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Sanitizer: Corona and Boom in the Market

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ABSTRACT

Background: Hand hygiene is a simple and efficient strategy for minimizing illness transmission in public and clinical settings. The development of SARS-CoV-2 has created enormous challenge to global public health. Currently, the efforts to prevent COVID-19 are supportive with a goal of minimizing transmission.

Method: In this review, an extensive literature search was performed with help of various search engines such as Google, Google Scholar, sci-hub, Science direct, Pub med. The authors have summarized the active ingredients and mechanism of action of benzalkonium chloride and alcohol against bacteria and viruses. Various research reports and patents that have been formulated hand sanitizers to prevent virus has been compiled in this article.

Results: From the literature, it was observed that alcohol-based hand sanitizers can efficiently disturb the activity of encapsulated bacteria's or viruses. Researchers found that there are various forms of hand sanitizer's i.e. liquid, gel, foam, spray and wipes and recommending best method of delivery out of these is difficult. Two basic requirements of hand sanitizers for maintaining hand hygiene is its compliance and its coverage to the whole hand.

Conclusions: The viruses and bacteria's causing disease should be successful in eliminating them with the help of current hand hygiene solutions. After reviewing the literature, it is concluded that there is a vast scope in development of hand hygiene products.

1. Introduction

Nowadays, hand hygiene is regarded as one of the most crucial parameter of infection control measures. In response to the rising number of health care associated infections (HCAIs), the severity of illness and complexity of treatment, as well as the multi-drug resistant pathogen infections, healthcare professionals are returning to the fundamentals of infection prevention by washing their hands (http://www.who.int/patientsafety/en/; http://www.who.int/patientsafety/en). In healthcare institutions, hand hygiene alone can significantly reduce the risk of infection cross-transmission (Daniels & Rees, 1999). Since 2015, the population with access to basic services has grown by nearly 500 million, from 5.0 billion to 5.5 billion, at a rate of 300,000 people per day. However, 2.3 billion people still lacked basic services. In 2020, 2.3 billion people were still in need of basic amenities, including 670 million who had no access to any hand washing stations (https://data.unicef.org/topic/water-and-sanitation/hygiene/). There are two types of bacteria's that reside and colonize hands *i.e.* resident flora, which consists of microorganisms living underneath the stratum corneum's surface cells and the transient flora, which colonizes skin's outermost layers and is more readily eradicated by regular hand hygiene. Transient bacteria can survive on the skin but they hardly replicates on skin. They are usually obtained by healthcare workers through close contact with patients or their nearby contaminated environmental surfaces. Healthcare workers are the only ones which are most frequently connected to HCAIs (Rotter, 1997).

New viral or bacterial infections have long constituted a serious risk to global public health problems (Golin *et al.,* 2020). Recently, coronavirus (COVID-19) has become major global public health problem in 2019. It is an infectious virus that is spreading all over the world. This pandemic has drawn people's attention to hand hygiene *via* using hand hygiene products (https://virusncov.com/; https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases). COVID-19 is a contagious ailment, which spreads through an infection caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)" strain. It can be passed from one person to another through close contact or by touching everyday objects. When a person sneezes 20,000 droplets of germs or viruses are released. If

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any infected person with SARS-CoV-2 touches any surface, the virus gets attached to that surface and can stay live up to 9 days at that surface and can infect others. As the virus enters the body, it attaches to the host, replicates its functions, assembles itself and then releases into the bloodstream (Kampf *et al.,* 2020). The hands of healthcare professionals are frequently colonized with pathogens such as methiciliin resistant *S. aureus*, multi-drug resistant-gram negative bacteria, vancomycin resistant *enterococcus*, *clostridium difficle* and candida species and can survive for more than 150 hr on hands. Critical care areas such as touching patient intact skin, artificial objects in patients, during cleaning processes and measuring patient blood pressure is said to have the greatest prevalence of hand contamination (Smith, 2009; Noble, 1975). Therefore, it is mandatory to keep hand hygiene from spreading transmission of virus or prevention of infection (Boyce & Pittet, 2002). Another ways established by the government by which we can avoid the viral infections is to maintain a 3-foot space from others in public space, wearing masks and staying at home (Chan *et al.,* 2020). Above all, the "centers for disease control and prevention" suggests hand cleanliness and wearing mask is the best method to prevent the spread of infection (https://www.cdc.gov/coronavirus/2019-ncov/prepare/prevention.html; Jing *et al.,* 2020; Mathur, 2011).

