A Review on Hand Sanitizer

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ABSTRACT

Current outbreak of Covid 19 has made us mandatory of using hand sanitizers everywhere. The hand hygiene is now being very essential in the public. Compliance with hand hygiene recommendations is critical to reducing colonization and infection of the hands of all people. Hand hygiene is of utmost importance because it may be contaminated easily from direct contact with airborne microorganism droplets from coughs and sneezes. Particularly in situations like pandemic outbreak, it is crucial to interrupt and cut the transmission chain of the virus by the practice of proper hand sanitization. The use of hand sanitizers drastically reduce the transmission of microorganisms to patients, ultimately reducing morbidity, mortality, and costs associated with healthcare-associated infections (HCAI). It can be achieved with contact isolation and strict infection control tool like maintaining good hand hygiene in hospital settings and in public. The success of the hand sanitization solely depends on the use of effective hand disinfecting agents formulated in various types and forms such as bath soaps, water-based or alcohol-based hand sanitizer, with the latter being widely used in hospital settings. To date, most of the effective hand sanitizer products are alcohol-based formulations containing 70%–95% of alcohol as it can denature the proteins of microbes and the ability to inactivate viruses. The present study correlated with the data available in Pubmed, and it will investigate the range of available hand sanitizers and their effectiveness as well as the formulation aspects, adverse effects, and recommendations to enhance the formulation efficiency and safety.

Keywords: hand sanitizer; hand disinfectants; infection control, SARS-CoV-2, COVID-19, hand hygiene.

INTRODUCTION

Study about hygiene is a branch of science which is involved in knowledge and practices related to promotion of health.1 Hygiene is defined as maintenance of cleanliness practices which carries utmost importance in maintenance of health. Keeping bodily hygiene and usage of cleansers are most requisites of healthy living. These concepts highlight the need of maintaining hygiene in prevention of diseases.2

The emergence of novel pathogens, bacterial or viral, has always posed serious challenges to public health around the globe. One of these dangerous pathogens is “severe acute respiratory syndrome coronavirus 2” or SARS-CoV-2, more commonly known for causing coronavirus disease 2019 or COVID-19, which has been declared a global pandemic by the World Health Organization in early 2020. Since its discovery in December 2019 in Wuhan, there have been over three million confirmed cases worldwide by April 2020.3 One of many ways implemented to prevent the spread of this virus, as with previous contagious pathogens, is frequent and effective hand washing. In both healthcare and community settings, alcohol-based hand sanitizers have become a popular alternative to the traditional hand washing with soap and water. Alcohol based hand sanitizers have been utilized as an effective alternative to handwashing with soap to prevent the spread of bacterial and viral infections, making it one of the essential protocols in decreasing healthcare burden.4,5

COVID-19 is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which can persist and remain infectious on surfaces for up to 9 days.6 7 Hence, it is crucial to interrupt the transmission chain of the virus through contact isolation and strict infection control tools.8 Following face masks, appropriate hand hygiene is of utmost importance as hands may be contaminated from direct contact with patients’ in direct contact via surfaces, which may then facilitate the transmission and spreading of the disease.9–11 The 2003 severe acute respiratory syndrome (SARS) outbreak was caused by a novel human coronavirus (CoV) (SARS-CoV) that could survive on surfaces for 24–72 h.10 The studies on SARS-CoV outbreak settings showed that providing efficient. CDC, the United States has promoted and encouraged hand hygiene through hand washing or use of hand sanitizer.11 Different types of delivery systems are also formulated—for instance, rubs, foams, or wipes. The World Health Organisation (WHO) recommends alcohol-based hand sanitizer (ABHS) in line with the proven advantages of their rapid action and a broad spectrum of microbicidal activity offering protection against bacteria
and viruses. However, the effectiveness against non-enveloped viruses is still debatable and questionable.  

**Ayurvedic Approach in Hand Hygiene**

Ayurveda is the traditional medicinal system of India and believed to have originated over 6000 years ago. It describes the ways to remain healthy as well as methods to treat disease. The name itself means “Knowledge (Veda) of life (Ayu)” Ayurveda is not only a curative medical science but also is a comprehensive way of healthy living. Guidelines related to healthy or “swastha” individual are termed as “Swastha vritta”.  

Considering ayurvedic approach; an attempt has been made to screen classical literature for the herbs with cleansing properties and found that, *Pancha Valkala* (the barks of five plants) has activities like, *Vrana prakashalana, Vrana ropana, Shothahara, Upadan shahara, Visar pahara.* *Pancha Valkala* is the combination of barks of five different plants (i.e.) *Vata- Ficus bengalensis* Linn.,; *Udambara- Ficus glomerata* Roxb.,; *Aswattha- Ficus religiosa* Linn.,; *Parisha- Thespesia populnea* Soland.Ex. Correa.; *Plaksha- Ficus lecor* Buch.Ham.  

