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Review

Efficacy of ethanol against viruses in hand disinfection

G. Kampf*

University Medicine Greifswald, Institute for Hygiene and Environmental Medicine, Greifswald, Germany

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SUMMARY

Ethanol is used worldwide in healthcare facilities for hand rubbing. It has been reported to have a stronger and broader virucidal activity compared with propanols. The aim of this review was to describe the spectrum of virucidal activity of ethanol in solution or as commercially available products. A systematic search was conducted. Studies were selected when they contained original data on reduction of viral infectivity from suspension tests (49 studies) and contaminated hands (17 studies). Ethanol at 80% was highly effective against all 21 tested, enveloped viruses within 30 s. Murine norovirus and adenovirus type 5 are usually inactivated by ethanol between 70% and 90% in 30 s whereas poliovirus type 1 was often found to be too resistant except for ethanol at 95% (all test viruses of EN 14476). Ethanol at 80% is unlikely to be sufficiently effective against poliovirus, calicivirus (FCV), polyomavirus, hepatitis A virus (HAV) and foot-and-mouth disease virus (FMDV). The spectrum of virucidal activity of ethanol at 95%, however, covers the majority of clinically relevant viruses. Additional acids can substantially improve the virucidal activity of ethanol at lower concentrations against, e.g. poliovirus, FCV, polyomavirus and FMDV although selected viruses such as HAV may still be too resistant. The selection of a suitable virucidal hand rub should be based on the viruses most prevalent in a unit and on the user acceptability of the product under frequent-use conditions.

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Introduction

Ethanol is widely used in hand rubs, gels, and foams for hand hygiene in healthcare settings [1–7]. The World Health Organization has even listed ethanol at 80% (v/v) as an essential medicine in the category ‘alcohol-based hand rub’ [8]. Since 1994 the US Food and Drug Administration considers ethanol between 60% and 95% as generally safe and effective for hand rubbing, although the safety aspect has been under review again since 2015 [9]. Recent studies indicated that there may be a risk from systemic absorption and long-term exposure. The aim of the new proposed rule is to demonstrate systemic safety

under daily and long-term use [10]. The spectrum of antimicrobial activity of a hand rub used in healthcare must include bacteria and yeasts according to EN 14885; virucidal activity, however, is not mandatory [11]. However, ~5% of all healthcare-associated infections are caused by viruses, so virucidal activity of hand rubs has relevance in some units with a high prevalence of viral disease and during viral outbreaks [12]. The European terminology allows three different claims on virucidal activity: ‘active against enveloped viruses’; ‘limited spectrum virucidal activity’ which includes enveloped viruses, adenoviruses, noroviruses and rotaviruses; and ‘virucidal activity’ which includes all viruses relevant in human medicine [13]. Numerous studies have been published on the virucidal activity of ethanol solutions and products but the spectrum of virucidal activity of ethanol has so far not been described in detail. The aim of this review is therefore to describe the spectrum of virucidal activity of ethanol *in vitro*

* Corresponding author. Address: University Medicine Greifswald, Institute for Hygiene and Environmental Medicine, Walter-Rathenau-Straße 49A, 17475 Greifswald, Germany.

E-mail address: gunter.kampf@uni-greifswald.de.

and *in vivo*. In addition, the European claims are evaluated regarding specific viruses that may not be covered by the test viruses selected for a specific claim.

Methods

A systematic literature search was conducted via the National Library of Medicine (PubMed) on October 10th, 2016, and updated on June 22nd, 2017, using the following terms: virucidal activity alcohol (85 hits), virucidal activity ethanol (41 hits), virucidal efficacy alcohol (38 hits), virucidal efficacy ethanol (22 hits), alcohol-based hand rub virus (22 hits), alcohol-based hand rub viruses (19 hits), ethanol-based hand rub virus (three hits), ethanol-based hand rub viruses (one hit), ethanol virucidal disinfectant (50 hits), ethanol-based sanitizer virucidal (four hits), alcohol-based sanitizer virucidal (three hits), virus inactivation ethanol hand (15 hits), virus inactivation ethanol hands (16 hits) and virus inactivation alcohol hand (24 hits). In addition, studies deemed suitable for this review were also included. Data were extracted from the publications and were selected when they provided original data on reduction of viral infectivity in suspension tests (49 studies) and on contaminated hands (17 studies). A solution or product was considered sufficiently effective against a virus in a suspension test when it achieved $\geq 4 \log_{10}$ reduction or the limit of detection was reached. There was no minimum criterion for the limit of detection so that solutions or products could have passed in an assay, although the initial viral titre may have been low or the cytotoxicity of the product may have been high, resulting in an overall low \log_{10} reduction of viral infectivity. Studies were not included when they provided data on the reduction of viral infectivity on inanimate surfaces or used other methods to determine efficacy (e.g. reduction of viral RNA).