Maintaining hand hygiene means washing your hands regularly with soap & water or sanitizers, not touching the surfaces or objects at public places. We should wash our hands with water and soap when they are visible soiled, contaminated with proteinaceous material such as blood or other bodily fluids; after using rest rooms and also, after and before having food (Pittet *et al.,* 2000). Hand sanitizers are required to have fungicidal, virucidal and bactericidal action. Hand hygiene healthcare compliance is affected by a number of factors including those that are specific to healthcare system, clinical issues, environmental, institutional and behavioral factors [Erasmus *et al.,* 2009]. Various hand hygiene products are available in market such as alcohol-based rub, antiseptic agent, antimicrobial soap, antiseptic hand wipe, detergents, plain soap and waterless antiseptic agents (https://pubmed.ncbi.nlm.nih.gov/23805438/) are discussed in Table 1.

Table 1: Various hand hygiene products available in market.

HAND HYGIENE PRODUCTS	DEFINITION	MARKETED FORMULATIONS
Alcohol based rub	A liquid, gel or foam that contains alcohol, intended to be applied to the hands to either inactivate or temporary restrict the growth of germs. These formulations might include humectants, additional active substances with excipients and containing one or more types of alcohol	Sterlomax (80% ethanol-based handrub)
Antimicrobial (medicated) soap	A detergent or soap that contains an antiseptic ingredient in a concentration high enough to kill bacteria or temporarily stop their growth.	Danil (Anti-fungal soap), Aknobest (Anti-acne medicated soap), Candid soap, Ketnex soap
Antiseptic hand wipe	An antiseptic-prewetted piece of fabric or paper used to wipe hands to inactivate or eliminate microbiological contamination. They are less effective than alcohol based hand rubs or washing hands.	WetOnes antibacterial hand wipes
Detergent (surfactant)	Compounds that are composed of hydrophilic and lipophilic part, possessing a cleaning action.	Cremphor RH 40, Span 20, Polysorbate 80, Gelucire 44
Plain soap	Products that do not contain antibacterial agents in them and consists only preservatives	Woosch, Olive, Dove
Waterless antiseptic agents	Antiseptics that does not need external water. The user rubs their hands together to make the skin feel dry after application.	Puridene Lupisafe

In the case, when water and soap is unavailable or occurrence of scaling and fissures on skin, then the hand sanitizers can be used. Hand sanitizer eliminates the bacteria and viruses on the hands and is a preventive measure in controlling infections. Alcohol is one of the important ingredients used in the preparation of sanitizers and it can inactivate bacteria/

virus *via* denaturation of proteins targeting primary site of action on cell membrane. In global market, alcohol-based hand sanitizers such as ethanol, propanol, iso-propanol *etc.* are effective against lipophilic viruses and these have the biggest market share (Suen *et al.,* 2019). Ethanol is widely used in preparation of hand sanitizers because it can act against enveloped as well as non-enveloped viruses whereas; propanol and iso-propanol alcohols are effective against only enveloped viruses (www.cdc.gov/handsanitizer). This review consists of various types of hand sanitizers, mechanism of alcohol and benzalkonium chloride against bacteria and viruses. Various research reports are also included in this article containing various sanitizer formulations inhibiting bacteria and viruses. Clinical data or patents that are filed or are in clinical trials is also included.

2. Types of Hand Sanitizer

Basically, hand sanitizers are separated into two types: alcohol-free sanitizers and alcohol-based sanitizers. Alcohol-free hand sanitizers are those which do not contain any alcohol and are inflammable. They keep skin moisturize and helps to prevent skin dryness. Alcohol-based hand sanitizers contain alcohol as its active ingredient, various excipients to make its volume and humectants. These are applied to hand to maintain their hand hygiene. Alcohols having a broad germicidal activity range can be used to stop or kill microorganisms present on hand. Alcohol based hand sanitizers do not act to protozoa, few non-enveloped bacteria and viruses' spores (Andal *et al.,* 2021). There are various advantages and disadvantages associated with hand sanitizers, described in Figure 1.

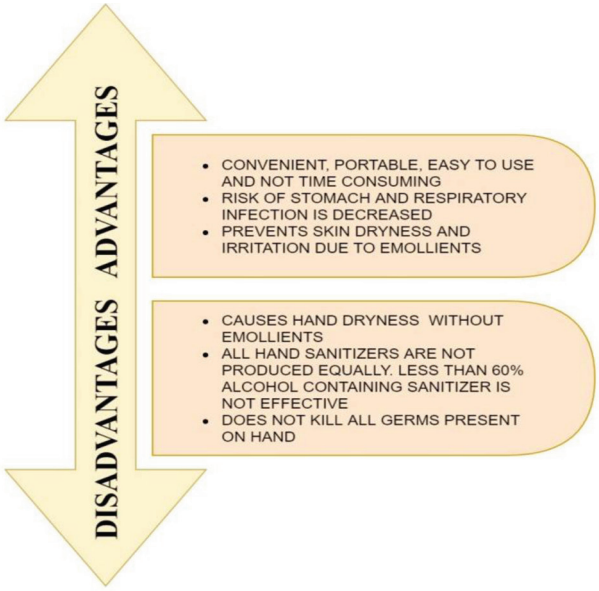

Figure 1: Advantages and disadvantages of hand sanitizer.

