and non-enveloped viruses [12,17]. It has a direct impact on crucial metabolic pathways and can lead to membrane damage and loss of cellular integrity [15].

Water is essential in alcoholic sanitizers because it facilitates the denaturation of proteins. Therefore, absolute alcohols are not a preferred component of sanitizers and disinfectants [15].

In the case of viruses, the alcohol-based sanitizers target the viral coat, constituted by host lipid envelopes and protein capsid. Although the mechanism of action is not well understood, it is well known that ethanol has greater viricidal activity than propanol. Ethanol has high efficacy against enveloped viruses which constitute a major proportion of clinically relevant viruses [15].

3.2. Alcohol-Free Sanitizers

With the increase in global consumption of sanitizers, non-alcohol-based sanitizers are also being greatly popularized. The mechanism of activity of some of the important constituents of such sanitizers is discussed hereafter.

3.2.1. Benzalkonium Chloride

Benzalkonium chloride is a widely used primary component of alcohol-free sanitizers. It targets the lipid membranes of viruses and bacteria, including SARS-CoV-2. The cationic head groups are adsorbed on the negatively charged phospholipid heads following the accumulation of the compound on the bilayer membrane, which consequently loses its fluidity creating hydrophilic gaps on it. Subsequently, the alkyl tail of the compound disrupts the lipid membrane [15]. Its mode of action is by reducing the surface tension, degrading the enzymes, and denaturing the cellular proteins [18,19].

3.2.2. Chlorhexidine

Chlorhexidine is primarily efficient against gram-positive bacteria and has minimal effectiveness against Gram-negative bacteria and enveloped viruses. It disrupts the arrangement of cytoplasmic membranes, therefore causing precipitation of cell contents [20].

3.2.3. Chloroxylenol

Chloroxylenol acts as an antimicrobial agent. It disrupts the synthesis of cell walls in microorganisms and is effective against bacteria as well as viruses [21].

3.2.4. Iodine/Iodophors

Iodine has a germicidal effect on Gram-positive, Gram-negative, spore-forming bacteria, as well as a number of fungi and viruses. It enters the cell wall of microorganisms and develops complexes with unsaturated fatty acids or amino acids that inhibit the synthesis of cellular components. Its characteristic mode of action includes oxidation/substitution by free iodine [22].

3.2.5. Triclosan

Triclosan disrupts the bacterial membranes leading them to death [22]. It has exceptional efficacy against Gram-positive bacteria [23]. However, the efficacy of triclosan can be affected by pH or ionic concentration [24]. As it is effective in disrupting the lipid membrane, it can be used for inactivating viruses [18].

The mechanism of key antimicrobial agents in sanitizers is summarized in Table 1.

Table 1. Mode of action of ingredients in Hand sanitizers.

Ingredients	Mechanism of Action
Alcohol	• Causes the death of organisms by denaturing the cellular proteins. • It is a lipid solvent that damages the lipid bilayer of the cell membrane and cell wall. • It is also a dehydrating agent and causes loss of water from cells.
Hydrogen peroxide	Releases highly reactive hydroxyl free radicals that can either cleave or form cross-links with the sulfydryl residues or double bonds of lipids, proteins, and nucleic acids, that are exposed, causing degradation.
Benzalkonium chloride	• Reduces the surface tension. • Degrades the enzymes. • Denatures the cellular proteins.
Iodophores/Iodine	• Iodine is a powerful oxidizing agent and irreversibly oxidizes cellular materials. • It brings halogenation of tyrosine residue of protein and enzymes and inactivates it.
Triclosan	• Bactericidal in nature. • Disrupts the membrane by degrading the enzymes that produce fatty acids for the membrane and cell wall.
Chlorhexidine	• Chlorhexidine is a widely used biocide in antiseptic products. It has broad-spectrum biocidal activity and skin tolerability. • In the case of viruses, its activity is restricted to lipid-enveloped viruses.

4. Role of Hand Sanitizers in Controlling COVID-19 Transmission

SARS-CoV-2 is a zoonotic virus [3], the classification of which is depicted in Figure 2. SARS-CoV-2 is a member of the family Coronaviridae and the order Nidovirales. The virus is categorized as a Sarbecovirus of the type Betacoronavirus, which also includes the viruses SARS-CoV-1 and MERS-CoV. The virus possesses rapid transmission with high mutation rates [25]. As a result, in a span of three years, multiple lineages and variants have emerged. The numerous rapid mutations in the viral genome have resulted in numerous variants in a short time span. These variants are classified into a variant of interest (VOI), a variant of concern (VOC), and a variant of high consequences (VOHC) [26].