Results

The concentrations of ethanol are described in w/w and were sometimes determined by calculation when they were originally in v/v. Some studies, however, did not specify whether the ethanol concentration was by volume or weight. In these cases, the ethanol concentration is described without w/w.

Efficacy against enveloped viruses

Ethanol has been shown to be effective against various enveloped viruses [14]. Beginning at a concentration of 42.6% (w/w) ethanol is effective within 30 s against SARS coronavirus, MERS coronavirus, ebolavirus, influenza A virus including the human type H3N2, the avian type H3N8 and human type H1N1, influenza B virus, HIV, HBV, vacciniavirus, duck hepatitis B virus, togavirus, pseudorabies virus, Newcastle disease virus, bovine viral diarrhoea virus, zikavirus, herpes simplex viruses type 1 and 2 and RSV [5,14–35]. Ethanol is effective at 73.6% (w/w) against HCV in 15 s and 30 s but not at 40% [16,35,36].

Efficacy against non-enveloped viruses in suspension tests

EN 14476 allows determining a partial activity against non-enveloped viruses described as 'limited spectrum virucidal activity' tested with adenovirus type 5 and murine norovirus. A

hand rub with limited spectrum virucidal activity is considered to be effective against enveloped viruses, adenovirus, norovirus, and rotavirus. In a first step, data from suspension tests according to the test principle of EN 14476 are reviewed for those viruses covered by the claim of 'limited spectrum virucidal activity'. These viruses have particular clinical importance as outbreak viruses. In 2016 a total of 1444 nosocomial outbreaks have been notified in Germany with 76.0% being caused by noroviruses and 6.4% being caused by rotaviruses [37].

Adenovirus

Ethanol as a solution has largely sufficient activity in 30 s against adenovirus type 5 (test virus of EN 14476) at concentrations between 45% (w/w; contains additional active ingredients) and 95% (w/w) although one study indicates sufficient activity only in 1 min with 77% (w/w) ethanol [3,30,35,38,39]. Ethanol at 70% (w/w) as a gel was sufficiently active in 2 min [3].

Adenovirus type 2 is less susceptible. Ethanol needs 2 min at 55% (w/w) and 85% (w/w) [5,21]. In 30 s, ethanol at 62.4% (w/w) was not sufficiently effective [40]. Ethanol at 50% required a 10 min exposure time to be effective [14]. The combination of ethanol 73.6% (w/w) and peracetic acid (0.2%), however, was effective in 30 s [41].

Data with other adenoviruses do not provide a clear picture. Ethanol at 72.5–77% (w/w) was effective in 60 s against adenovirus type 7 but not against adenovirus type 8 [42].

Rotavirus

Gels based on 85% ethanol (w/w) or the combination of 62.4% (w/w) ethanol with additional citric acid were effective against rotavirus in 30 s as well as a hand rub based on 55% ethanol (w/w), 0.7% phosphoric acid and three other alcohols [5,21,40].

Norovirus

Today, the murine norovirus (MNV), a gastrointestinal tract virus, is widely used to determine the activity against noroviruses. Ethanol at concentrations between 62.4% (w/w) and 85.8% (w/w) is usually effective against MNV in 30 s or 1 min [30,35,38,43–45]. Lower concentrations were less effective. A gel based on 53.2% (w/w) ethanol was only effective in 1 h [46]. According to one study, ethanol at 42.6% (w/w) reduced MNV in 1 min by 0.3 \log_{10} and in 5 min by 0.4 \log_{10} [44]. In another study, ethanol at 42.6% (w/w) reached $\sim 3 \log_{10}$ reduction in 30 s whereas ethanol at 24.7% (w/w) or 8% (w/w) is ineffective within 3 min [43].

