



# Hand sanitizers: Science and rationale

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Received: May, 2020  
Accepted: September, 2020  
Published: March, 2021

**DOI:**  
10.25259/IJDVL\_598\_20

**PMID:**  
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## Introduction

Owing to the coronavirus disease 2019 pandemic, there has been a run on hand sanitizers with shipments back-ordered and supplies hoarded. A bottle of a hand sanitizer is often in sight at a dermatologist's office and as a product, it presents both benefits and challenges. Adequate knowledge about their role, effectiveness, usage and adverse effects is a must for a dermatologist.

A hand sanitizer or a hand rub is a liquid, gel or foam-based product containing suitable antimicrobial agents, that is left on and not rinsed off with water and is intended to reduce hand contamination.

They are considered over-the-counter products and are regarded as critical in reducing colonization of the hands with potential disease-causing organisms.<sup>1</sup>

Endorsed by the World Health Organization as a part of its global campaign (SAVE LIVES: Clean Your Hands) which is celebrated on May 5<sup>th</sup> every year, hand sanitizers, especially alcohol-based formulations, have become an international standard for hand hygiene.<sup>2</sup>

## Classification

Hand sanitizers can be categorized into three main classes:<sup>3</sup>

1. Alcohol-based
2. Alcohol-based supplemented = alcohol plus other antimicrobial agents
3. Non-alcohol-based = majority of the product is water plus surfactant and antimicrobial agent.

The alcohol-based version is on the World Health Organization's List of Essential Medicines and it is the most frequently used one.<sup>4</sup>

## Alcohol-Based Hand Sanitizer

According to the World Health Organization, an alcohol-based hand rub is an "alcohol-containing preparation (liquid, gel or foam) designed for application to the hands to inactivate microorganisms and/or temporarily suppress their growth. Such preparations may contain one or more types of alcohol, other active ingredients being excipients and humectants."<sup>5</sup>

## Mechanism of Action

Alcohols have been used as disinfectants for more than 100 years and they are highly effective because they non-specifically denature proteins.<sup>6</sup> Hand sanitizers are designed to reduce transient flora on the skin which are the organisms most frequently associated with healthcare-associated infections. They are often acquired during direct contact with patients or contaminated environmental surfaces adjacent to the patient. The fate of the resident skin flora is disregarded in this process.<sup>7</sup>

Alcohols are rapidly germicidal when applied to the skin but have no appreciable persistent activity. However, regrowth of bacteria on the skin occurs slowly after the use of alcohol-based hand antiseptics, presumably because of the sub-lethal effect of the alcohol on some of the cutaneous bacteria.<sup>8</sup>

## Antimicrobial Coverage

Alcohols are effective against most of the bacteria, fungi and viruses [summarized in Table 1]. It should be kept in mind

**How to cite this article:** Kumar S, Das A. Hand sanitizers: Science and rationale. Indian J Dermatol Venereol Leprol. 2021;87:309-14.

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that the efficacy of alcohol-based hand rub is affected by numerous factors which include the type of alcohol used, its concentration, the contact time, the volume of solution used and whether the hands are wet when the alcohol is applied (which reduces efficacy).<sup>9-12</sup>

**Testing Standards**

This applies to all types of hand sanitizers. They evaluate a formulation’s ability to inactivate all the transient microorganisms on the hands, employing a method that simulates bacterial exposure and the use of hand rub in clinical settings.<sup>13</sup> The methods have been tabulated. In Europe, the most commonly used method for testing hand rubs is the European 1500. However, in the United States of America, hand rub agents are evaluated using the American Society for Testing and Materials standards. The testing standards have been summarized in Table 2.

**Constituents and Formulation**

Alcohol-based hand rubs may contain ethanol, isopropanol or *n*-propanol or a combination of any two.