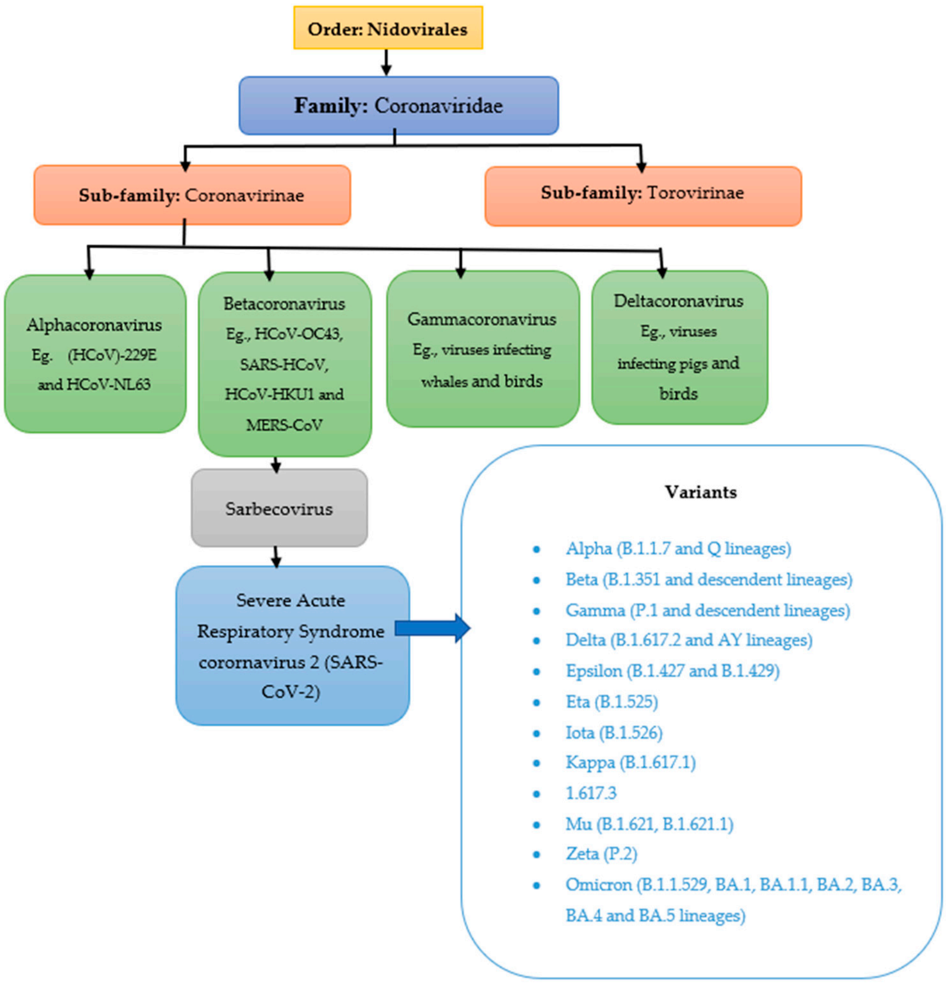

Figure 2. Classification of SARS-CoV-2 [26–28] (created by Vuppu et al.).

The virus has challenged the domain of health care, all across the globe, questioning the current understanding of the virus life cycle, disease prognosis, drug, and vaccine development [26]. The mode of transmission of SARS-CoV-2 is through the air via respiratory droplets (sneezing, coughing, or talking) or contact with the infected person. The virus is deposited on the surfaces within 1 to 4 m of the source of ejection.

The virus has a structural protein called Spike (S) which binds to the angiotensin-converting enzyme 2 (ACE 2) receptor on the surface of the host cell facilitating the release of viral genetic material, resulting in the infection [29]. The symptoms of the COVID-19 infection range from asymptomatic (in patients with mild infection) to serious complications that could eventually lead to mortality [30]. Thus, preventive measures like regular hand sanitation, and the use of masks, gloves, and face shields should be adhered to in order to avoid transmission of infection, especially from asymptomatic patients.

Globally, a large amount of research is being carried out to develop effective treatments or therapies, vaccines, and prevention strategies [31]. Although COVID-19 primarily spreads through aerosols and droplets, and most infections are attributed to these methods, good hand hygiene may limit community transmission [32]. Consequently, this approach is supported and promoted by governments across the globe, along with the aid of public health agencies and organizations [33]. Several epidemiological studies have identified that the risk of infection transmission is dependent on the type of preventive intervention employed, as well as the duration and nature of exposure [34]. A study found that the practice of hand hygiene reduces the transmission of infections by approximately 16% [35]. The World Health Organization has encouraged the use of hand sanitizers as an alternative to hand washing due to their simplicity of use, efficacy in decreasing the microbial count on hands, rapid drying upon application, and independence from soap and water, which are not always accessible [33]. A study conducted in Germany revealed that compliance with hand hygiene increased from 47% prior to the COVID-19 pandemic to approximately 95% during the pandemic [35]. Sanitizers are effective disinfectants for eliminating the SARS-CoV-2 virus, with their efficacy dependent on the characteristics of the viral strains, the properties and composition of sanitizers, and the virus's environment or habitat. For instance, hand sanitizers reduce the virus from epidermal layers of hands and consequently clean it. The persistence time of SARS-CoV-2 is shown in Table 2. The sanitizers and disinfectants cancel out this persistent duration by immediately eliminating the pathogens present on the surface [31].

Table 2. Duration of persistence on the surface of different materials [31].

Surface of Materials	Duration of Persistence
Surgical masks	Up to 7 days
Glass, plastic, bank notes, stainless steel	4–7 days
Printing and tissue papers	Up to 3 h
Treated wood and cloth	Up to 2 days
Copper and cardboard	Up to 72 h

There is a wide range of compounds that are effective against the SARS-CoV-2 virus, which includes ethanol (predominantly at 75%), formaldehyde (>0.7%), isopropanol (>70%), povidone-iodine (>0.23%), sodium hypochlorite (>0.21%), and hydrogen peroxide (>0.5%) [31]. Consequently, these compounds are extensively used for developing novel hand sanitizer formulations.

Different alcohols display varying levels of effectiveness against viruses in the case of alcohol-based hand sanitizers. Ethanol has a broad range of effectivity against viruses, isopropanol has relatively greater lipophilic activity than ethanol. The activity of alcohols against viruses is by attacking and disrupting the membrane proteins that are crucial for viral replication and survival. In the case of SARS-CoV-2, the M and E proteins constitute the envelope in addition to the lipid layer that safeguards the core of the virus. The lipid layer facilitates easy disruption by most commonly used disinfectants, including alcohols and soaps. The addition of other compounds in the composition of alcohol-based sanitizers like emollients and fragrances has been reported to reduce antimicrobial activity. However, natural emollients like *Aloe vera* are found to exhibit antimicrobial activity independently, and so are better alternatives to the chemical emollients in the composition. The alcohol-based sanitizer formulations recommended by WHO are also found to be efficacious in inactivating the virus. Another antimicrobial compound that exhibits antimicrobial activity is hydrogen peroxide (H_2O_2). It is a biocide that acts as an oxidant by releasing highly reactive hydroxyl free radicals that can either cleave or form cross-links with the sulfydryl residues or double bonds of lipids, proteins, and nucleic acid that are exposed to it. In a study conducted to study the effectivity of H_2O_2 on N95 filters, it was found that the virus was eliminated within the time duration of 10 min. However, it cannot be used as an active compound in hand sanitizers because high concentrations of it are harmful to the skin [18].

The sanitizers available on the market, however, are found to be associated with numerous harmful effects associated with both environmental as well as human health [31]. According to the recommendation by WHO, the main ingredients of alcohol-based sanitizers include different combinations of ethanol, isopropyl alcohol, and hydrogen peroxide. However, abuse and misuse of these components can result in toxic implications on human health as well as the environment. Studies have attributed the toxicity of alcohol-based hand sanitizers to methanol contamination. On the other hand, hydrogen peroxide on ingestion can result in conditions such as gastrointestinal problems, vomiting, mild mucosal irritation, and portal vein embolism. Excessive usage of hand sanitizers containing alcohol can raise the risk of infections owing to skin damage. The alcoholic components of the sanitizers can enter the environment through evaporation or spillage. They reportedly are more hazardous to aquatic life compared to terrestrial life [36]. Thus, extensive research is required in this domain to obtain formulations that are safe and free of limitations in addition to being cost-effective to make them accessible and affordable to people from low-income countries.

