THE FACTS COMPARING ALCOHOL BASED SANITIZERS TO MEDITIZER WATER-BASED SANITIZER

The emergence of the SARS-CoV-2 virus, the causative agent of COVID-19, prompted the introduction of a number of community public health measures to try and control spread of the virus. One of these was the widespread use of hand sanitizers; this has now become a routine operation for many individuals and continues to be an entry requirement for a wide variety of public places such as hospitals, GP surgeries and even shops and theaters.

FACT ONE - ENOUGH TIME TO KILL IS NOT ACHIEVED BY ALCOHOL BASED SANITIZERS. IT IS BY MEDITIZER.

One key finding was that, in keeping with other well-characterised Coronaviruses, SARS-CoV-2 was not readily inactivated by alcohol (ethanol and propan-2-ol) based disinfectants unless extended contact times of up to 10 minutes were employed[1]. The caveat here is that contact times of 1 minute resulted in approximately a 3-log reduction in viable Corona viruses when concentrations of ethanol between 62% – 71% were used, but all of these tests were performed according to statutory surface disinfection protocols where metal or other non-porous materials are coated in virus particles and then immersed in the disinfectant solution for the required time and the viable virus particle number remaining is determined. <u>Although this is a standard test method, it does not accurately represent the way in which hand sanitizers are used.</u>

For surface acting disinfection agents to work effectively there are two critical considerations. The first of these is the concentration of the active compound and the second is the contact time. For effective bacterial and viral knock-down by alcohol-based sanitizers, a concentration of between 62% and 71% of the alcohol is required. In order of effectiveness, propan-1-ol is the most effective alcohol disinfectant, followed by propan-2-ol and then ethanol and most alcohol-based hand sanitizers use ethanol[2,3] as propan-2-ol is more typically used in surface disinfectants or wipes to sterilize the skin surface prior to injection.

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1 Kampf, G *et al.* "Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents." The Journal of hospital infection vol. 104,3 (2020): 246-251. doi:10.1016/j.jhin.2020.01.022

To exert its disinfectant properties, alcohols require water to be present in the formulation as they act by denaturing proteins in the bacteria or viruses so somewhat counter-intuitively higher concentrations of alcohols are less effective[4]. Despite this, there are several products available which use up to 90% or 95% alcohol in their formulation. Thus, we have already seen that the active ingredient concentration is critical to optimal performance measured in terms of microbial reduction or knock-down.

A recent review[5] of the effectiveness of a range of hand sanitizers with varying alcohol concentrations as well as those which are alcohol free, indicated that a minimum contact time of 30 seconds was required to inactivate a range of enveloped viruses, including SARS-CoV-2 and reduce the number of viable viruses by between 3 and 5-logs (logarithmic reduction is the universal way of describing disinfection efficacy and thus a 3-log reduction would reduce the number of viable organisms by a factor of 1,000) but that a contact time of 1 minute resulted in greater efficacy. Herein lies one of the potential problems with alcohol-based hand sanitizers, in that these extended contact times for effective reduction of pathogenic microorganisms on the skin may never be reached due to the inherent volatility of the active ingredient, alcohol. One of the other important factors to consider when using skin sanitizers is the duration of action. Alcohol-based sanitizers have recently been shown to have a very short duration of action and therefore protection against re-contamination.[6] Formulating alcohol-based hand sanitizers with varying

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[2] Jain VM, Karibasappa GN, Dodamani AS, Prashanth VK, Mali GV. Comparative assessment of antimicrobial efficacy of different hand sanitizers: An *in vitro* study. Dent Res J (Isfahan). 2016;13(5):424-431. doi:10.4103/1735-3327.192283

[3] Siddharta, Anindya *et al.* "Virucidal Activity of World Health Organization-Recommended Formulations Against Enveloped Viruses, Including Zika, Ebola, and Emerging Coronaviruses." The Journal of infectious diseases vol. 215,6 (2017): 902-906. doi:10.1093/infdis/jix046

[4] Morton HE. The relationship of concentration and germicidal efficiency of ethyl alcohol. Ann N Y Acad Sci. 1950;53:191–196.