**Types of hand sanitizers**

Hand sanitizer are generally classified into two groups as,

- Alcohol-based hand sanitizer (ABHS)
- Alcohol-free (NABHS).

An ABHS may contain one or more types of alcohol, with or without other excipients and humectants, to be applied on the hands to destroy microbes and temporarily reduces the spreading. ABHS can effectively and quickly reduce microbes covering a broad germicidal spectrum without the need for water or drying with towels. Nevertheless, there are a few shortcomings with the effectiveness against non-enveloped (non-lipophilic) viruses and bacterial spores. On the other hand, the alcohol-free sanitizer makes use of chemicals with antiseptic properties to exert the antimicrobial effects. These chemicals have a different mode of action and function according to their chemical functional groups (Table 1). As they are non-flammable and often used at low concentrations, they are relatively safer to use among children as compared to ABHS. ABHS is available in different dosage forms, namely gel, liquid and aerosol. As each type has its own characteristics, a study was conducted to understand the impact on sensory attributes that may affect user’s acceptance of the product and ultimately influence usage leading to hand hygiene compliance.  

**Ingredients of Sanitizers**

**Table 1:** List of alcohol, non-alcohol compounds, and commonly used excipients in hand sanitizers

<table>
<thead>
<tr>
<th>Alcohol based sanitizer</th>
<th>Commonly used excipients</th>
<th>Alcohol free sanitizer</th>
</tr>
</thead>
<tbody>
<tr>
<td>70-95% V/V alcohol</td>
<td>• Glycerin</td>
<td>Antiseptic</td>
</tr>
<tr>
<td>Ethanol</td>
<td>• Fragrance</td>
<td>Chlor hexidine</td>
</tr>
<tr>
<td>Isopropanol</td>
<td>• Colorants</td>
<td>Chloro xylanol</td>
</tr>
<tr>
<td>n-propanol</td>
<td></td>
<td>Quaternary ammonium compounds</td>
</tr>
</tbody>
</table>

**Types of Hand Sanitizers**

<table>
<thead>
<tr>
<th>Chemical group</th>
<th>Example</th>
<th>Mechanism of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>• Ethanol</td>
<td>Denaturation of proteins in the plasma membrane</td>
</tr>
<tr>
<td></td>
<td>• Isopropanol</td>
<td></td>
</tr>
<tr>
<td>Chlorine compounds</td>
<td>• Hypochlorites (ClO₂) (e.g., Sodium hypochlorite)</td>
<td>Halogeneration/oxidation of cellular proteins</td>
</tr>
<tr>
<td></td>
<td>• Chlorine dioxide (ClO₂)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Chloramine-t trihydrate (C₅H₆ClNaO₃S)</td>
<td></td>
</tr>
<tr>
<td>Iodine compounds</td>
<td>• Povidone-iodine (polyvinylpyrrolidone with iodine)</td>
<td>Iodine can easily penetrate through the cell membranes of pathogens Followed by attacking vital proteins, nucleotides and fatty acids of cell</td>
</tr>
</tbody>
</table>
Quaternary ammonium compounds
- Benzalkonium chlorides, including
  - Alkyl dimethyl benzyl ammonium chloride (C_{22}H_{40}N\textsuperscript{+})
  - Benzyl dimethyl octyl ammonium Chloride (C_{17}H_{30}ClN)
  - Didecyl dimethyl ammonium chloride (C_{22}H_{48}ClN).

Peroxygens
- Hydrogen peroxide (H_{2}O_{2})
- Peracetic acid (PAA) (C_{2}H_{4}O_{3})