The concentration of the alcohol is expressed either as a percentage of weight (= g/100 g, abbreviated % w/w) which is not affected by temperature or other variables, as a

percentage of volume (= mL/100 mL, abbreviated % v/v) or as a percentage of weight/volume (= g/100 mL, abbreviated % w/v). The latter two may be affected by temperature, specific gravity or reaction concentration. For example, 70% alcohol by weight is equivalent to 76.8% by volume if prepared at 15 °C or 80.5% if prepared at 25 °C.<sup>14</sup> Most often alcohol concentrations in hand rubs are expressed as a percentage of volume.<sup>15</sup>

Hand sanitizers containing 60–95% alcohol are most effective, and lower or even higher concentrations are less potent, as proteins are not denatured easily in the absence of water.<sup>9</sup> Besides, pure alcohol or higher concentrations would evaporate too quickly to exert any germicidal effect. The World Health Organization recommended formulations contain either 80% v/v ethanol or 75% v/v isopropanol.<sup>5</sup> Mostly, concentrations between 60 and 80% are used for hand rubs. As alcohols are volatile, containers should be designed to minimize evaporation, so that the initial concentration is preserved.

Alcohol-based hand rubs are available as solutions (with low viscosity), gels and foams. Though most studies have demonstrated that gel-based formulations are somewhat less effective than solutions,<sup>16,17</sup> greater emphasis should be placed on compliance, because, if a gel with lower *in vitro* activity

**Table 1: Antimicrobial coverage of sanitizers**

Alcohol-based hand sanitizer	Non-alcohol based hand sanitizer
Most gram-positive and gram-negative bacteria – including methicillin-resistant <i>Staphylococcus aureus</i> and <i>Vancomycin</i> -resistant <i>Enterococci</i> , <i>Mycobacterium tuberculosis</i>	Bacteriostatic against Gram-positive and some Gram-negative bacteria <sup>5</sup> QACs have greater activity against lipophilic viruses <sup>5</sup> They are not active against nonenveloped viruses
Fungi Enveloped (lipophilic) viruses Most nonenveloped viruses (e.g., rotavirus, adenovirus, rhinovirus). Other nonlipophilic viruses such as hepatitis A and enteroviruses (e.g., poliovirus) may require 70–80% v/v alcohol to be reliably inactivated. <sup>9,10</sup> The inactivation of naked viruses is influenced by temperature, the ratio of alcohol to virus volume, protein load and time <sup>10</sup> Alcohols have virtually no activity against bacterial spores (so, they are not suitable for spore-forming organisms such as anthrax, <i>Clostridium difficile</i> <sup>11</sup> ); or protozoan oocysts (e.g., <i>Cryptosporidium</i> ) and have reduced activity against some nonenveloped (nonlipophilic) viruses like norovirus. <sup>12</sup> In general, ethanol has shown greater activity against viruses than isopropanol <sup>9</sup>	
QAC: Quaternary ammonium compounds	

**Table 2: Testing standards for hand sanitizers**

Testing standard	Salient features
EN 1500	The mean acceptable reduction of viable bacteria (usually a pure culture of a nonpathogenic strain of <i>Escherichia coli</i> is used as the inoculum) with a test formulation should not be significantly inferior to that obtained with the reference alcohol-based hand rub (isopropyl alcohol 60% v/v)
ASTM E-1174	The criteria for efficacy is a 2-log <sub>10</sub> reduction of the indicator organism on each hand within 5 min after the first use, and a 3-log <sub>10</sub> reduction of the indicator organism on each hand within 5 min after the tenth use <sup>5</sup>
ASTM E-2755 (whole-hand method for bacteria-eliminating effectiveness of hand sanitizer formulations)	This test method which may use either <i>Staphylococcus aureus</i> or <i>Serratia marcescens</i> as the test organism, can be used to test any form of hand sanitizer. It can be an alternative to E-1174 <sup>13</sup>

ASTM: American Society for Testing and Materials, EN: European

is more frequently used, the overall outcome is expected to be better.<sup>18</sup>

In addition to alcohol, hand sanitizers also contain additional antiseptics (chlorhexidine digluconate (0.5–1%), benzalkonium chloride, octenidine dihydrochloride or triclosan (0.2% to 0.5%);<sup>7</sup> sporicides (hydrogen peroxide, 0.125% v/v);<sup>19,20</sup> moisturizers like isopropyl myristate, glycerol, etc; gelling agent (cellulose derivatives), water and other additives like colorants and fragrances.