[5] Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents [published correction appears in J Hosp Infect. 2020 Jun 17;:]. J Hosp Infect. 2020;104(3):246-251. doi:10.1016/j.jhin.2020.01.022

[6] Kampf G, Kramer A, Suchomel M. Lack of sustained efficacy for alcohol-based surgical hand rubs containing 'residual active ingredients' according to EN 12791. J Hosp Infect. 2017 Feb;95(2):163-168. doi: 10.1016/j.jhin.2016.11.001. Epub 2016 Nov 12. PMID: 27912980.

concentrations of glycerol results in increased contact times but with the negative effect that it leaves the skin surface “sticky” which is obviously a contra-indication for skin cleanliness[7]. In fact, several studies looking at the effectiveness of alcohol-based hand sanitizers on the removal of Noroviruses indicate exactly the opposite and that use of alcohol-based sanitizers increases the risk in Norovirus outbreaks[8],[9].

FACT TWO - ALCOHOL BASED SANITIZERS HAVE MANY NEGITIVE SIDE EFFECTS

This same study also suggested that the widespread and frequent use of alcohol-based sanitizers could result in oral, dermal and/or pulmonary absorption and subsequent systemic toxicity[7] from the alcohol . Moreover, alcohol-based hand sanitizers can cause a number of unwanted side-effects such as skin dehydration, contact dermatitis and skin cracking.

We must not forget that our skin is the largest human organ and given its direct contact with the environment, is frequently exposed to environmental microorganisms in addition to its’ own natural bacterial micro-flora[10]. Microorganisms live both on the skin surface and within the living epidermal layer; recent evidence also now indicates that this micro-flora also comprises a small number of viral species[11], so it is important to understand that irrespective of the amount and degree of handwashing and use of hand sanitizers, most of these commensal species will not be removed. The entire reason for hand hygiene is the removal of pathogenic microorganisms capable of causing disease and being transmitted (particularly in a healthcare setting) to more vulnerable persons.

[7] Basak D, Deb S. Sensitivity of SARS-CoV-2 towards Alcohols: Potential for Alcohol-Related Toxicity in Humans. Life (Basel). 2021;11(12):1334. Published 2021 Dec 3. doi:10.3390/life11121334

[8] Blaney DD, Daly ER, Kirkland KB, Tongren JE, Kelso PT, Talbot EA. Use of alcohol-based hand sanitizers as a risk factor for norovirus outbreaks in long-term care facilities in northern New England: December 2006 to March 2007. Am J Infect Control. 2011;39:296–301.

[9] Vogel L. Hand sanitizers may increase norovirus risk. CMAJ 2011;183:E799.

[10] Rosenthal M, Goldberg D, Aiello A, Larson E, Foxman B. Skin microbiota: microbial community structure and its potential association with health and disease. Infect Genet Evol. 2011;11(5):839-848. doi:10.1016/j.meegid.2011.03.022

[11] Kampf G, Kramer A. Epidemiologic Background of Hand Hygiene and Evaluation of the Most Important Agents for Scrubs and Rubs. Clin Microbiol Rev. 2004;17(4):863–893.

FACT THREE – MEDITIZER WATER-BASED SANITIZER KILLS IN REAL-LIFE NEEDED SECONDS AND HAS BEEN PROVEN TO KILL THE HARDEST AND MOST DEADLY BACTERIA (AND VIRUSES). ALCOHOL-BASED SANITIZERS DON'T.