5. Growing Market of Sanitizers during COVID-19

Hand sanitizers have become an indispensable component of our daily existence, especially after the COVID-19 pandemic. Their popularity has skyrocketed in recent years, and the demand for these products has been steadily increasing [37].

5.1. Factors Facilitating Market Growth

- Increased Awareness of Hygiene

The COVID-19 pandemic has caused people to become more aware of the importance of hygiene, particularly hand hygiene. People have become more conscientious about using hand sanitizers to prevent the transmission of viruses [32]. Hand sanitizers, along with other preventive measures, may aid in reducing community transmission. Governments, health organizations, and the media have all emphasized the importance of hygiene, which has led to increased awareness among people. This results in increased purchases of sanitizers contributing to the growing market [38].

- Convenience

Sanitizers are easy to use, portable, and can be carried around. They do not require water or soap, making them ideal for use when traveling, or when access to water and soap is limited [15]. With the increasing popularity of on-the-go lifestyles, the convenience of sanitizers has become more appealing to consumers.

- Increased Demand from Healthcare Industry

The healthcare industry has always been a significant consumer of sanitizers. However, the outbreak of the COVID-19 pandemic has caused a surge in demand. Hospitals, clinics, and other healthcare facilities have had to increase their use of sanitizers to prevent the spread of the virus [36]. The increased demand leads to a shortage of supplies. Consequently, production has to be increased in order to meet the rising demand. This leads to growth in the market of hand sanitizers and increased research for the development of novel formulations with easy-to-access ingredients.

- Improved Formulations

Sanitizer formulations have improved significantly over the years, making them more effective and appealing to consumers. Sanitizers now come in a variety of formulations, including gels, sprays, and wipes. Manufacturers have also introduced sanitizers with moisturizing properties to prevent skin dryness, which can occur with frequent use [7].

- Availability

The availability of sanitizers has also contributed to their growing market. In the past, sanitizers were primarily used in hospitals and other healthcare facilities. However, with the increasing demand, they are now widely available in stores, online, and even in vending machines [39].

- Affordability

The affordability of sanitizers has also played a significant role in their growing market. With a wide range of brands and commercialized formulations, sanitizers are now available at different price points, making them accessible to consumers across different income levels [40].

5.2. Economics of Market of Sanitizers

The economics of a sanitizer market can be understood through the principles of supply and demand. As the demand for sanitizers increases, manufacturers seek to produce more to meet this demand. However, the cost of producing sanitizers can vary depending on factors such as the formulation, packaging, and raw materials used [41]. Sanitizers typically contain alcohol, which can be expensive depending on the source and quality. Manufacturers may need to adjust their pricing strategies in response to fluctuations in the cost of raw materials [32]. In a free market, the price of sanitizers will be determined by the interaction of supply and demand [37]. The pricing of sanitizers is influenced by a range of additional factors, including production costs, competition, and consumer demand. As the demands return to the pre-pandemic level, a decline in the price of sanitizers may be experienced [39].

The market for sanitizers is highly competitive, with a range of brands and formulations available. There are several large manufacturers, as well as smaller players who specialize in niche products. The market is characterized by low barriers to entry, meaning that new players can enter the market relatively easily. In recent years, there has been a trend towards consolidation in the market, with larger manufacturers acquiring smaller players. This has led to increased concentration in the market, with a small number of large players dominating the industry. The sanitizer market is also subject to external factors such as regulation and the availability of raw materials [40]. For example, regulations regarding the ingredients used in sanitizers and GMP requirements can impact the production costs and pricing strategies of manufacturers. Similarly, shortages of raw materials can lead to supply disruptions and an increase in prices.

Another important factor in the sanitizer market is brand loyalty. Consumers may develop a preference for a particular brand based on factors such as perceived product quality, price, and packaging. Manufacturers must work to differentiate their products from those of their competitors and develop brand loyalty among consumers [42].

Finally, the economics of the sanitizer market are influenced by distribution and marketing strategies. Manufacturers must ensure that their products are widely available to consumers through a range of channels such as supermarkets, drugstores, and online retailers. Effective marketing can help to drive demand for sanitizers and increase brand loyalty among consumers [43]. Marketing is an essential component of the economics of the sanitizer market. Manufacturers must develop effective marketing strategies to promote their products and differentiate themselves from their competitors. Marketing costs can vary depending on the channels used, such as television, social media, or influencer marketing. Effective marketing can help to drive demand for sanitizers and increase brand among consumers.

6. Challenges in Effective Sanitation Due to COVID-19

During the COVID-19 pandemic, despite guidelines outlined by the WHO such as regular handwashing or maintaining social distancing, there were a number of complications in some aspects that prevented effective arrest of the spread of the virus. One of these was the absence of facilities that are important for the maintenance of good hygiene practices, as well as the use of common locations like water sources or toilets. As a result, many of the surfaces (walls, faucets, door handles) function as fomites through which the virus can be indirectly transmitted. This is an issue that is common in densely populated locations including both cities and rural areas [44]. Approximately 3 billion people lacked access to basic hygiene facilities such as water and soap during the pandemic. Masks and other personal protective equipment (PPE) were mandated to prevent the spread of the coronavirus, which transmits through the air and contact with people or surfaces. However, there was a lack of these protective materials, despite their importance in preventing the spread of the virus in the population (particularly among patients and frontline employees). A key inference to learn from in the future would be to maintain large stocks of such important supplies in advance [45].

A recent study identified substandard preparations as well as detected toxic contaminants (like methanol and 3-methyl-butanol) in many hand sanitizer brands in Johannesburg, South Africa. The public should be made aware of this lack of compliance with the guidelines resulting in poor quality formulation, which could have a negative impact on health [46]. Another study on commercial sanitizers in South Africa found that only 4 sanitizers out of 18 test samples were effective against *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Enterococcus faecalis*, and *Staphylococcus aureus*, while other sanitizer samples were completely ineffective against the aforementioned test pathogens. Seven samples claimed to exhibit an efficiency of 99.99% and showed effectiveness against only *E. coli* [47]. A similar study was performed in Ethiopia recently to analyze the quality and efficacy of local brands of hand sanitizers. The results of this study revealed that over one-third of the analyzed hand sanitizers failed to comply with the guidelines of WHO with respect to the limit of ethanol and hydrogen peroxide in the formulation [48]. Similar results were also obtained in a study conducted on marketed hand sanitizers in Kenya. It was found that out of 74, only 3 sanitizer samples showed compliance with the regulatory guidelines. The majority of the commercial samples were substandard and exposed the public to toxic contaminants [49]. In the context of Saudi Arabia, a similar study identified 196 samples out of 1409 that did not comply with international standards. They contained toxic impurities like acetaldehyde, methanol, and 1-propanol [50].