In the past, the feline calicivirus (FCV) was often used as a surrogate for human noroviruses although it is a respiratory tract virus. FCV is difficult to inactivate by ethanol. Ethanol solutions at 42.5% and 62.4% (both w/w) were effective at 3 min; ethanol at 73.6% (w/w) required 5 min [47]. Formulations with 72.5% ethanol (w/w) did not reach a 4 \log_{10} reduction in 60 s [42]. A solution based on 77% ethanol (w/w) showed only little activity against FCV in 60 s ($< 1 \log_{10}$) [42]. Even after 5 min the efficacy was still insufficient ($< 2 \log_{10}$) [39]. A hand rub based on $> 85.8\%$ (w/w) ethanol was almost ineffective in 30 s ($< 1 \log_{10}$) [30]. Finally, ethanol at 42.6%, 62.4%, and 85.8% (all w/w) revealed insufficient efficacy in 5 min with the highest \log_{10} reduction of 2.6 [44].

Whenever different types of acid are added, ethanol in hand rubs has been described to be effective in 30 s at 45%, 50.2%,

55%, 62.4%, and 67.9% (all w/w) [21,30,40,48]. Malic acid at 0.35% has also been reported to improve the efficacy of ethanol against FCV to some extent [49].

Enteroviruses

EN 14476 allows determining a full virucidal activity (test viruses: adenovirus type 5, murine norovirus, and poliovirus type 1). In a second step, data from suspension tests according to the test principle of EN 14476 are reviewed for enteroviruses that should be covered by the claim 'virucidal activity'.

Coxsackievirus

Data on the efficacy of ethanol against coxsackievirus are conflicting. Ethanol at 72.5–92.4% (w/w) has been reported to be effective against coxsackievirus B5 within 60 s and also against coxsackievirus B1 within 10 min but not against coxsackievirus A7 [42,50]. Higher ethanol concentrations (85–90%) are effective against coxsackievirus B3 in 15–60 s [51].

Echovirus

The efficacy of ethanol against echoviruses is rather good. One study shows that ethanol at 92.4% (w/w) is effective against echovirus 11 in 20 s [52]. Another study found a \log_{10} reduction ≥ 3 within 1 min for ethanol at 92.4% (w/w) against the same virus, whereas ethanol at 67.9% (w/w) was almost ineffective ($< 1 \log_{10}$) at the same exposure time [53]. Against echovirus 6 ethanol was effective at 50% within 10 min [14].

Human enterovirus 71

Against the human enterovirus 71 ethanol had only little activity at 62.4% (w/w) and 67.9% (w/w) within 10 min ($< 1 \log_{10}$). At 79.6% (w/w) a 3.21 \log_{10} reduction was achieved in the same exposure time, and at 92.4% (w/w) the \log_{10} reduction was 5.78 [54].

Poliovirus

All formulations with ethanol up to 80% (w/w) and without acid were not sufficiently effective in up to 5 min against poliovirus type 1 when tested under standard conditions with 80% product proportion in the suspension (Table I). When the product proportion is increased in the suspension test to 97%, some formulations with 73.5% or 80% ethanol (w/w) were effective within 1 min. One formulation with 95% (w/w) ethanol was effective in 30 s. Gels were mostly less effective compared to solutions.

The addition of various types of acids can substantially improve the activity of ethanol against poliovirus type 1 so that the formulations are often sufficiently effective in 30 s (Table II).

Poliovirus type 2 is somewhat less susceptible to ethanol compared to poliovirus type 1 [57].

Rhinovirus

A hand rub based on 55% ethanol (w/w), 0.7% phosphoric acid, and three other alcohols was effective in 30 s [21].

Other non-enveloped viruses

In a third step, data from suspension tests according to the test principle of EN 14476 are reviewed for other non-

enveloped viruses that should be covered by the claim 'virucidal activity'.