It has long been recognised[12] that the hands of healthcare workers may provide a reservoir for the circulation and transmission of drug-resistant bacteria and other pathogenic micro-organisms in the hospital environment. Conventional hand washing with soap and water is an effective means of reducing the microbial burden of pathogens such as *Staphylococcus aureus* which has been found to colonize between 10% and 78% of healthcare workers hands with up to 1×10^7 bacteria present. In situations where access to soap and water is not available, bodies such as the US Centers for Disease Control (CDC) have recommended the use of hand sanitizers containing either 80% ethanol or 75% propan-2-ol. Evaluation of the World Health Organization (WHO) recommended formulations alongside a large number of commercially available alcohol-based hand sanitizers indicated that whilst the WHO formulations resulted in complete bacterial inactivation within 1 minute of exposure (only bacterial strains were tested, not viruses) most of the commercially-available, over the counter preparations required at least 5 minutes exposure, which as we have seen earlier does not occur with alcohol-based products due to the rapid evaporation of the alcohol[13]. Interestingly this same study also indicated that the presence of thickening agents such as glycerol further impacted the efficacy of the bacterial kill and the authors hypothesized that this was due to the slower release of the active ingredient.

Now water-based formulations have been extensively evaluated, for a recent example see Bondurant *et al.* (2019)[13] and for activity against SARS-CoV-2 see Herdt *et al.* (2021)[14]. Meditizer has developed an innovative and novel preparation which relies on mechanical rather than biocide killing of bacterial cells and viruses. The active ingredients are metal ions, specifically copper and magnesium in

[12] Chojnacki M, Dobrotka C, Osborn R, et al. Evaluating the Antimicrobial Properties of Commercial Hand Sanitizers. mSphere. 2021;6(2):e00062-21. Published 2021 Mar 3. doi:10.1128/mSphere.00062-21
[13] Bondurant SW, Duley CM, Harbell JW. Demonstrating the persistent antibacterial efficacy of a hand sanitizer containing benzalkonium chloride on human skin at 1, 2, and 4 hours after application. Am J Infect Control. 2019 Aug;47(8):928-932. doi: 10.1016/j.ajic.2019.01.004. Epub 2019 Feb 16. PMID: 30777389.
[14] Herdt BL, Black EP, Zhou SS, Wilde CJ. Inactivation of SARS-CoV-2 by 2 commercially available Benzalkonium chloride-based hand sanitizers in comparison with an 80% ethanol-based hand sanitizer. Infect Prev Pract. 2021;3(4):100191. doi:10.1016/j.infpip.2021.100191

a nano-matrix formulation. Using this proprietary formulation against a range of bacterial species indicates excellent bactericidal effect, with most bacterial species completely inactivated in under 30 seconds exposure, including spores of *Clostridium difficile*. A couple of bacterial species showed resistance to killing at 30s exposure but these were completely inactivated by 60s exposure to the preparation. Results from these tests are shown in the table below:

Organism (Exposure Time)	**Inoculum Level (cfu/mL)**	**Growth Average (cfu/g)**	**Log_{10} Reduction**
E. coli (30 seconds)	8.59×10^5	No Growth	5.93
MRSA (30 seconds)	7.55×10^5	No Growth	5.88
P. aeruginosa (30 seconds)	5.56×10^5	No Growth	5.75
B. cepacia (30 seconds)	6.24×10^5	310	3.30
B. cepacia (60 seconds)	6.24×10^5	No Growth	5.8
S. enterica (30 seconds)	5.91×10^5	No Growth	5.77
L. monocytogenes (30 seconds)	5.98×10^5	No Growth	5.78
C. jejuni (30 seconds)	2.42×10^5	No Growth	5.38
C. difficile (30 seconds)	2.40×10^5	No Growth	5.38
C. difficile (Spore form) (30 seconds)	1.67×10^5	No Growth	5.22
S. pyogenes (30 seconds)	2.25×10^5	No Growth	5.41
K. pneumoniae (30 seconds)	3.81×10^5	15	4.40
K. pneumoniae (60 seconds)	3.81×10^5	No Growth	5.58
E. faecalis (30 seconds)	8.84×10^5	No Growth	5.95

FACT FOUR - ALCOHOL-BASED SANITIZERS DECLINE IN THEIR EFFEVTIVNESS OVER TIME WHILE MEDITIZER WATER-BASED SANITIZER MAINTAINS A CONSISTANT 99.99% KILL RATE.