Hand sanitizers can be divided into several categories based on the active ingredients they contain and are classified as:

1. **Alcohol-based:** Alcohol-based products typically contain 60-95% of alcohol. Various alcohols are used in preparation of hand sanitizers such as ethanol, propanol and isopropanol. Alcohols have polar and non-polar end. The non polar end of alcohol helps to penetrate into membrane and is effective in denaturing the proteins and thus, inactivates the microorganism. Alcohol based hand sanitizers either inactivates the microorganism or temporarily suppresses microorganism growth (Jing *et al.,* 2020; Sax *et al.,* 2007).
2. **Alcohol-free:** Alcohol-free hand sanitizers are those which do not contain any alcohol, generally based on disinfectants, such as benzalkonium chloride or on antimicrobial agents, such as triclosan. These are basically inflammable in nature. The efficiency of antimicrobials or disinfectants may be immediate or persistent (Pittet *et al.,* 2009; kampf, 2018).

Diagrammatically, the active ingredients of alcohol-based hand sanitizers and alcohol free hand sanitizers are shown in Figure 2.

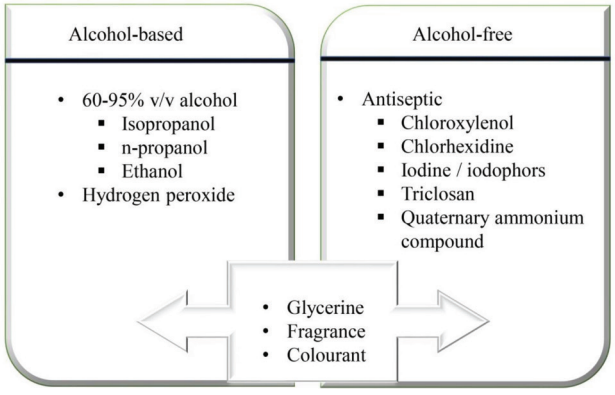

Figure 2: Classification of hand sanitizers.

Many hand sanitizers also contain emollients, thickening agents and fragrance. Instead of alcohol, quaternary ammonium compounds (also known as benzalkonium chloride) are used in alcohol-free hand sanitizers to kill microorganisms. These compounds are not as effective as alcohols based. Thus, alcohol- based sanitizers are preferred over alcohol-free sanitizers. In public places, hands may become quite oily or soiled after handling food, working in garden, participating in sports, and while camping and fishing. Hand sanitizers are frequently used since they are simple to find, don't require water or plumbing and have been shown to be effective at lowering microbial load (Thomas, 2012).

3. Mechanism of Action of Hand Sanitizers Against Viruses and Bacteria's

3.1. Alcohol Mechanism of Action Against Bacteria

Alcohol's antibacterial effects are associated with membrane damage, protein denaturation and inhibition or decoupling of mRNA and protein synthesis *via* RNA polymerase and ribosomes. For activity against bacteria, 60-90% concentration of alcohol is required for effective bactericidal activity. It has an impact on vital metabolic processes, membrane damage and cellular integrity (shown in Figure 3). It has bactericidal effect against vegetative bacteria but not against spores. Absolute alcohol or alcohol with a water content of less than 1% has a lower bactericidal effect than alcohol in the middle of the range. Water is therefore essential for the denaturation of proteins (Dastider *et al.,* 2020; Wood & Payne, 1998).

3.2. Alcohol Mechanism of Action Against Viruses

The host lipid, a protein capsid that contains and protects the genetic material envelope is used to generate viral envelope. The main viral targets of alcohol-based hand sanitizers are the genetic components themselves. It makes sense to think that altering the structure or function of any one of these components will make the virus ineffective because they are all necessary for the viral life cycle (e.g., attachment, penetration, biosynthesis, maturation and lysis) (shown in Figure 3). Although the specific method by which alcohols interact with viruses is less understood than the mechanism by which they interact with bacteria, it is known that ethanol has a broader and stronger virucidal effect than propanol. High ethanol concentrations have been shown to be quite effective against enveloped viruses, which make up the majority of clinically significant viruses. Acids can be added to ethanol solutions to increase their potency against viruses that are resistant to just ethanol. Even with the potential synergy between ethanol and acidity, non-enveloped viruses are still resistant to the majority of hand sanitizers (Wessels & Ingmer, 2013).