(Bis) phenols
- Triclosan

Biguanide
- Chlorhexidine

Table 3: Mechanism of action of alcohols and non-alcohol compounds

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Functions</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol based hand sanitizer (ABHS)</td>
<td>Denatures protein and lipid membrane of Microorganisms</td>
<td>Optimum concentration 60%–95%.</td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Hydrogen peroxide           | Inactivates contaminating spores in the bulk solutions or excipients. | Concentration is as low as 3%.
|                             |                                                | May fade the coloring agent        |
|                             |                                                | Corrosive in nature                |
| Non-alcohol-based hand sanitizer (NABHS) | Good activity | Gram-positive bacteria |
| Chlor hexidine gluconate    |                                                | Enveloped viruses                 |
|                             | Good activity                                  | Weak activity                      |
|                             | Gram-positive bacteria                         | Gram-negative bacteria             |
|                             | Gram-negative bacteria                         | Fungi                              |
|                             | Enveloped viruses                             | Non-enveloped viruses              |
| Chloro xylanol              | Good activity                                  | Gram-positive bacteria             |
|                             | Gram-positive bacteria                         | Gram-negative                      |
|                             | Gram-negative                                   | Enveloped viruses                  |
|                             | Pseudomonas aeruginosa                         |                                    |
| Iodine/ Iodophors           | Inhibits the growth of microorganisms on living tissues. | Gram-positive bacteria |
|                             | Gram-negative bacteria                         | Fungi                              |
|                             | Enveloped viruses                              | Spore-forming bacteria             |
| Quaternary ammonium compounds | Good activity | Gram-positive bacteria |
|                             | Gram-positive bacteria                         | Enveloped viruses                  |
|                             | Gram-negative                                   | Mycobacteria                       |
|                             | Mycobacteria                                    | o Fungi                            |
| Triclosan                   | Good activity                                  | Gram-positive bacteria             |
|                             | Gram-positive bacteria                         | Mycobacteria                       |
|                             | Mycobacteria                                    | Candida spp.                       |
|                             | Candida spp.                                    | Filamentous fungi                  |

Lower surface tension
Inactivate enzymes
Degrade cell-proteins
Free-radical oxidation of essential cell components
Penetrate cytoplasmic bilayer
Ionic interaction
Disrupt cell membrane
H$_2$O$_2$:
While alcohol is the active component in the formulations, certain aspects of other components should be respected. All raw materials used should be preferably free of viable bacterial spores. The low concentration of H$_2$O$_2$ is incorporated in the formulations to help eliminate contaminating spores in the bulk solutions and excipients and is not an active substance for hand antisepsis. While the use of H$_2$O$_2$ adds an important safety aspect, the use of 3–6% of H$_2$O$_2$ for the production might be complicated by its corrosive nature and by difficult procurement in some countries. Further investigation is needed to assess H$_2$O$_2$ availability in different countries as well as the possibility of using a stock solution with a lower concentration.

Glycerol

Glycerol is added to the formulation as a humectant to increase the acceptability of the product. Other humectants or emollients may be used for skin care, provided that they are affordable, available locally, miscible (mixable) in water and alcohol, nontoxic, and hypoallergenic. Glycerol has been chosen because it is safe and relatively inexpensive. Lowering the percentage of glycerol may be considered to further reduce stickiness of the handrub.

Alcohol mechanism of action against Bacteria

The compound, n-propanol, is the most commonly used alcohol compound in biocides. It is not known with much confidence the exact mechanism of alcohol’s antimicrobial activity, however, it may be related membrane damage, and inhibition or uncoupling of mRNA and protein synthesis through effects on ribosomes and RNA polymerase, or associated with protein denaturation. For activity against bacteria, its optimal bactericidal efficacy is achieved at concentrations between 60% to 90%.

Alcohol mechanism of action against Viruses

The viral targets of alcohol-based hand sanitizers are predominantly the viral envelope, if present, which is derived from host lipid envelopes, the protein capsid, which contains and protects the genetic material. Given that all these components are essential for the viral life cycle (e.g., attachment, penetration, biosynthesis, maturation, lysis), and thus critical for its ability to transmit to another host, it can be presumed that altering the structure or function of any of the aforementioned components will typically render the virus ineffective. While less is known regarding the specific mechanism of action of alcohols agents against viruses compared to bacteria, it is understood that ethanol has a broader and stronger virucidal activity than propanols. In fact, high concentrations of ethanol have shown to be highly effective against enveloped viruses and thus are effective against the majority of clinically relevant viruses. It is also interesting to note that adding acids to ethanol solutions can increase its efficacy against viruses that are more resistant to ethanol alone.

Benzalkonium chloride

The cationic “headgroup” of BC is progressively adsorbed to the negatively charged phosphate heads of phospholipids in the lipid bilayer, and as a result, increase in concentration. The consistent increase of BC concentration results in reduced fluidity of the membrane and thus the creation of hydrophilic gaps in the membrane. In addition, the alkyl chain “tail” component of BC further perturbs and disrupts the membrane bilayer by permeating the barrier and disrupting its physical and biochemical properties. Protein function is subsequently disturbed and the combination of the aforementioned effects results in the solubilization of the bilayer constituents into BC/phospholipid micelles. BC also interrupts intercellular targets and compromises the conformational behavior of DNA.

Chlorhexidine

Similar to alcohol, chlorhexidine works by disrupting the arrangement of cytoplasmic membranes, thereby leading to precipitation of cell contents. It is most effective against Gram-positive bacteria and has modest activity against a Gram-negative bacteria, as well as enveloped viruses. As chlorhexidine is cationic, it is advisable to avoid using chlorhexidine-containing products with natural soaps and hand creams that contain anionic emulsifying agents as they may cause inactivation or precipitation of chlorhexidine, thus reducing its efficacy. Chlorhexidine gluconate 0.12% is likely to have antiviral activity against the coronavirus as it does against other enveloped viruses.