A study[15] evaluated immediate and persistent antimicrobial effectiveness comparing alcohol-containing sanitizers to the novel surfactant Benzalkonium Chloride (BZK)

[15] AORN J68 (Aug 1998) 239-251

used in Meditizer™ sanitizer. It was proven that all three products were equally effective after a single application, but after repeated use the alcohol-based sanitizer continued to decline in its effectiveness while the BZK product maintained the highest level of efficacy.

FACT FIVE - ALCOHOL-BASED SANITIZERS ARE FLAMMABLE AND EXPENSIVE TO SHIP AND STORE - MEDITZER WATER-BASED SANITIZER IS NIETHER.

The Safety Data Sheet for Ecolab's "Best Gel Hand Sanitizer" clearly states not only that the hand sanitizer is flammable but also states this: "Skin: In case of contact, immediately wash with plenty of soap and water for at least 15 minutes. Seek medical attention if irritation or redness occurs."

FACT SIX - MEDITIZER WATER-BASED SANITIZER HAS EXTENSIVE PROOF OF KILLING COVID-19 AT A RATE OF 99.99% AND THAT IT DOES SO FOR FOUR HOURS AT 99.99%. ALCOHOL-BASED SANITIZERS HAS NIETHER.

In February of 2021, the Arizona State University's Biodesign institute in conjunction with the Southwest College Of Naturopathic Medicine & Health Sciences conducted an assay to characterize the long term antimicrobial properties of our sanitizing products. The results of this study, conducted in a certified Biosafety Level 3 facility, support that the 2 in 1 Invisible Glove products are all able to kill the SARS-CoV-2 virus even after drying on a surface for 1 hour or 4 hours. [16]

THE PROBLEM IS REAL

Prior to the COVID-19 pandemic, each year, 135,000 deaths in Europe and 99,000 deaths in the United States had been reported from health care-associated infections. In the U.S., more than three-quarters of a million people die of sepsis each year. These numbers are likely under-reported, and they do not account for the number of deaths from infections outside of healthcare institutions. A leading cause of these deaths is the lack of hand hygiene.[17]

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[16] Arizona State University, Southwest College of Naturopathic Medicine, Characterization of the long-term anti-SAR-CoV-2 properties of novel hand sanitizer solution. February 23, 2021

[17] WHO (2009). WHO guidelines on hand hygiene in health care. Page 6, available at http://whqlibdoc. who. int/ publications/ 2009/ 9789241597906_ eng. pdf?ua= 1

So, the question remains, why have alcohol-based hand sanitisers continued to be so widely used? The answer lies in the evidence base surrounding the introduction of hand-sanitizers into routine clinical practice. For most of the 20th Century, alcohol was avoided, and plain soap and water were recommended for hand hygiene by the U.S Public Health Service, the CDC, and the Professionals in Infection Control. In 1961, the U.S. Public Health Service recommended hand-washing techniques for health care workers, but antiseptics were believed to be inferior to soap and water. The 1975 and 1985 hand-washing guidelines for hospitals, published by the CDC, featured plain soap and water and recommended waterless antiseptics only if sinks were not available. In 1988 and 1995, hand-washing guidelines from professionals in infection control were similar to those of the CDC but allowed alcohol hand rubs in some clinical settings. The resident flora of the skin microbiome is not normally pathogenic but transient microorganisms can be pathogenic and contagious. Transient flora can be mechanically removed by proper hand-washing protocols but frequent handwashing can also cause a minimal reduction or sometimes an increase in bacterial population on clean hands. Also, normal handwashing alone cannot always prevent the spread of fatal infection. Indeed, simple handwashing before patient care can, in some cases, result in higher counts of microorganism colonies.[18]