3.3. Benzalkonium Chloride Mechanism of Action

The main component of non alcoholic hand sanitizer, benzalkonium chloride, is typically efficient against non-enveloped viruses. The lipid envelopes of bacteria and viruses are important components of benzalkonium chloride efficacy. The fluidity of the membrane declines as benzalkonium chloride concentration increases, causing the membrane to develop hydrophilic pores. Additionally, by infilterating the barrier and disturbing its physical and biological characteritics, the alkyl chain component of benzalkonium chloride further perturbs and disrupts the membrane bilayer. Protein function is then disrupted, resulting in the solubilization of bilayer materials into benzalkonium chloride/ phospholipid micelles as a result of the aforesaid impacts. Benzalkonium chloride also disturbs DNA structural behavior and intercellular targets (Zinchenko *et al.,* 2004; Jing *et al.,* 2020).

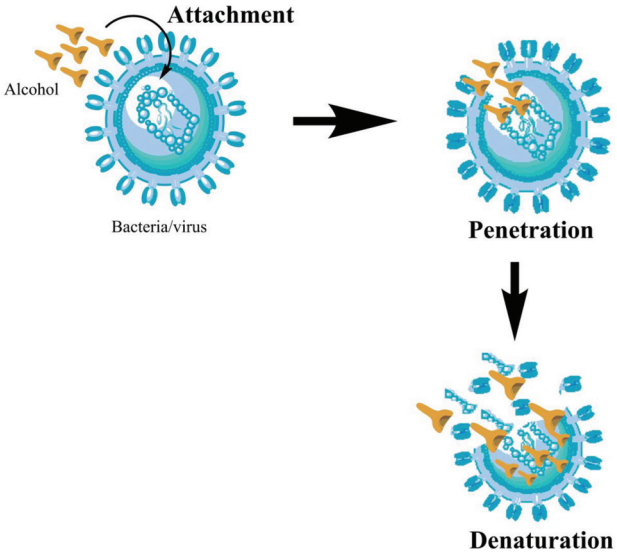

Figure 3: Basic mechanism of alcohol on bacteria and virus.

4. Agents Used in Hand Hygiene Products

Hand hygiene efficiency combines hand drying and washing efficiency. According to empirical data, hand washing is about 85% successful in removing bacteria from hands and hand drying further reduces transient flora. Comparatively to fully dried hands, inadequately dried hands are more likely to spread microbes (Suen *et al.,* 2019). The most crucial variables to take into account when selecting a hand hygiene solution are the antimicrobial profile, user approval and price (Kampf & Kramer, 2004). Post contamination hand hygiene products must have bactericidal, fungicidal and virucidal activities. One of the most crucial ways to increase hand cleanliness is to use alcohol-based hand rub instead of soap and water (Larson, 1999; Boyce, 2001; Trampuz & Widmer, 2004). Compared to an alcohol-based hand rub, traditional hand washing with soap and water takes longer, is less efficient against microorganisms and causes greater skin irritation (https://aapcc.org/tra ck/hand-sanitizer). The various hand hygiene products such as non-

medicated soaps, chlorhexidine, alcohols, chloroxylenol, iodine and iodophores, hexachlorophene, quaternary ammonium compounds and triclosan has been described in Table 2 with its concentration, activity, advantages and disadvantages (https://www.techsciresearch.com/report/india-hand-sanitizer-market/4484.html).

Table 2: Various hand hygiene products with its concentration, action, advantages and disadvantages.

Agents	Concentration	Activity	Advantages	Disadvantages
Non-medicated soaps	-	Non-microbicidal	Removes dirt or any other material	Do not have any antimicrobial activity
Alcohols	60-95%	Active against gram positive, gram negative bacteria, enveloped viruses, mycobacteria, Fungi	Fast action effectively reduces bacterial counts	They cannot be used when hands are clearly dirty or contaminated with protein-containing substances
Chlorhexidine	0.5-4%	Active against gram positive	Safe and completely allergy free Lightly impacted by organic material, including blood	Slower acting than alcohol Toxic to meninges, brain, eyes and ears Skin irritability depending on concentration
chloroxylenol	0.5-4%	Active against gram positive	Organic matter has a negligible impact on activity Rare allergic responses	Compared to chlorhexidine, its activity is slower and leaves less traces.
Hexachlorophene	3%	Active against gram positive	Several hours of residual activity Following repeated use, gradually lowers the number of bacteria on the hands	The drug is absorbed cutaneously Cannot be used to newborns due to its neurotoxicity
Iodine & iodophors	0.5-10%	Active against gram positive, gram negative	Less skin irritant Fewer allergic reactions	Activity is reduced in the presence of organic and inorganic compounds
Quaternary ammonium compounds	-	Active against gram positive	Usually well tolerated	Antimicrobial activity is adversely affected by presence of organic material Not compatible with anionic detergent
Triclosan	0.2-2%	Active against gram positive	Persistent skin activity Activity not significantly impacted by organic matter	Activity is easily affected by pH, surfactants, emollients and humectants