**Directions for Use**

- Hand sanitizer should be applied to dry hands. Efficacy is reduced when alcohol is applied to wet hands.
- The ideal volume of product to apply may vary for different formulations. Small volumes (0.2–0.5 mL) of alcohol applied to the hands are not better than washing hands with plain soap and water.<sup>21,22</sup> If hands feel dry after being rubbed together for less than 10–15 s, an insufficient volume of product was likely applied.<sup>9</sup> In general, it is recommended to apply at least 3 mL or enough to wet the entire surface of hands.<sup>23</sup> However, most hand rub dispensers dispense amounts between 0.6 and 1.5 mL.
- Hands should be rubbed together covering all surfaces for at least 20–30 s until dry. The six steps “How to Hand rub” technique outlined by the World Health Organization underscores the importance of entire coverage of the hands [Figure 1].<sup>5</sup>

**Local Production**

The guidelines for local production of hand sanitizers are now revamped in the wake of the novel coronavirus pandemic. As per World Health Organization, alcohol-based hand rubs should contain at least 60% alcohol, should be certified and in regions where suitable commercial products are either unavailable or cost-prohibitive, they can be made locally by following the World Health Organization guide. The two formulations which have been recommended for local production to ensure safety in production and storage, have been mentioned in Table 3.<sup>5</sup>

The two World Health Organization-recommended formulations are as per European standards (European 1500). However, healthcare settings currently using commercially-available hand rubs should continue to use them, provided that they meet recognized standards for microbicidal efficacy (American Society for Testing and Materials or European standards) and are well tolerated.<sup>5</sup>

**Pros and Cons of Alcohol-Based Hand Sanitizer<sup>24-43</sup>**

These have been summarized in Table 4.

**Non-alcohol-based hand sanitizer**

Quaternary ammonium compounds such as benzalkonium chloride or benzethonium chloride are the primary



**Figure 1:** Hand hygiene technique with an alcohol-based hand sanitizer (reproduced from reference number 5)

**Table 3: WHO recommended formulation for hand sanitizers**

Formulation 1	Formulation 2
Ethanol 80% (v/v)	Isopropyl alcohol 75% (v/v)
Glycerol 1.45% (v/v)	Glycerol 1.45% (v/v)
Hydrogen peroxide 0.125% (v/v)	Hydrogen peroxide 0.125% (v/v)
Sterile distilled water or boiled and cooled water	Sterile distilled water or boiled and cooled water

WHO: World Health Organization

constituents in most alcohol-free hand sanitizers today. They are most often procured in the form of water-based foams.<sup>44-47</sup>

**Mechanism of action**

They adsorb to the cytoplasmic membrane of microbes with subsequent leakage of low molecular weight cytoplasmic constituents.<sup>48</sup>

**Antimicrobial coverage**

The coverage is poor, in comparison to alcohol-based hand rubs [Table 1]. Several outbreaks of pseudo-infections have been reported with quaternary ammonium compounds contaminated with gram-negative bacilli.<sup>49,50</sup> The widespread use of quaternary ammonium compounds in hospitals