Hepatitis A virus

A gel based on 54.2% ethanol (w/w) showed no effect at all ($0 \log_{10}$) against hepatitis A virus (HAV) after 30 s [40]. Ethanol at 80% or 95% (both w/w) was not sufficiently effective within 2 min [58]. A hand rub based on 80% ethanol showed only little reduction of viral infectivity within 30 s (0.47), but it was higher after 2 min ($\geq 2.2 \log_{10}$) [24]. When 0.7% phosphoric acid and three other alcohols are added to ethanol at 55% (w/w) the formulation was effective against HAV in 30 s [21]. Ethanol at 62.4% (w/w) with additional 0.25% citric acid, however, was not sufficiently effective in 30 s with 1.75 \log_{10} [40].

Table I

Efficacy of different formulations based on ethanol without additional acids in suspension tests against poliovirus type 1

| Ethanol concentration (w/w) | Viscosity (type of product) | Exposure time | Mean \log_{10} reduction | Reference |
|-----------------------------|-----------------------------|---------------|----------------------------|-----------|
| 62.4% ^a | Solution (S) | 1 min | 2.3 | [55] |
| | | 5 min | 1.0 | [55] |
| | | 10 min | 5.0 | [55] |
| 70% | Gel (C) | 3 min | 0–0.87 ^b | [3] |
| | | 3 min | 0.75–3.25 ^c | [3] |
| 73.5% ^a | Solution (F) | 0.5 min | 0.9 | [35] |
| | | 1 min | 2.9 | [55] |
| | | 1 min | 2.2 | [35] |
| | | 2 min | 2.0 | [38] |
| | | 2 min | 2.8 | [35] |
| | | 3 min | 3.1 | [35] |
| | | 5 min | 2.9 | [55] |
| | | 5 min | 2.2 | [38] |
| | | 5 min | 3.5 | [35] |
| | | 10 min | 5.4 | [55] |
| 73.5% ^{a,d} | Solution (S) | 30 min | < 4 | [41] |
| | | 30 s | 3.4 | [38] |
| | | 1 min | 4.5 | [38] |
| 78.8% ^a | Solution (S) | 30 s | 0.4 | [39] |
| | | 1 min | 1.3 | [39] |
| | | 5 min | 2.9 | [39] |
| 80% | Solution (F) | 2 min | 2.0 | [38] |
| | | 5 min | 2.8 | [38] |
| 80% ^d | Solution (F) | 30 s | 3.1 | [38] |
| | | 1 min | 4.2 | [38] |
| 85% | Gel (C) | 3 min | 4.25 | [5] |
| 85.7% ^a | Solution (S) | 1 min | 1.6 | [55] |
| | | 5 min | 1.2 | [55] |
| | | 10 min | 1.7 | [55] |
| 95% | Solution (C) | 30 s | ≥ 4 | [30] |
| 100% | Solution (S) | 1 min | 1.5 | [55] |
| | | 5 min | 2.3 | [55] |
| | | 10 min | 2.3 | [55] |

(C), commercially available product; (F), formulation with auxiliary agents or additional active agents; (S), solution of ethanol.

^a Determined by calculation (originally in v/v).

^b Four experiments.

^c Three experiments.

^d Tested in suspension with 97% product proportion.

Table II

Efficacy of different formulations based on ethanol with additional acids in suspension tests against poliovirus type 1

| Ethanol concentration (w/w) | Type of acid | Viscosity (type of product) | Exposure time | Mean log ₁₀ reduction | Reference |
|-----------------------------|----------------------------------|-----------------------------|---------------|----------------------------------|-----------|
| 45% | Phosphoric acid | Solution (C) | 30 s | ≥4 | [30] |
| 55% ^a | 0.7% phosphoric acid | Solution (C) | 30 s | ≥4 | [21] |
| | | | 1 min | ≥4 | [21] |
| 62.4% ^b | 0.25% citric acid | Gel (C) | 30 s | 3.5 | [40] |
| 69.39% ^c | 0.2% citric acid, 0.2% uric acid | Solution (F) | 1 min | 4.0 | [56] |
| 73.5% ^b | 0.2% peracetic acid | Solution (F) | 30 s | ≥4 | [41] |
| 78.8% ^b | 0.1% citric acid, 1% lactic acid | Solution (F) | 30 s | ≥4 | [39] |

(C), commercially available product; (F), formulation with auxiliary agents or additional active agents.