5. Biosafety and Environmental Concerns of Alcohol-Based Hand Sanitizers

The flammability of alcohol and toxicity from accidental intake of the sanitizer are the general safety concerns related to alcohol-based hand sanitizers. Alcohol and isopropyl alcohol are poisonous to aquatic life when they spill in bodies of water, but they can also contaminate groundwater when they spill in significant quantities on the soil. Although the main ingredients in hand sanitizers such as alcohol and hydrogen peroxide are not hazardous from the outside, excessive use of hand sanitizers raises concerns about skin damage, which might impair the skin's capacity to defend against other viruses or bacteria (Tambekar *et al.,* 2007). Children under the age of 12 are particularly vulnerable to accidental intake. Even a modest amount of alcohol can result in alcohol can result in alcohol toxicit in youngsters. Hand sanitizers are therefore considered emergent dangers by the the American association of poison control center (AAPCC). According to the AAPCC, poison control centres have handled 23,529 exposure incidents involving hand sanitizer in children aged 12 and under as of December 2021 (Stauffer *et al.,* 2013).

6. Basic Requirements of Hand Sanitizer

The most widely used brands of alcohol hand rubs include Allsept S, Aniosgel, Avant, Sterillium, and Desderman. Since 1995, Aplet E3 plus Hand Sanitizer Spray, Aplet E3 Hand Sanitizer Spray, and Smart-San Hand Sanitizer are just a few of the several hand sanitizers that Best Sanitizers, Inc. offers. Aplet E3 plus Hand Sanitizer Spray is created with moisturisers to keep hands soft and healthy, and it eliminates 99.9999% of 26 tested germs in 15 seconds (Lens *et al.,* 2011). The Lifebuoy brand created a color-changing hand sanitizer to make washing hands enjoyable for kids. The innovative liquid hand wash offers 99.9% germ prevention and transforms from white to green in just 10 seconds. According to requirements like EN 12054 for hygienic treatment and surgical disinfection by hand-rubbing, all hospital hand rubs must be compliant. Since the reduction must be greater than "99.99%," products that make claims of "99.99% reduction" or "4-log reduction" are ineffective in a hospital ward. (https://www.health.state.mn.us/people/handhygiene/clean/howrub.html). Hospital hand sanitizer dosing systems are made to give staff members a precise dosage of the product. There are dosage pumps that screw onto bottles or there are dispensers with refill bottles that are particularly made. In order to prevent any contact with the pump, dispensers for surgical hand disinfection are typically fitted with elbow-controlled mechanisms or infrared sensors. Reckitt Benckiser (India) Private Limited, ITC Limited, Dabur India Limited, Hindustan Unilever Limited, The Himalaya Drug Company, Pristine Care Products Private Limited, Wipro Consumer Care Limited, Colgate Palmolive (India) Limited, Godrej Consumer Products Limited, Herbal Strategy, and others are significant market participants in the Indian hand sanitizer market. To accommodate rising customer demand, major market participants are concentrating on increasing their production capacity and implementing cutting-edge technology (Khadse & Murthy, 2021).

6.1. Procedure to Use Hand Sanitizer

Utilize a hand sanitizer with at least 60% alcohol in it. The protective covering of the germ is broken down by the sanitizer, which kills the microbe. According to the CDC, users should apply the recommended amount of a product to one palm, and then cover all hand surfaces and massage them together until they feel dry. If you remove the hand sanitizer from your hands before it has dried, it won't be as effective and could let some bacteria get out and possibly mutate (Ghosh *et al*., 2020).