On the other hand, after the outbreak of the COVID-19 pandemic, Health Canada executed some major modifications in the regulatory guidelines with respect to labeling, packaging, and ethanol levels. These changes reportedly result in increased susceptibility of the population to various health risks. The permission to use technical-grade ethanol for sanitizer formulation, as well as increased permittance or threshold level of toxic contaminants in the formulation, are important alterations with drastic negative implications on human health. Furthermore, improper labeling has also resulted in increased incidences of toxicity due to accidents or unintended uptake of alcohol-based hand sanitizers [51]. Thus, these findings signify the importance of adequate regulatory guidelines to promote the health of the citizens and lower the susceptibility to toxicity and adverse effects due to exposure to substandard or poor-quality hand sanitizers. The safety and efficacy of the sanitizer formulations should be prioritized and strictly monitored to avoid unintended negative implications on health.

The dissemination of SARS-CoV-2 through wastewater is a concern that focuses more on sanitation. While the likelihood of the disease spreading through water has been eliminated to a large extent, it has been discovered in the excrement of patients with the disease as well as in effluent in outbreak-affected areas. Concern has also been identified regarding the disposal of waste from COVID-19 patients in low-income areas [44]. The disposal of this waste necessitated a distinct waste disposal area and toilets that must be cleaned twice daily by a worker wearing the proper PPE clothing for handling such hazardous material [52].

An important aspect of COVID-19 and sanitation is properly planned and funded logistics, which enable the acquisition and distribution of the necessary resources for maintaining sanitary and hygienic conditions. Approximately 62% of excrement-based effluent is improperly managed, especially with respect to the treatment of wastewater. One reason for this is the inadequacy of data required for proper planning and administration of sanitation resources, especially in areas such as water scarcity/availability in a particular area. This problem is exacerbated by the fact that data collection efforts of this type are hampered by a lack of manpower or infrastructure [52].

Certain diagnostic procedures, such as RT-PCR (Reverse Transcription-Polymerase Chain Reaction), necessitate a certain level of expertise in order to guarantee accurate diagnosis. This alone necessitates the presence of trained professionals who are able to operate the instrument and complete the procedure [53].

As a result, the major challenges in maintaining hygiene and sanitation during the pandemic include the availability of resources such as water and soap, the use of common areas such as bathrooms, the proper disposal of waste from infected patients, and the logistical constraints that come with attempting to design and manage such a system. Other significant challenges include the availability of necessary supplies of PPE kits and equipment, as well as aspects at testing centers such as testing methodologies and sanitation, as well as the knowledge required to carry out said diagnostic operations. Solutions to these problems can be advantageous for the preparation of any future pandemic outbreaks.

7. Advancements in Sanitizer Formulation

In the wake of COVID-19, the world has found itself increasingly dependent on sanitation practices and products to help maintain hygienic conditions and curb the spread of the virus. The increased use of hand sanitizers has bolstered pharmaceutical companies to identify or develop compounds with potential for use as hand sanitizers.

Many of the synthetic hand sanitizers available on the market cause side effects like itching, peeling, and redness in the skin. They can also cause ocular injury on accidental contact [19]. Consequently, alternative actives and formulations for hand sanitizers that do not inherently irritate the skin upon application are being researched. One example of this is the development of sanitizer using methanolic extract derived from the *Lawsonia inermis* plant, which has demonstrated antimicrobial activity on a broad scale [54].

Electrolyzed water (EW) has gained popularity as a general disinfectant. It possesses a disinfectant effect mainly attributed to the reduced pH and enhanced oxidation-reduction potential in addition to the complementary influence of the compounds HClO, H_2O_2, hydroxyl group, and Cl_2. Conditions such as low pH have a detrimental impact on the permeability of microbial membranes inhibiting their multiplication. The increased oxidation-reduction potential is an important factor responsible deaths of bacterial cells by affecting their metabolism. The hydroxyl ions and H_2O_2 molecules result in damage to the lipid membrane, denaturation of cellular proteins to inhibit multiplication as well as cleavage of bacterial DNA [55].

Sanitation is also important in preventing the spread of diseases like COVID-19, and several countries implemented a number of approaches to help with this endeavor throughout the epidemic. One of the most fundamental strategies that was implemented was better dissemination of WASH (water, sanitation, and hygiene) methods like ensuring access to a clean supply of water and soap, as well as sharing knowledge of how to properly wash hands, through campaigns and multiple channels of communication.

Other secondary measures that were employed were applied more at a smaller scale in homes or institutions. This included measures such as quarantining symptomatic individuals, avoiding sharing of items, or the availability of domestic sanitation products such as bleach or filters, at homes. In the case of public places like schools, transport stations, or offices, legislation advocated for the addition of measures such as facilities for handwashing, which are fully functional and modified to suit the needs of the individuals who use it or the frequent disinfection and cleaning of facilities such as bathrooms with multiple users.

The third facet of the sanitation strategies employed by governments entails legislation, which permits the availability of sanitation resources at all times, as well as increasing the availability of these services to as many people as possible. This includes measures such as ensuring a minimum amount of water is available at all times for use, as well as the provision of essential sanitary facilities such as toilets to avoid resorting to measures such as defecating in open environments or sharing facilities.

Initiatives by governments that support the continuous availability of these essential resources in their fullest possible capacity through various means are being used to support the prior strategy of ensuring sanitation facilities are available in as many places as possible. Included in these measures is the routine maintenance of sanitation apparatus, which ensures that all treatment and sanitation processes are operating at peak efficiency. Regular logistical support is provided for systems such as wastewater treatment, along with adequate safety equipment (masks and gloves) for workers and engineers handling these appliances or working on the processes, and a dependable power supply to consistently support these sanitation processes and techniques. In addition, it is necessary to develop infrastructure that can adapt to the requirements of communities and individuals who rely on these systems [56].

An overview of the recent advancements in the development of sanitizer formulations and techniques is presented in Table 3. It includes some of the aforementioned formulations and techniques like *Lawsonia inermis* methanolic extract-based sanitizer, and electrolyzed water. Advanced technologies expand the possibilities for solving existing problems and challenges.

Table 3. Advancements in sanitizer formulations and techniques.