^a With three additional alcohols.^b Determined by calculation (originally in v/v).^c With one additional alcohol.

Foot-and-mouth disease virus

The infectivity of the foot-and-mouth disease virus (FMDV) was insufficiently reduced by ethanol between 55.2% and 72.5% (both w/w) within 5 min [59]. Hand rubs with 70–75.2% ethanol (w/w) and additional phosphoric acid (0.6%) or 50% (w/w) ethanol and additional citric acid (0.5%), however, were effective within 30 s [59].

Polyomavirus

Ethanol has only little activity against polyomavirus SV 40, an additional test virus that was chosen due to its resistance to alcohols by experts for the German test method to determine virucidal activity [60]. A gel based on 85% ethanol (w/w) revealed sufficient activity in 15 min [5]. A hand rub based on 78.2% (w/w) ethanol had insufficient activity within 10 min (~2 log₁₀) [57]. When 0.7% phosphoric acid and three other alcohols are added to ethanol at 55% (w/w) the formulation was able to reduce infectivity sufficiently in 60 s [21]. Ethanol at 73.6% (w/w) in combination with 0.2% peracetic acid was effective in 30 s [41].

Parvovirus

Ethanol has almost no virucidal activity against parvovirus. At 80% ethanol the infectivity of the canine parvovirus was reduced in 5 min only by 0.1 log₁₀ [24].

Virucidal activity on hands

Some data can be found for the enveloped influenza A virus. A gel based on 61.5% ethanol completely reduced viral infectivity of the H1N1 influenza A virus after one application [61]. The formulations with ethanol between 54.2% and 58.1% (both w/w) ethanol effectively reduced viral infectivity of the same virus within 30 s by 3.25–3.35 log₁₀ [62].

First results with non-enveloped viruses were reported in 1978. One millilitre of a solution based on 70% ethanol reduced rhinovirus on hands by 1.5 log₁₀ [63]. Table III shows data obtained for ethanol-based formulations with current methods for various non-enveloped viruses. Overall, the majority of non-enveloped viruses can only be reduced partially by ethanol-based formulations. Exceptions are rotavirus and MNV for which most data indicate sufficient activity. When ethanol is combined with different types of acids the efficacy on hands can be improved substantially with HAV as an exception (Table IV).

Non-quantitative data were found in addition for rhinovirus. When hands artificially contaminated with rhinovirus were treated with 1.5 mL ethanol (65%) once or twice, rhinovirus was no longer be detected on 13 of 15 hands or 13 of 16 hands, respectively [70]. A similar result was described after the application of 1.5 mL ethanol (83%) [70].

Discussion

The evidence for sufficient activity of ethanol against enveloped viruses is very broad. Hand rubs must fulfil the EN 1500 efficacy requirement, hence they often contain ≥80% ethanol when applied for 30 s [4,71]. At this concentration hand rubs have comprehensive activity against different types of enveloped viruses.

Hand rubs with 'limited spectrum virucidal activity' are deemed suitable for inactivation of noroviruses and adenoviruses. Based on data obtained for MNV, hand rubs with 70–90% ethanol are usually effective against norovirus within 30 s. For adenovirus, however, the situation is somewhat different. The EN 14476 test virus (adenovirus type 5) is mostly inactivated by ethanol between 45% and 95% in 30 s. Other types of adenovirus, however, are less susceptible to ethanol such as adenovirus types 2 and 8. Both types of adenovirus have been reported before to have only little susceptibility to other biocidal agents such as povidone iodine or peracetic acid, indicating a general reduced susceptibility [72]. The in-vitro data are supported by the description of an outbreak with adenovirus type 8 which was successfully controlled by various measures including use of a virucidal hand rub [73].