7. Hand Sanitizer: Market

The market for hand sanitizers is expected to grow as consumers become more aware of the value of good hand hygiene for preventing the spread of infectious diseases through advertising efforts and media coverage. The worldwide hand sanitizer market is showing signs of a new trend as a result of advancements in hand sanitizers, such as novel formulations with fragrances. One of the main factors contributing to the growth of the hand sanitizer market in emerging countries is anticipated to be the people's shifting lifestyle and adoption of western values in their habits (Neufeld *et al.,* 2020). The largest portion of the worldwide hand sanitizers market is accounted well by hospitals. The majority of hand sanitizers are produced by licenced pharmacists, according to the world health organisation (WHO). The majority of the manufacturing takes place in national drug corporations and hospital pharmacies. To stop the transmission of contagious infections, employees, patients, physicians, and visitors all use hand sanitizers (Aodah *et al.,* 2021). Recent research reports from IndustryARC estimate the market's size to be between $1,350 million and $1,400 million as of 2018, and the demand for the product is anticipated to increase at a strong CAGR of 6.5% to 7.5% from 2019 to 2025.

8. Various Research Reports on Hand Sanitizers

The majority of hand sanitizers on the market are made comprised of isopropyl alcohols, hydrogen peroxide and ethanol in different combinations. Misuse of hand sanitizers or not knowing the accurate procedure to use hand sanitizers can be hazardous to environment and human health. According to the AAPCC, aforementioned exposure caused nausea, confusion, respiratory arrests, lethargy and even deaths in children. Repeated usage of hand sanitizers has also been connected to a higher risk of developing antibiotic resistance and viral infections. The risks to human health and the environment linked with the regular use of alcohol-based hand sanitizers were recently detailed in above section of this review. The toxicity problem might be resolved by modifying alternative hand sanitizer formulations based on natural and botanical resources. During COVID-19, medicinal plants with proven antiviral and disinfection properties can be used as a substitute to hand massages containing alcohol. Numerous plants with broad-spectrum antiviral activities have been reported and published which are discussed below:

Benzalkonium chloride containing non-alcoholic hand sanitizer gel was prepared and evaluated for irritancy and persistency. Results concluded that hand gel was having pH 6.3, low viscosity, high spreadability. Ten people were tested with the hand gel, and the results revealed no skin irritation nor redness after use. As a result, this alcohol-free hand sanitizer is recommended as a possible substitute for hand

gels that include alcohol (Aodah et al., 2021). Another study was reported with preparing benzalkonium chloride hand sanitizer and was tested for activity against SARS-CoV-2. The findings demonstrated that the prepared hand sanitizer showed virucidal activity against SARS-CoV-2. It can reduce SARS-CoV-2 action in 30 seconds. Therefore, it was determined that hand washing with benzalkonium chloride could be another successful method of inactivating the SARS-CoV-2 virus and could be taken into consideration for pandemic response (Herdt et al., 2021). Akpeteshie, a traditional beverage from Ghana, was used as the source of ethanol for the creation of a high-quality, reasonably priced sanitizer. Using the microbial time-kill kinetics experiment, the formulation's effectiveness against Vibrio cholerae was assessed. The results showed that akpeteshie was efficient against Vibrio cholerae and had a higher than 70% alcohol content. There was a gradual decrease in the number of microbes present after exposure to the organisms for different amounts of time, such as 0, 5, 15, 30, 60, and 120 minutes (Osei-Asare et al., 2020). 0.12% benzalkonium chloride containing hand sanitizer was prepared and concluded that prepared formulation showed significant results in reduction of S. aureus bacterial count within a week as compared to using 70% ethanol sanitizers (Bondurant et al., 2020). Researchers used 3 commercially available quaternary ammonium compound disinfectants and one prepared in lab with 0.2% benzalkonium chloride solution to conduct suspension tests against SARS-CoV-2. Even in the presence of dirt load or diluted with hard water, three of the four formulations was effective in inactivating the virus within 15 seconds of contact. Quaternary ammonium compound was potentially useful for inactivating SARS-CoV-2 quickly, making its potential use for preventing SARS-CoV-2 transmission in hospitals and general public (Ogilvie et al., 2021). The goal of the study was to create a natural hand sanitizer gel that contained essential oils and was efficient against a variety of infections. The outcomes demonstrated that the formulations' organoleptic properties were satisfactory. The formulation had an acidic pH. The hand gel proved efficient against several gram-positive and gram-negative bacteria, according to in-vitro antibacterial investigations. Clove oil hand sanitizers demonstrated efficiency against all microbes, including Candida albicans, while tea tree oil hand sanitizers had the strongest antibacterial impact but no activity against the yeast. The antibacterial effectiveness of the lavender hand sanitizer was the lowest. The hand sanitizer gel with 1.25% (v/v) clove oil did not cause any skin irritation, according to the acceptance study on 20 human volunteers. According to this study, a natural hand sanitizer gel produced with 1.25% (v/v) clove oil may be an effective replacement for routinely used alcohol-based hand sanitizers (ABHS) (Booq et al., 2021). The goal of the study was to describe the antibacterial activity of different herbal oils, including eucalyptus, cinnamon, lavender, and menthol. It was discovered that cinnamon oil had stronger antimicrobial properties. The formulation and evaluation of a polyherbal hand wash gel including Ocimum sanctum, Azadirachta indica, and Citrus limon extracts were also the subjects of investigation. By using spread plate techniques, the anti-microbial activity of the developed herbal hand wash gel was assessed against Staphylococcus aureus, Escherichia coli, and Salmonella. The results were then compared to industry antibacterial standards. Additionally, volunteers were used to test the effectiveness of the hand wash gel. The findings of this study suggested that prepared formulations produced superior results (Acharya et al., 2018). The leaves of tulsi and eucalyptus globules were combined with other plant extracts to create a herbal hand sanitizer (Nilgiri). The produced formulation's antibacterial effectiveness and hand safety were assessed. Pseudomonas aeuroginosa, E. coli, Bacillus subtilis, Staphylococcus aureus, and Fungi-saccharomyces cerevisiae, Candida albicans) were used to evaluate the formulation by a culture sensitivity test. The findings were discovered to be more significant than the reference (Wani et al., 2013). By combining extracts from readily accessible plants like ginger, andrographis paniculata, and lemon juice, researchers created a herbal hand wash. The formulation's physical characteristics were assessed, and the findings showed that the combination of these plant extracts acted as a reliable hand sanitizer (Grace et al., 2015). Salam bark extract was used in the formulation of and evaluation of hand sanitizer gels, which were then tested to see how well they worked against bacteria on the hands' palms. The findings showed that salam bark extract worked better in reducing the amount of bacteria on the palms (Surini et al., 2018). The focus of the study is on the potency and encouraging results of a herbal hand sanitizer made with Psidium guajava leaf extract. The majority of study has been on maintaining hygiene by preventing germs from entering the body through hands. The findings showed that organic herbal hand sanitizers are affordable, effective, and environmentally friendly (Shaikh & Bhosale, 2020). By reducing alcohol consumption, researchers created a curcumin-based herbal gel sanitizer and tested its antibacterial effectiveness. The efficacy of curcumin's anti-bacterial activity was also assessed, and it is safe and effective againstpathogens. The curcumin gel sanitizer was tested for its phytochemical constituents present in curcumin, organoleptic properties, irritancy test, and detection of the active constituent of curcumin, which was primarily responsible for the anti-microbial activity through HPTLC. The results indicated that curcumin, a common household