Sl. No	Formulation/ Technique	Innovation	Description	Advantages	Limitations	References
1	*Lawsonia inermis* methanolic extract-based sanitizer	Tested extracts demonstrated a multitude of beneficial qualities, such as anti-inflammatory and antibacterial qualities.	Dried and powdered leaves, methanol, phosphate buffer saline (PBS), acetate-HCl and Tris Base-HCl buffers are analyzed, with each buffer being tested in separate solutions.	Antimicrobial agent with a broad spectrum of activity. The source plant is not a food crop, so food supply is unaffected. Exhibited potential activity against both *E. coli* and *B. subtilis*, as well as the MS2 bacteriophage.	Further cytotoxicity analyses are pending for this extract. An evaluation of antiviral activity against COVID-19 is still pending for this plant extract.	[54]
2	Alternative hand sanitizers derived from mandelic acid and other phytochemical compounds	Mandelic acid is an effective antimicrobial compound against the likes of *S. aureus*, and *Pseudomonas* sp. Similarly, other components of essential oil like eugenol or vanillin have been shown to have synergistic effects against microbes when used in conjunction with other compounds.	Gels that contain the mandelic acid or essential oil are similar to standard hand sanitizer.	The essential oils derived from cinnamon, clove, and thyme demonstrated good antimicrobial activity against multiple bacteria, particularly *S. aureus* and *E. coli.* Some essential oils also demonstrated good sensory qualities even after storage for prolonged periods (60 days) at higher temperatures like 50 °C.	Certain essential oils derived from specific plants did not demonstrate good antimicrobial activity after storage at increasing temperatures leading to alteration of chemical properties as well as stability.	[57]
3	Electrolyzed water (sanitizer alternative)	The reagents are fairly simple to acquire in order to produce a sanitizer alternative that has potential efficacy.	This is prepared via electrolysis of a 10% *w/v* sodium chloride solution.	Cytotoxicity tests and studies showed that electrolyzed water is safe for use as a sanitizer by the majority of people. The ions present in the solution produced from electrolysis (like hypochlorite ions) demonstrated good antimicrobial activity.	For some individuals, both within the test sample population and in general application, the chemicals/ions present have the potential to cause inflammatory responses on the skin, opening it up to spread the infection in those affected.	[58]
4	Processing of COVID-19 biomedical waste through the use of cement kilns	The acidic gases produced by waste burning are countered and neutralized by the alkaline conditions within the kiln. This process also leaves no waste residues after burning.	The waste is burned inside a cement kiln at a temperature of 1450 °C.	Biomedical waste is completely destroyed and leaves no residues. Acidic gases are negated by the kiln's internal alkaline conditions. This method also reduces the demand for non-renewable energy sources like coal.	The limitations of this method are yet to be known.	[59]

8. Limitations

As the COVID-19 pandemic continues to evolve, new variants of the virus are emerging, some of which are believed to be more contagious and potentially more dangerous than the original strain. This has raised concerns about the effectiveness of currently available sanitizers in combating these emerging variants [10].

Sanitizers are an essential tool in the fight against COVID-19. They are designed to kill or inactivate the virus on surfaces and hands, helping to prevent its spread. Sanitizers typically contain alcohol, which is known to be effective against viruses, including coronaviruses [32]. However, the emergence of new variants of COVID-19 has raised concerns about the effectiveness of sanitizers against these emerging variants. Some experts believe that these variants may be more resistant to sanitizers and other disinfectants, which could make them more difficult to control [31].

8.1. Limitations of Currently Available Sanitizers

One of the primary limitations of currently available sanitizers is their effectiveness against emerging variants of COVID-19. While sanitizers are effective against the original strain of the virus, there is evidence to suggest that they may be less effective against certain variants [15]. For example, the B.1.1.7 variant, which was first identified in the UK, has been shown to be more contagious than the original strain of the virus. Some studies have suggested that this variant may be more resistant to certain sanitizers, which could make it more difficult to control [60]. While sanitizers can be effective on smooth, non-porous surfaces, such as doorknobs and countertops, they may not be as effective on porous surfaces, such as fabrics and carpets [15].

Hand sanitizers can be efficient at killing viruses on the surface of hands. However, washing with soap and water is still the most efficient method for cleaning hands of dirt, grime, and germs. Additionally, there is evidence to suggest that the overuse of sanitizers can lead to the development of antimicrobial resistance. This is because the chemicals in the sanitizer formulation such as hydrogen peroxide can induce mutations that can result in the development of antimicrobial resistance [61].

8.2. Potential Solutions

Despite the limitations of currently available sanitizers, there are potential solutions that could help to address these issues. One approach is the development of new sanitizers that are specifically designed to target emerging variants of COVID-19 [32]. Some researchers are exploring the use of alternative disinfectants, such as hydrogen peroxide and ultraviolet light, which may be more effective against certain variants of the virus. Others are exploring the use of antimicrobial coatings and materials that can kill or inactivate the virus on contact [62]. Another potential solution is the development of better sanitizing protocols. This could include increasing the frequency of cleaning and disinfection, particularly in high-traffic areas such as hospitals and public transportation [63]. Education and awareness campaigns may also be important in helping to reduce the spread of COVID-19 and its emerging variants. Educating the public on the proper use of sanitizers and other disinfectants, as well as promoting handwashing and other hygiene practices are important strategies [38].

In addition to COVID-19, novel sanitizer formulations can also be designed for various opportunistic pathogens that include bacteria like *Escherichia coli*, *Enterobacter aerogenes*, *Bacillus cereus*, *Pseudomonas aeruginosa*, *Enterococcus* sp., *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Listeria monocytogenes*, as well as fungal pathogens like *Aspergillus* sp. and *Candida albicans*. These are dominantly present on surfaces like mobile phones and currencies, resulting in frequent exposure due to direct contact with palms. The prolonged exposure to these pathogens can cause the development of several infectious diseases, which can lead to increased hospitalization [64]. Therefore, it is important to develop novel sanitizer formulations to target various other classes of pathogenic microbes as they also increase the burden on global health. Numerous pathogenic infections have serious implications on human health that result in increased morbidity and mortality.

9. Conclusions

The COVID-19 pandemic has emphasized the importance of developing adequate hand hygiene behaviors to avoid infections and break the transmission chain. This has led to a rapid rise in the market demand for hand sanitizers. Hand sanitizers are broadly classified into two categories, namely, alcohol-based and alcohol-free sanitizers. The drastic increase in demand for hand sanitizers cannot be fulfilled with only alcohol-based hand sanitizers and so alcohol-free hand sanitizers were designed. However, both classes of sanitizers are reported to be associated with numerous adverse events, consequently demanding innovative alternatives that are safer and exhibit comparable efficacy. With the advancement in technology, various novel formulations are being designed with adequate efficiency and safety. Thus, to promote public health, it is important to focus on the development of efficient prevention strategies especially hand hygiene to avoid the viral infection caused by SARS-CoV-2 as well as the newly emerging pathogenic outbreaks or future outbreaks.