**Table 4: Pros and cons of alcohol-based hand sanitizer versus non-alcohol-based hand sanitizer**

Sanitizer	Pros	Cons
Alcohol-based hand sanitizer	<p>Quick and easy to use</p> <p>Fast-acting; hand washing takes at least twice as much time. The shorter time (20–30 s) required for hand antisepsis increases acceptability and compliance<sup>24</sup></p> <p>Immediately available at the point of care and where hand contamination is likely (e.g., at the bedside, OPD)</p> <p>More accessible – hand rub can be used in areas that are unsuitable for sinks; without need for any particular infrastructure (clean water supply network, washbasin, soap, hand towel); so are suitable for resource-limited or remote areas</p> <p>Better acceptability and tolerance than traditional hand washing; less incidence of cutaneous adverse reactions<sup>5</sup></p> <p>Fewer chances of cross-contamination with surrounding objects</p> <p>Broad-spectrum microbicidal activity with minimal risk of generating resistance to antimicrobial agents. Alcohol-based rubs are more efficacious than antiseptic detergents and that the latter are usually more efficacious than plain soap<sup>5</sup></p>	<p>Not appropriate for use when hands are visibly soiled (if organic matter viz. dirt, food, etc., is visible on hands). However, when relatively small amounts of proteinaceous material (e.g., blood) are present, ethanol and isopropanol may reduce viable bacterial count<sup>25</sup></p> <p>There are certain situations where handwashing is preferred over a hand sanitizer. According to WHO, hands should be washed with soap and water when visibly dirty or soiled with blood or other body fluids; after using the toilet; or if exposure to potential spore-forming pathogens is strongly suspected or proven, including outbreaks of <i>Clostridium difficile</i><sup>5</sup></p> <p>Hand sanitizers are not effective in removing chemicals such as pesticides and heavy metals like lead<sup>26</sup></p> <p>Contamination of alcohol-based hand sanitizers can occur.</p> <p>A pseudo-epidemic of infections caused by contamination of ethanol by <i>Bacillus cereus</i> spores has been reported<sup>27</sup></p> <p>Cutaneous adverse reactions: Potential skin reactions from hand rubs include</p> <p>A brief stinging reaction at the site of breached skin (e.g., abrasions). ABHRs with isopropanol may be less stinging<sup>28</sup></p> <p>Irritant contact dermatitis- Hand sanitizers are a known cause of recalcitrant hand dermatitis. Alcohol-based hand sanitizers effectively solubilize components of intercellular lipids,<sup>29</sup> eventually compromising skin barrier, leading to dermatitis and more frequent colonization by staphylococci and Gram-negative bacilli.<sup>30</sup> The lipid-dissolving effect of alcohol is inversely related to their concentration<sup>31</sup> although ethanol tends to be less irritating than n-propanol or isopropanol.<sup>32</sup> Added emollients or humectants may improve the product's skin tolerability</p> <p>Contact allergy-It may present as delayed-type reactions (allergic contact dermatitis) or less commonly as immediate reactions (contact urticaria).<sup>33,34</sup></p> <p>Allergic reactions to alcohol-based formulations may represent true allergy to the alcohol or allergy to an impurity or aldehyde metabolite or to compounds that may be present as inactive ingredients in alcohol-based hand rubs including fragrances, propylene glycol, parabens or emulsifiers.<sup>33</sup> Allergic contact dermatitis attributable to alcohol-based hand rubs is uncommon<sup>35</sup></p> <p>Irritant contact dermatitis and allergic reactions to supplemental antiseptic agents including chlorhexidine, triclosan, etc., have also been reported<sup>36-39</sup></p> <p>The propensity to fires-undiluted ethanol is highly flammable and may ignite at temperatures as low as 10°C. The flashpoints of ethanol 80% (v/v) and isopropyl alcohol 75% (v/v) are 17.5°C and 19°C, respectively.<sup>5,40</sup> Although the risk of fires associated with alcohol-based hand sanitizer is very low,<sup>5</sup> they should be stored away from high temperatures or flames and users should be aware of this risk</p> <p>There are occupational safety concerns with the chronic use of alcohol. The minimal absorption of alcohol through the skin or by inhalation of vapors that occurs with the normal use of ABHRs does not pose a health risk to health-care workers. Although cutaneous absorption appears to be minimal, accidental and intentional ingestion of alcohol-based hand rubs have been reported.<sup>41-43</sup> For this reason, careful product placement and vigilance is required, particularly in areas where young children or patients with psychiatric illness are managed, such as pediatric wards and OPDs, geriatric/dementia wards and psychiatric facilities</p>
Non-alcohol-based hand sanitizer	<p>It is non-flammable and can be safely used around electrocautery devices whereas alcoholic-based sanitizers have flammability concerns<sup>44</sup></p> <p>They are less irritating to the skin alcohol-based hand rubs are more damaging to the skin, especially after repeated use<sup>45</sup></p> <p>Benzalkonium dries 10–15 s later than alcohol-based hand sanitizers, allowing more than the minimum contact time for complete efficacious coverage.</p> <p>Besides, benzalkonium chloride-based hand sanitizers deliver 2 to 4 h of residual protection<sup>46</sup></p> <p>They are relatively nontoxic at low concentrations (sanitizers usually contain less than a 0.1% concentration of benzalkonium) and are much less of a threat in cases of accidental ingestion<sup>44</sup></p>	<p>The spectrum of coverage against microbes is poor</p> <p>Not active against nonenveloped viruses</p> <p>The widespread use of QACs in hospitals contributes to the emergence of disinfectant-resistant bacteria</p> <p>Benzalkonium chloride has less reliable activity against coronavirus than alcohols<sup>47</sup></p> <p>Their antimicrobial activity is adversely affected by the presence of organic material<sup>7</sup></p>