chemical, may be used to make a sanitizer that lowers the negative effects of alcoholic sanitizer solutions and is the best source for fighting a variety of diseases (Maddi *et al.*, 2021). Researchers found that the phenolic, flavonoid, saponin, and steroid terpenoids component in binahong leaf (Anredera cordifolia) may potentially be employed as the active ingredient in hand sanitizer gel. A hand sanitizer gel infused with binahong leaves was tested for its antibacterial activity and physical chemical characteristics against Staphylococcus aureus. By measuring the inhibition zone of each preparation, the disc diffusion method was used to test this formulation's effectiveness against a particular bacterial strain. The gel's physicochemical properties demonstrated exceptional qualities. The antibacterial test revealed that hand sanitizer gel infused with binahong's leaves has an inhibition zone that is virtually as large as a positive control (6.02 mm, 6.24 mm, and 6.55 mm) (9.15 mm). In conclusion, the developed hand sanitizer gel has the antibacterial ability to prevent S. aureus (Rahmasari et al., 2020). Moringa silver nanoparticles (MSN) were created by researchers to be used in personal hygiene products and to stop the spread of infectious illness outbreaks. The efficiency of MSN's antibacterial action in lowering the microbial population was assessed. MSN had PDI and ZP values ranging from 0.11-0.39 and 22-33 mV, respectively, and were negatively charged, stable, and modestly distributed. For manufacturing scale up and formulation investigations, formulations with yields above 50% and mean particle sizes of roughly 30 and 38 nm were chosen. As a result, it was possible to draw the conclusion that alcohol-based herbal hand sanitizers were successfully blended with synthetic MSN, showing an improvement over the industry norm and the capacity to completely remove microbial load. To stop the spread of communicable diseases outbreaks like the present COVID-19 pandemic, these innovative herbal hand sanitizers could be quickly put to use (Oyeniyi *et al.*, 2021). The hand sanitizer for snow fungus, snow mushrooms, and white jelly mushrooms was created as a moisturising alcohol-based hand rub gel. It has been demonstrated that the snow mushroom hand sanitizer moisturises skin more effectively than a placebo. The anti-septic action of the hand sanitizer was validated. The produced gel demonstrated its effectiveness in moisturising and sanitising. The product's proven skin-hydrating effectiveness allows for frequent application, which helps to maintain proper hand hygiene (Lourith *et al.*, 2021).