Chloroxylenol

Chloroxylenol is a common agent as a preservative in cosmetics or as an antimicrobial agent in soap. The
antimicrobial effect of chloroxylenol is attributable to its ability to deactivate enzyme systems and alter cell wall synthesis in microbes. It is good at killing bacteria and enveloped viruses but less active against *Pseudomonas aeruginosa*.

**Iodine/iodophors** 48-53

Iodine was once an effective antiseptic used for skin disinfection. It can penetrate the microbial cell wall and form complexes with amino acids or unsaturated fatty acids to impair the synthesis of cellular components. Nonetheless, due to its potential to cause skin irritation and discoloration, iodophors have come into play to replace iodine as the active ingredient in antiseptics. The FDA has not cleared any liquid chemical sterilant or high-level disinfectants with iodophors as the main active ingredient.

Iodophors are a combination of iodine, iodide or triiodide, and a high molecular weight polymer carrier such as polyvinyl pyrrolidone. This carrier is responsible for improving the solubility of iodine, enhancing the sustained release of iodine, and minimizing skin irritation. The degree of antimicrobial activity determined based on the amount of free iodine present in the structure. Having said so, formulations with lower iodophor concentration may have significant antimicrobial activity as well because the amount of free iodine tends to increase after dilution.

Both iodine and iodophors exhibit germicidal activity against a Gram-positive, Gram-negative, and spore-forming bacteria, as well as various fungi and viruses. However, the concentration of iodophors used in antiseptics (e.g., povidone-iodine 5%-10%) is usually insufficient to achieve sporicidal action. Furthermore, the nasal povidone-iodine formulation has shown acceptable tolerability and favorable risk/benefit profile to help mitigate the perioperative spread of COVID-19 in patient decolonization.

**Quaternary Ammonium Compounds** 54

Quaternary ammonium compounds are composed of four alkyl groups connected to nitrogen atom in the centre. The typical examples include benzalkonium chloride, benzethonium chloride, and cetyl peridium chloride. They act by adsorbing to the cytoplasmic membrane, thus causing leakage of the constituents. They are more active against Gram-positive bacteria and lipophilic viruses. The activity against fungi, mycobacteria, and Gram-negative bacilli is comparatively weak.

**Triclosan** 55-57

At low concentration, triclosan is bacteriostatic due to its harmful effects to bacterial enzymes responsible for the composition of fatty acid from cells wall and membranes. At high concentrations, triclosan disrupts the bacteria membrane, leading it to death. It has good activity against gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus*, *Candida spp.* and *Mycobacteria*. The efficacy of triclosan may be affected by pH, use of emollients, and the ionic nature of certain skin formulations.

**Other additives to the formulations**

It is strongly recommended that no ingredients other than those specified here be added to the formulations. In the case of any additions, full justification must be provided together with documented safety use of the additive, its compatibility with the other ingredients, and all relevant details should be given on the product label. In general, it is not recommended to add any bittering agents to reduce the risk of ingestion of the handrubs. Nevertheless, in exceptional cases where the risk of ingestion might be very high (paediatric or confused patients), substances such as methylethyl ketone and denatonium benzoate may be added to some household products to make them less palatable and thus reduce the risk of accidental or deliberate ingestion. However, there is no published information on the compatibility and deterrent potential of such chemicals when used in alcohol based handrubs to discourage their abuse. It is important to note that such additives may make the products toxic and add to production costs. In addition, the bitter taste may be transferred from hands to food being handled by individuals using handrubs containing such agents. Therefore, compatibility and suitability, as well as cost, must be carefully considered before deciding on the use of such bittering agents.

A colorant may be incorporated to differentiate the handrub from other fluids as long as such an additive is safe and compatible with the essential components of the handrubs. However, the H₂O₂ in the handrubs may tend to fade any coloring agent used and prior testing is recommended.

**CONCLUSION**

With the current study in the literature, it is difficult to confidently suggest one mode of hand sanitizing delivery over the other. A sufficient volume of sanitizer is important to ensure complete hand coverage, and compliance is critical for appropriate hand hygiene. The use of ABHS is becoming more common because of their rapid action and efficiency in killing microorganisms, mainly when hand washing using soap and water is always not practical and convenient. There are, however, some situations in which hand washing is preferred as ABHS are less effective when handrubs from other fluids as long as such an additive is safe and compatible with the essential components of the handrubs. However, the H₂O₂ in the handrubs may tend to fade any coloring agent used and prior testing is recommended.
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