Virucidal activity according to EN 14476 aims to include all enveloped and non-enveloped viruses relevant in human medicine [13]. After reviewing published data, some viral species are unlikely to be sufficiently inactivated by ethanol alone, even at high concentrations: polyomavirus and coxsackieviruses B5 and B1. Other viruses are only sufficiently inactivated by ethanol at 95% such as poliovirus, echovirus 11, human enterovirus, and coxsackievirus B3 (≥85% ethanol). The majority of ethanol-based hand rubs with concentrations up to 90% are therefore likely to yield <4 log₁₀ reduction against these viruses, suggesting insufficient efficacy. The addition of acids to the formulation such as phosphoric acid, citric acid, or peracetic acid can substantially improve the virucidal efficacy of ethanol, as shown with adenovirus type 2,

Table IIIMean log₁₀ reduction of viral infectivity on artificially contaminated hands or finger tips by treatment of hands with ethanol-based formulations without additional acids

| Type of virus | Ethanol concentration (w/w) | Viscosity (type of product) | Application time | Mean log ₁₀ reduction | Reference |
|-------------------------------|-----------------------------|-----------------------------|------------------|--------------------------------------|-----------|
| Poliovirus type 1 | 74.5% | Solution (S) | 10 min | 1.0 ^a 2.5 ^b | [57] |
| | 80% | Solution (S) | 30 s | 0.42 | [64] |
| | 80% | Solution (S) | 10 min | 2.2 | [65] |
| Poliovirus type 2 | 96.8% | Solution (S) | 10 min | 3.2 | [65] |
| | 74.5% | Solution (S) | 10 min | 0.2 ^a 0.7 ^b | [57] |
| Coxsackievirus B3 | 74.5% | Solution (S) | 10 min | 1.1 ^a 2.9 ^b | [57] |
| Coxsackievirus B4 | 74.5% | Solution (S) | 10 min | 1.3 ^a 3.0 ^b | [57] |
| Echovirus type 9 strain Hill | 74.5% | Solution (S) | 10 min | 0.7 ^a 2.6 ^b | [57] |
| Echovirus type 9 strain Barty | 74.5% | Solution (S) | 10 min | 1.3 ^a 2.2 ^b | [57] |
| Polyomavirus SV 40 | 74.5% | Solution (S) | 10 min | 0.9 ^a 1.8 ^b | [57] |
| Murine norovirus | 54.1% ^c | Gel (C) | 20 s | 2.8 | [66] |
| | 54.1% ^c | Gel (C) | 30 s | 3.5 | [66] |
| | 62.4% ^c | Solution (S) | 30 s | 4.69 | [43] |
| | 68% ^c | Solution (S) | 30 s | 0.91 | [40] |
| | 67.8% ^c | Solution (S) | 20 s | 3.0 | [66] |
| | 67.8% ^c | Solution (S) | 30 s | 2.7 | [66] |
| | 73.5% ^c | Solution (S) | 20 s | 1.7 | [66] |
| Human enterovirus 71 | >90% | Solution (C) | 30 s | 3.91 | [30] |
| | 68% ^c | Solution (S) | 30 s | 0.86 | [54] |
| Rotavirus | 92.9% ^c | Solution (S) | 30 s | 4.06 | [54] |
| | 70% ^d | Solution (S) | 30 s | 2.85 | [67] |
| Feline calicivirus | 54.1% ^c | Gel (C) | 20 s | 1.4 | [66] |
| | 54.1% ^c | Gel (C) | 30 s | 2.1 | [66] |
| | 62% ^d | Solution (S) | 30 s | 0.50 | [68] |
| | 62% ^d | Solution (S) | 2 min | 0.55 | [68] |
| | 62.4% ^c | Solution (S) | 30 s | 3.78 | [47] |
| | 62.4% ^c | Solution (S) | 30 s | 0.68 | [21] |
| | 67.8% ^c | Solution (S) | 20 s | 1.5 | [66] |
| | 67.8% ^c | Solution (S) | 30 s | 2.2 | [66] |
| | 70% | Solution (S) | 30 s | 2.66 | [69] |
| | 70% | Solution (S) | 30 s | 2.62 | [69] |
| | 70% | Solution (S) | 30 s | 1.18 | [69] |
| | 70% | Solution (S) | 30 s | 1.45 | [69] |
| | 70% | Solution (S) | 30 s | 1.33 | [69] |
| | 75.1% | Solution (C) | 30 s | 0.93 | [69] |
| 80% | Solution (C) | 30 s | 1.34 | [69] | |
| 85.7% ^c | Solution (S) | 30 s | 2.84 | [47] | |
| 95% | Solution (C) | 30 s | 1.90 | [69] | |
| 99.5% ^d | Solution (S) | 30 s | 1.00 | [68] | |
| 99.5% ^d | Solution (S) | 2 min | 1.30 | [68] | |

(C), commercially available product; (S), solution of ethanol.