Author Contributions: The author S.V. conceptualized the idea for the work. All authors (S.V., T.M. and A.C.) have substantially contributed to the design of work, data acquisition, analysis and interpretation; and drafting, reviewing and revising the work. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: The authors want to express their gratitude to honorable Chancellor G. Viswanathan, VIT University, Vellore, for his constant support and encouragement. Suneetha Vuppu wants to Acknowledge ICMR (Indian Council of Medical Research) India for sponsoring to carry out this research. Toshika would like to express special gratitude to ICMR for granting her the JRF position.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Chavda, V.P.; Mishra, T.; Vuppu, S. Immunological Studies to Understand Hybrid/Recombinant Variants of SARS-CoV-2. *Vaccines* **2023**, *11*, 45. [CrossRef]
2. Chavda, V.P.; Vuppu, S.; Mishra, T.; Kamaraj, S.; Patel, A.B.; Sharma, N.; Chen, Z.-S. Recent review of COVID-19 management: Diagnosis, treatment and vaccination. *Pharmacol. Rep.* **2022**, *74*, 1120–1148. [CrossRef] [PubMed]
3. WHO Coronavirus (COVID-19) Dashboard with Vaccination Data. Available online: https://covid19.who.int/ (accessed on 26 July 2022).
4. Chavda, V.P.; Mishra, T.; Kamaraj, S.; Punetha, S.; Sengupta, O.; Joshi, Y.; Vuppu, S.; Vaghela, D.; Vora, L. Post-COVID-19 Fungal Infection in the Aged Population. *Vaccines* **2023**, *11*, 555. [CrossRef] [PubMed]
5. Pradhan, D.; Biswasroy, P.; Kumar Naik, P.; Ghosh, G.; Rath, G. A Review of Current Interventions for COVID-19 Prevention. *Arch. Med. Res.* **2020**, *51*, 363–374. [CrossRef]
6. Prashar, N. Comparative evaluation of efficacy of alcoholic vs. non-alcoholic hand sanitizers. *Int. J. Life Sci. Biotechnol. Pharma Res.* **2012**, *1*, 173–177.
7. Booq, R.Y.; Alshehri, A.A.; Almughem, F.A.; Zaidan, N.M.; Aburayan, W.S.; Bakr, A.A.; Kabli, S.H.; Alshaya, H.A.; Alsuabeyl, M.S.; Alyamani, E.J.; et al. Formulation and Evaluation of Alcohol-Free Hand Sanitizer Gels to Prevent the Spread of Infections during Pandemics. *Int. J. Environ. Res. Public Health* **2021**, *18*, 6252. [CrossRef]
8. The History of Hand Sanitizer—History News Network. Available online: https://historynewsnetwork.org/article/174779 (accessed on 24 July 2022).
9. Mcdonnell, G.; Russell, A.D. Antiseptics and disinfectants: Activity, action, and resistance. *Clin. Microbiol. Rev.* **1999**, *12*, 147–179. [CrossRef] [PubMed]
10. Singh, P.; Potlia, I.; Malhotra, S.; Dubey, H.; Chauhan, H. Hand Sanitizer an Alternative to Hand Washing—A Review of Literature. *J. Adv. Oral Res.* **2020**, *11*, 137–142. [CrossRef]