9. Clinical Status of Hand Sanitizers

There are several patents that are filed on invention of novel hand sanitizers that are discussed below and briefly in Table 3. Researchers formulated a hand sanitizer comprises of 50-95%.

Table 3: Various patents on invention of novel hand sanitizers.

S. No.	Patent Number	Title	Reference
1	EP 3 187 045 A1	Gel hand sanitizers	Chris *et al.,* 2005
2	WO2006085907A3	Sanitizing composition and method of preparation	Steven, 2004
3	US20090082472A1	Hand sanitizer and method of Preparation	Peters, 2009
4	WO2009109870A3	Moisturizing hand sanitizer	Berendes *et al.,* 2009
5	CA 2763063	Hand sanitizer	Bruce, 2014
6	201911043540	Alcohol free hand sanitizer and method of preparation thereof	Sindhu *et al.,* 2019

The hand sanitizers in the form of a gel, as well as techniques for making and using them, with a focus on gel-type hand sanitizers with alcohol and an enhanced antimicrobial action, as well as methods for making and using them (Chris *et al.,* 2005). The invention provides a sanitizing composition in the form of a viscous liquid or gel suitable for use as a handwash composition comprising alcohol, water and thickner wherein the viscous liquid or gel has particle suspended therein. The particles may deliver agents such as antimicrobial, antibacterial or antiviral to skin with addition of emollients, moisturizers, fragnances, coloring agents has been added in preparation of sanitizers (Steven, 2004). A sanitizing composition or hand gel composition containing a mixture of stearidonic acid and isopropyl alcohol to kill germs and bacteria. An acrylic polymer as a thickener, stabilizer or polymer acrylic acid neutralizer such as polyoxyethylene coconut alkylamine, octyl isononanoate as an emollient, glycerin as an additional moisturizer, water and other additives were used in preparation of hand sanitizer (Peters, 2009). A present study formulated moisturizing hand sanitizers including hand sanitizers including alcohols that are effective in killing microorganism while providing a moisturizing benefit to the user's skin (Berendes *et al.,* 2009). The present study relates to a hand sanitizer. The rise of hospital-acquired infections such methicillin- resistance *staphylococcus aureus* and clostridium difficile has emphasized the need for cleanliness. Effective hand sanitizing is needed for people working in a clinical environment (Bruce, 2014). The current invention is concerned with a hand sanitizer composition. The present invention is directed to an antimicrobial hand sanitizer

i.e. substantially alcohol-free and comprises of a mixture of natural oils selected from cinnamon oil, tea tree oil, lemon oil, and lavender oil. Thickening agents, moisturising agents, and water was included in preparation of hand sanitizer. The present invention's hand sanitizer compound has outstanding antibacterial characteristics (Sindhu *et al.,* 2019).

Conclusion

In conclusion, maintaining good hand hygiene is the best strategy to stop the spread of pathogens. The best way to protect oneself and patients is, if available, to properly wash one's hands with soap and water. When soap and water are not readily available, using hand sanitizer as directed is a suitable alternative. The ultimate objective of encouraging a strong patient safety culture is an improvement in hand hygiene procedures. The need to practice good hand hygiene has grown recently as a result of the corona virus. The main components of SARS-CoV-2 virus are RNA enveloped by a protein and surrounded by a lipid bilayer. The connection between these components is weak as there is no covalent link to keep the connection stable. Connection between SARS-CoV-2 lipids and alcohol-based hand sanitizer will break up the weak interactions, causing the viral component to separate from hands. Hand hygiene is one of the strategies for controlling infection as it can significantly reduce the risk of microorganism transmission. Alcohol based hand sanitizers are becoming popular because of their quick action and efficacy in destroying microbes. Hand washing with soap and water is convenient when alcohol based hand sanitizer are less effective such as in case when hands are unclean or soiled. To guarantee that all bacteria are properly eliminated, choose alcohol based hand sanitizer with the appropriate amount of alcohol and use proper hand hygiene techniques when cleansing hands. Hand hygiene products and various research reports have been compiled in the above sections. The patents filed on formulating hand sanitizer with novel agents have been also compiled in this section. Hence, emphasizing on appropriate hand hygiene is a critical first line defense against the spread of infections.

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Conflict of Interest

The authors declared no conflicts of interest.

Authorship Contribution

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