^a Hand test.^b Finger test.^c Determined by calculation (originally in v/v).^d No information on v/v or w/w.

Table IV

Mean log₁₀ reduction of viral infectivity on artificially contaminated hands or finger tips by treatment of hands with ethanol-based formulations containing additional acids

| Type of virus | Ethanol concentration (w/w) | Viscosity (type of product) | Application time | Mean log ₁₀ reduction | Reference |
|--------------------|-----------------------------|-----------------------------|------------------|----------------------------------|-----------|
| Adenovirus type 5 | 62.4% ^a | Gel (C) ^b | 15 s | ≥3.16 | [40] |
| | | | 30 s | ≥3.12 | [40] |
| Poliovirus type 1 | 55% | Solution (C) ^b | 30 s | 3.04 | [21] |
| | | | 1 min | 3.13 | [21] |
| | | | 30 s | 2.98 | [40] |
| Murine norovirus | 62.4% ^a | Gel (C) ^c | 30 s | 2.98 | [40] |
| | 45% | Solution (C) ^b | 30 s | 3.94 | [30] |
| | 55% | Solution (C) ^b | 30 s | 3.91 | [30] |
| Hepatitis A virus | 62.4% ^a | Gel (C) ^c | 30 s | 2.48 | [40] |
| | 62.4% ^a | Gel (C) ^c | 30 s | 1.32 | [40] |
| Rotavirus | 62.4% ^a | Gel (C) ^c | 15 s | ≥4.32 | [40] |
| | | | 30 s | ≥3.84 | [40] |
| Feline calicivirus | 55% | Solution (C) ^b | 30 s | 2.38 | [21] |

(C), commercially available product.

^a Determined by calculation (originally in v/v).

^b Additional phosphoric acid.

^c Additional citric acid.

poliovirus type 1, polyomavirus, HAV, FMDV, and FCV. Although the efficacy is better, the dermal tolerance is likely to be worse. Post-marketing surveillance of an ethanol-based hand rub with phosphoric acid revealed frequent and significant skin lesions among the users [74]. Improved formulations, however, may have better user acceptability [75,76]. It would be beneficial in any case to look at the user acceptability of a virucidal hand rub locally before healthcare workers are asked to use it [77].

A European work item (WI 00216088) exists with the aim of measuring the virucidal activity on hands artificially contaminated with murine norovirus. Ethanol, probably at 70%, has been selected as the reference alcohol. Ethanol as an alcohol has a superior efficacy against non-enveloped viruses compared with the propanols. Against MNV, for example, most studies indicate that iso-propanol is considerably less effective compared with ethanol [43,44,46]. Against FCV iso-propanol has overall only poor virucidal activity [44,47]. And enteroviruses have been reported to be more or less resistant to iso-propanol at various concentrations within 10 min [14,51,54,55,78].

A look at the efficacy data of ethanol against non-enveloped viruses, however, shows that MNV is one of the most susceptible non-enveloped viruses. In addition, ethanol at 70% would not be considered to be virucidal according to EN 14476 due to the insufficient activity against poliovirus. A non-virucidal reference alcohol may therefore be found in the future as a positive control for the phase 2, step 2 test for virucidal efficacy on hands, which may reduce the credibility and acceptance of the upcoming standard. Perhaps it will be an option to select MNV for a phase 2, step 2 test to support 'limited spectrum virucidal activity' and another more resistant non-enveloped virus to support virucidal activity under practical conditions.

In conclusion, the spectrum of virucidal activity of ethanol at high concentrations covers the majority of clinically relevant viruses. Additional acids can substantially improve the virucidal activity against, for example, poliovirus, FCV, polyomavirus, and FMDV, although selected viruses such as HAV may still be too resistant. The selection of a suitable virucidal hand rub should

be based on the most prevalent viruses in a unit and on the user acceptability of the product under frequent-use conditions.

Conflict of interest statement

None declared.

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