11. Dyer, D.L.; Gerenraich, K.B.; Wadhams, P.S. Testing a new alcohol-free hand sanitizer to combat infection. *AORN J.* **1998**, *68*, 239–251. [CrossRef]
12. Gold, N.A.; Mirza, T.M.; Avva, U. *Alcohol Sanitizer*; StatPearls: Tampa, FL, USA, 2021.
13. Alghamdi, H.A. A need to combat COVID-19; herbal disinfection techniques, formulations and preparations of human health friendly hand sanitizers. *Saudi J. Biol. Sci.* **2021**, *28*, 3943–3947. [CrossRef]
14. Chemical Disinfectants: Disinfection & Sterilization Guidelines. Guidelines Library, Infection Control, CDC. Available online: https://www.cdc.gov/infectioncontrol/guidelines/disinfection/disinfection-methods/chemical.html (accessed on 10 July 2022).
15. Golin, A.P.; Choi, D.; Ghahary, A. Hand sanitizers: A review of ingredients, mechanisms of action, modes of delivery, and efficacy against coronaviruses. *Am. J. Infect. Control* **2020**, *48*, 1062–1067. [CrossRef] [PubMed]
16. Food and Drug Administration (FDA). *Consumer Updates Is Your Hand Sanitizer on FDA's List of Products You Should Not Use?* FDA: Silver Spring, MD, USA, 2020.
17. Song, X.; Vossebein, L.; Zille, A. Efficacy of disinfectant-impregnated wipes used for surface disinfection in hospitals: A review. *Antimicrob. Resist. Infect. Control* **2019**, *8*, 139. [CrossRef] [PubMed]
18. Marumure, J.; Makuvara, Z.; Alufasi, R.; Chapungu, L.; Gufe, C. Effectiveness of hand sanitizers in the prevention of COVID-19 and related public health concerns: A review. *Cogent Public Health* **2022**, *9*, 2060904. [CrossRef]
19. Jing, J.L.J.; Yi, T.P.; Bose, R.J.C.; McCarthy, J.R.; Tharmalingam, N.; Madheswaran, T. Hand Sanitizers: A Review on Formulation Aspects, Adverse Effects, and Regulations. *Int. J. Environ. Res. Public. Health* **2020**, *17*, 3226. [CrossRef] [PubMed]
20. APIC Guideline for Hand Washing and Hand Antisepsis in Health-Care Settings—Semantic Scholar. Available online: https://www.semanticscholar.org/paper/APIC-Guideline-for-Hand-Washing-and-Hand-Antisepsis-Larson/393a7a66a4698f7a9cc10442b85fa3656e5bd0b9 (accessed on 10 July 2022).
21. Larson, E. Guideline for use of topical antimicrobial agents. *Am. J. Infect. Control* **1988**, *16*, 253–266. [CrossRef]
22. Kampf, G.; Kramer, A. Epidemiologic background of hand hygiene and evaluation of the most important agents for scrubs and rubs. *Clin. Microbiol. Rev.* **2004**, *17*, 863–893. [CrossRef]
23. Jones, R.D.; Jampani, H.B.; Newman, J.L.; Lee, A.S. Triclosan: A review of effectiveness and safety in health care settings. *Am. J. Infect. Control* **2000**, *28*, 184–196. [CrossRef]
24. Fahimipour, A.K.; Ben Maamar, S.; McFarland, A.G.; Blaustein, R.A.; Chen, J.; Glawe, A.J.; Kline, J.; Green, J.L.; Halden, R.U.; Van Den Wymelenberg, K.; et al. Antimicrobial Chemicals Associate with Microbial Function and Antibiotic Resistance Indoors. *mSystems* **2018**, *3*, e00200-18. [CrossRef]
25. Cosar, B.; Karagulleoglu, Z.Y.; Unal, S.; Ince, A.T.; Uncuoglu, D.B.; Tuncer, G.; Kilinc, B.R.; Ozkan, Y.E.; Ozkoc, H.C.; Demir, I.N.; et al. SARS-CoV-2 Mutations and their Viral Variants. *Cytokine Growth Factor Rev.* **2022**, *63*, 10–22. [CrossRef]
26. SARS-CoV-2 Variant Classifications and Definitions. Available online: https://stacks.cdc.gov/view/cdc/105817 (accessed on 26 July 2022).
27. Basit, A.; Ali, T.; Ur Rehman, S. Truncated human angiotensin converting enzyme 2; a potential inhibitor of SARS-CoV-2 spike glycoprotein and potent COVID-19 therapeutic agent. *J. Biomol. Struct. Dyn.* **2021**, *39*, 3605–3614. [CrossRef]
28. Monpara, J.D.; Sodha, S.J.; Gupta, P.K. COVID-19 associated complications and potential therapeutic targets. *Eur. J. Pharmacol.* **2020**, *886*, 173548. [CrossRef] [PubMed]
29. Harapan, H.; Itoh, N.; Yufika, A.; Winardi, W.; Keam, S.; Te, H.; Megawati, D.; Hayati, Z.; Wagner, A.L.; Mudatsir, M. Coronavirus disease 2019 (COVID-19): A literature review. *J. Infect. Public Health* **2020**, *13*, 667. [CrossRef]
30. Schoch, C.L.; Ciufo, S.; Domrachev, M.; Hotton, C.L.; Kannan, S.; Khovanskaya, R.; Leipe, D.; McVeigh, R.; O'Neill, K.; Robbertse, B.; et al. NCBI Taxonomy: A comprehensive update on curation, resources and tools. *Database* **2020**, *2020*, baaa062. [CrossRef]
31. Dhama, K.; Patel, S.K.; Kumar, R.; Masand, R.; Rana, J.; Yatoo, M.I.; Tiwari, R.; Sharun, K.; Mohapatra, R.K.; Natesan, S.; et al. The role of disinfectants and sanitizers during COVID-19 pandemic: Advantages and deleterious effects on humans and the environment. *Environ. Sci. Pollut. Res. Int.* **2021**, *28*, 34211. [CrossRef] [PubMed]
32. Prajapati, P.; Desai, H.; Chandarana, C. Hand sanitizers as a preventive measure in COVID-19 pandemic, its characteristics, and harmful effects: A review. *J. Egypt. Public Health Assoc.* **2022**, *97*, 6. [CrossRef] [PubMed]
33. Abuga, K.; Nyamweya, N. Alcohol-Based Hand Sanitizers in COVID-19 Prevention: A Multidimensional Perspective. *Pharmacy* **2021**, *9*, 64. [CrossRef]
34. McIntosh, K. COVID-19: Epidemiology, virology, and prevention—UpToDate. *UpToDate Off. Repr.* **2022**, *202*, 126981.
35. Natnael, T.; Adane, M.; Goraw, S. Hand hygiene practices during the COVID-19 pandemic and associated factors among barbers and beauty salon workers in Ethiopia. *PLoS ONE* **2022**, *17*, e0269225. [CrossRef]
36. Mahmood, A.; Eqan, M.; Pervez, S.; Alghamdi, H.A.; Tabinda, A.B.; Yasar, A.; Brindhadevi, K.; Pugazhendhi, A. COVID-19 and frequent use of hand sanitizers; human health and environmental hazards by exposure pathways. *Sci. Total Environ.* **2020**, *742*, 140561. [CrossRef]
37. Berardi, A.; Perinelli, D.R.; Merchant, H.A.; Bisharat, L.; Basheti, I.A.; Bonacucina, G.; Cespi, M.; Palmieri, G.F. Hand sanitisers amid COVID-19: A critical review of alcohol-based products on the market and formulation approaches to respond to increasing demand. *Int. J. Pharm.* **2020**, *584*, 119431. [CrossRef]
38. Alzyood, M.; Jackson, D.; Aveyard, H.; Brooke, J. COVID-19 reinforces the importance of handwashing. *J. Clin. Nurs.* **2020**, *29*, 2760–2761. [CrossRef]