OPD: Outpatient department, QAC: Quaternary ammonium compounds, ABHR: Alcohol-based hand rub, WHO: World Health Organization

contributes to the emergence of disinfectant-resistant bacteria.<sup>51,52</sup> The *qac*-resistant genes have been identified in clinical staphylococcal isolates.<sup>53,54</sup>

### Pros and Cons of Non-alcohol-Based Hand Sanitizer<sup>44-47</sup>

They have been summarized in Table 4.

#### Hand washing versus hand sanitizing

Although healthcare professionals often perceive that rubbing hands with a hand sanitizer is more damaging to the skin than washing, numerous studies have confirmed that hand rubs cause less disruption of the skin barrier, in comparison to detergent-based soaps and antiseptics.<sup>55</sup> This misconception, consequently leads to higher rates of dermatitis because staff prefers the procedure of traditional handwashing.<sup>56</sup> Importantly, the epidermal water content decreases significantly with soap-and-water handwashing (skin becomes dryer) compared to hand rubbing with alcohol-based hand rubs.<sup>57</sup>

However, the main concern raised for reluctance to accept hand rubbing as a substitute for handwashing is the lack of confidence about its efficacy.<sup>58</sup> Nevertheless, it has been seen that during routine patient care, hand rubbing with alcohol-based hand rub is significantly more efficient in reducing hand contamination than handwashing with an antiseptic soap.<sup>59</sup> Alcohol-based hand rubs work faster than medicated soap and water, are less irritating to the skin and avoid recontamination by contaminated water while rinsing hands. Contamination of the hands may also occur in the process of hand washing by contacting the surrounding environment, tap, paper towel handle or the sink edge.<sup>9</sup> Furthermore, bacteria adhere more readily to wet hands, increasing the risk of cross-contamination.<sup>60</sup>

The large numbers of patients examined each day in the dermatology office requires quite some hand hygiene interventions and a commitment of substantial time and effort. Hand hygiene compliance rates in one study increased from 48% to 66% after hospital workers switched from a reliance on washing with soap and water to alcohol-based hand rubs.<sup>61</sup>

### Conclusion

Hand sanitizers have become an important part of hand hygiene for both healthcare professionals and consumers. At present, alcohol-based hand rubs are the only known means for rapidly and effectively inactivating a wide array of potentially harmful microbes on hands; reducing morbidity, mortality and costs associated with healthcare-associated infections. However, it is important to keep in mind that their efficacy is dependent upon which and how much product is used, proper technique and consistency of use. There are also situations where they are not ideal, for example, in preventing the spread of certain infections or when the hands are significantly soiled and the bacterial load is too

high. Therefore, as we combat this coronavirus disease 2019 pandemic, hand sanitizers have become our most reliable companion; and this should be routinely included in our day to day practice, even when the pandemic fades away.

#### Financial support and sponsorship

Nil.

#### Conflicts of interest

There are no conflicts of interest.

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