In the 1990s, multidrug-resistant pathogens emerged, typified by Vancomycin-resistant Enterococci (VRE) and methicillin-resistant Staph. aureus (MRSA). In 1995, the Healthcare Infection Control Practices Advisory Committee recommended antimicrobial soap or waterless antiseptics for the hands of health care workers who were treating patients infected by such multidrug-resistant pathogens. In 2019, the CDC published a report on "Antibiotic Resistance Threats in the United States.[19]"

This report is: "dedicated to the 48,700 families who lose a loved one each year to antibiotic resistance or Clostridioides difficile, and the countless healthcare providers, public health experts, innovators and others who are fighting back with everything they have." [20]

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[18] . Larson, E. (1999). Skin hygiene and infection prevention: More of the same or different approaches? Clin Infect Dis 29 1287-94. 15.

[19] Larson, E., McGinley, K.J., Grove, G.L., Leyden, J.J. and Talbot, G.H. (1986). Physiologic, microbiologic and seasonal effects of hand-washing on the skin of health care personnel. Am J Infect Control 14 51-9.

Viral respiratory infections are a leading cause of morbidity and mortality.[21] Viruses can be divided into two main groups: enveloped and nonenveloped viruses.[22] Enveloped viruses are coated with a lipid bilayer and they enter a host cell by merging this lipid bilayer with the cell membrane.[23] Examples of enveloped viruses are the Human Immunodeficiency Virus (HIV), Influenza Virus and coronaviruses (CoVs).[24]

MEDITIZER WATER-BASED SANITIZER IS UNIQUE – WHY OUR COPPER/ MAGNESIUM SET US APART FROM ANY OF THE COMPETITION.

While FDA has indicated that hand sanitizers should generally be considered medical products, or especially drug products, there has been no final rule that specifies that a claim to "hand sanitization" fits within the definitional sections of 21 U.S.C. §§ 321(g) or (h). Most recently, in the Consumer Antiseptic Rub Final Rule (84 FR 14847, 18478, April 12, 2019), the agency was studious to use the term "sanitizer" only in quotation marks. And, in response to Comment 4, specifically declined to adopt the term "hand sanitizer" as potential claim for a consumer antiseptic rub (defined as an antiseptic used without water). This is well-advised since the plain meaning of the term "sanitizer" references cognate terms such as cleanse (a cosmetic claim by statute), hygienic, as well as "disinfect."

OVERVIEW OF NON-CHEMICAL AND NON-METABOLIC ACTION OF COPPER IN THE MEDITIZER HAND SANITIZER.

Copper's antimicrobial activity in the present formulation when used on the skin of the hand is based on creation of an induced micro-electromagnetic field surrounding the metallic-coordination complex that induces electrical and/or paramagnetic distortions in microbial systems in proximity resulting in eventual bacterial, fungal, or viral death. The metallic-coordination complex that induces electrical and/or paramagnetic distortions in microbial systems in close proximity resulting in eventual bacterial, fungal, or viral death.

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[20] Meers, P.D. (1980). The shedding of bacteria and skin squames after handwashing. In: Newsom, S.W.B. and Caldwell, A.D.S., eds. Problems in the Control of Hospital Infection. London, Royal Society of Medicine 13-8; International Congress and Symposium Series vol 23

[21] WHO website (2017). Available at http://www. who. int. en/

[22] . Harrison, S. (199). Principles of virus structure. In: Fields, B.N., Krupe, D.M., et al., eds, Virology, 2nd edn. Raven Press, Ltd., New York.

[23] Falanga, A. Cantisani, M., Pedone, C. and Galdiero, S. (2009). Membrane fusion and fission: Enveloped viruses. Protein & Peptide Letters 16 751-759.

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