39. Chen, X.; Rahman, M.K.; Rana, M.S.; Gazi, M.A.I.; Rahaman, M.A.; Nawi, N.C. Predicting Consumer Green Product Purchase Attitudes and Behavioral Intention During COVID-19 Pandemic. *Front. Psychol.* **2022**, *12*, 760051. [CrossRef]
40. Chalkidou, K.; Claxton, K.; Silverman, R.; Yadav, P. Value-based tiered pricing for universal health coverage: An idea worth revisiting. *Gates Open Res.* **2020**, *4*, 16. [CrossRef]
41. Lee, J.; Lee, J.-Y.; Cho, S.-M.; Yoon, K.-C.; Kim, Y.J.; Kim, K.G. Design of Automatic Hand Sanitizer System Compatible with Various Containers. *Healthc. Inform. Res.* **2020**, *26*, 243–247. [CrossRef]
42. Jang, Y.; Kim, H.; Yang, S.Y.; Jung, J.; Oh, J. Bioactive multiple-bent MWCNTs for sensitive and reliable electrochemical detection of picomolar-level C-reactive proteins. *Nanoscale* **2020**, *12*, 9980–9990. [CrossRef]
43. Sheth, J. Impact of COVID-19 on consumer behavior: Will the old habits return or die? *J. Bus. Res.* **2020**, *117*, 280–283. [CrossRef]
44. Donde, O.O.; Atoni, E.; Muia, A.W.; Yillia, P.T. COVID-19 pandemic: Water, sanitation and hygiene (WASH) as a critical control measure remains a major challenge in low-income countries. *Water Res.* **2021**, *191*, 116793. [CrossRef]
45. To, K.K.-W.; Sridhar, S.; Chiu, K.H.-Y.; Hung, D.L.-L.; Li, X.; Hung, I.F.-N.; Tam, A.R.; Chung, T.W.-H.; Chan, J.F.-W.; Zhang, A.J.-X.; et al. Lessons learned 1 year after SARS-CoV-2 emergence leading to COVID-19 pandemic. *Emerg. Microbes Infect.* **2021**, *10*, 507–535. [CrossRef]
46. Matatiele, P.; Southon, B.; Dabula, B.; Marageni, T.; Poongavanum, P.; Kgarebe, B. Assessment of quality of alcohol-based hand sanitizers used in Johannesburg area during the COVID-19 pandemic. *Sci. Rep.* **2022**, *12*, 4231. [CrossRef]
47. Muleba, L.; Van Wyk, R.; Pienaar, J.; Ratshikhopha, E.; Singh, T. Assessment of Anti-Bacterial Effectiveness of Hand Sanitizers Commonly Used in South Africa. *Int. J. Environ. Res. Public. Health* **2022**, *19*, 9245. [CrossRef]
48. Selam, M.N.; Habte, B.M.; Marew, T.; Bitew, M.; Getachew, T.; Getachew, S.; Abate, A.; Mitiku, M.; Matsabisa, M.; Birhanu, G. Evaluation of quality and antimicrobial efficacy of locally manufactured alcohol-based hand sanitizers marketed in Addis Ababa, Ethiopia in the era of COVID-19. *Antimicrob. Resist. Infect. Control* **2022**, *11*, 126. [CrossRef]
49. Abuga, K.; Nyamweya, N.; King'ondu, O. Quality of Alcohol Based Hand Sanitizers Marketed in the Nairobi Metropolitan Area. *East Cent. Afr. J. Pharm. Sci.* **2021**, *24*, 29–37.
50. Othaim, I.A.A.; Al-Mutari, T.F.; Bakiri, N.S.; Shehail, K.M.B.; Al-Enazi, F.K.; Aldawsari, F.S.; Suhaibani, A.S.A.; Alshehri, Y.M. Evaluation of the Quality and Safety of Hand Sanitizers Marketed in Saudi Arabia. *Health* **2022**, *14*, 523–534. [CrossRef]
51. Mustafa, R.; Purdy, S.K.; Nelson, F.B.; Tse, T.J.; Wiens, D.J.; Shen, J.; Reaney, M.J.T. Canadian policy changes for alcohol-based hand rubs during the COVID-19 pandemic and unintended risks. *World Med. Health Policy* **2021**, *13*, 1–13. [CrossRef] [PubMed]
52. Desye, B. COVID-19 Pandemic and Water, Sanitation, and Hygiene: Impacts, Challenges, and Mitigation Strategies. *Environ. Health Insights* **2021**, *15*, 11786302211029448. [CrossRef]
53. Long, M.J.C.; Aye, Y. Science's Response to COVID-19. *ChemMedChem* **2021**, *16*, 2288–2314. [CrossRef]
54. Majiya, H.; Galstyan, A. Potential of a methanolic extract of *Lawsonia inermis* (L.) leaf as an alternative sanitiser in the time of COVID-19 Pandemic and beyond. *J. Herb. Med.* **2023**, *38*, 100633. [CrossRef]
55. Rahman, S.; Khan, I.; Oh, D.-H. Electrolyzed Water as a Novel Sanitizer in the Food Industry: Current Trends and Future Perspectives. *Compr. Rev. Food Sci. Food Saf.* **2016**, *15*, 471–490. [CrossRef]
56. Giné-Garriga, R.; Delepiere, A.; Ward, R.; Alvarez-Sala, J.; Alvarez-Murillo, I.; Mariezcurrena, V.; Sandberg, H.G.; Saikia, P.; Avello, P.; Thakar, K.; et al. COVID-19 water, sanitation, and hygiene response: Review of measures and initiatives adopted by governments, regulators, utilities, and other stakeholders in 84 countries. *Sci. Total Environ.* **2021**, *795*, 148789. [CrossRef]
57. Egner, P.; Pavlačková, J.; Sedlaříková, J.; Pleva, P.; Mokrejš, P.; Janalíková, M. Non-Alcohol Hand Sanitiser Gels with Mandelic Acid and Essential Oils. *Int. J. Mol. Sci.* **2023**, *24*, 3855. [CrossRef]
58. Hidayat, R.; Wulandari, P. The efficacy and safety of electrolyzed water against COVID-19 as an alternative hand sanitizer. *Med. Glas. Off. Publ. Med. Assoc. Zenica-Doboj Cant. Bosnia Herzeg.* **2022**, *19*, 229–233. [CrossRef]
59. Dehal, A.; Vaidya, A.N.; Kumar, A.R. Biomedical waste generation and management during COVID-19 pandemic in India: Challenges and possible management strategies. *Environ. Sci. Pollut. Res. Int.* **2022**, *29*, 14830–14845. [CrossRef] [PubMed]
60. Dhawan, M.; Saied, A.A.; Mitra, S.; Alhumaydhi, F.A.; Emran, T.B.; Wilairatana, P. Omicron variant (B.1.1.529) and its sublineages: What do we know so far amid the emergence of recombinant variants of SARS-CoV-2? *Biomed. Pharmacother. Biomed. Pharmacother.* **2022**, *154*, 113522. [CrossRef] [PubMed]
61. Lobie, T.A.; Roba, A.A.; Booth, J.A.; Kristiansen, K.I.; Aseffa, A.; Skarstad, K.; Bjørås, M. Antimicrobial resistance: A challenge awaiting the post-COVID-19 era. *Int. J. Infect. Dis.* **2021**, *111*, 322–325. [CrossRef] [PubMed]
62. Lin, Q.; Lim, J.Y.C.; Xue, K.; Yew, P.Y.M.; Owh, C.; Chee, P.L.; Loh, X.J. Sanitizing agents for virus inactivation and disinfection. *View* **2020**, *1*, e16. [CrossRef]
63. Dancer, S.J. Controlling hospital-acquired infection: Focus on the role of the environment and new technologies for decontamination. *Clin. Microbiol. Rev.* **2014**, *27*, 665–690. [CrossRef]
64. Majumder, S. Antimicrobial Assessment of a Novel Humectant-Hand-Sanitizer against Microbes Transferred to Human Palms from Mobile Phones With/Without Flip Covers. *Ann. Adv. Biomed. Sci.* **2022**, *5*, 000176. [CrossRef]