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Review Article

A Review on Hand Sanitizers: Types of Hand Sanitizers, Mechanism of action, Toxicity and Adverse Effects COVID-19

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Abstract: The latest COVID -19 corona virus disease outbreak is responsible for a highly pathogenic corona virus (SARS-CoV-2). Since no vaccines or licensed drugs are currently available, sanitization interventions appear to be important to help delay the transmission of COVID -19. For regular hand hygiene, WHO suggested alcohol-based hand sanitizers, containing predominantly of hydrogen peroxide, ethanol, and isopropyl alcohol in various combinations. When misused, these preparations can become harmful to human health. The key goal of the new analysis is to demonstrate the toxicity and serious adverse effects.

Keywords: COVID -19, Alcohol Hand sanitizers, WHO, Toxicity, Ethanol.

1. INTRODUCTION

The new epidemic spreads by corona virus 2 (SARS-CoV-2) via Wuhan, China [1]. Respiratory disturbances, pneumonia, cough, fever, body pains and mortality rates, are characterized by the disease particularly in elderly people and with those chronic health conditions [2]. In the middle of March 2020, the global spread of the disease was such that the World Health Organization(WHO) publicly labeled epidemic of covid-19 as a pandemic outbreak [3]. Strict preservative steps, including frequent hand washing with hand sanitizer or with water and soap when water and soap are not available, are important for controlling the spread of virus [4]. Because of their quick intervention and widespread microbial existence, the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) have recommended the use of hand sanitizers based on alcohols to reduce contamination and transmission [5-7]. Since no vaccines or licensed drugs are currently available, sanitation interventions appear to be important to help delay the transmission of COVID -19 [8, 9]. Alcohol based hand sanitizer have been used to deter the spread of viral and bacterial infections as an efficient alternative to hand washing, making them one of the main protocols to reduce burden on healthcare [10, 11]. There is an active ingredient in every hand sanitizer, which may be ethanol or iso propanol. The use of hand sanitizers dependent on alcohol can decrease the chances of infection spreading. Others may include compounds of quaternary ammonium (QACs). Alcohol broad spectrum disinfectants that destroy bacteria and fungi. QACs include benzalkonium chloride, benzylakoniumchloride are active surfactants and domestic application of broad spectrum antimicrobials [12]. In compliance with the profound consequences of their rapid response and wide variety of microbial process providing protection towards bacteria and viruses, the WHO recommended alcohol-based hand sanitizer, the efficacy with non-enveloped viruses is however still datable [13-18]. The key goal of ongoing study was to demonstrate the toxicity and severe adverse effects.

2. Types of hand sanitizers

Hand sanitizers are of two types (1) hand sanitizers that are not based on alcohol (NABHS) and (2) hand sanitizers that are based on alcohol (ABHS). A widely used disinfectant is the main active component of NABHS is benzalkonium chloride, it is a quaternary ammonium. Benzalkonium chloride disinfectants is normally less harmful than alcohol disinfectants [7]. On the other side, n- propanol, ethanol, iso propyl alcohol or mixture of these, water,

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humectants and excipients can be a alcohol based hand sanitizer [19]. And they are forms of hand sanitizer based on falsified alcohol: (1) methanol containing sanitizers, an additive that will not be identified as an ingredient [10, 2] alcohol containing sanitizers below 60%. Since it is extremely poisonous and can cause serious reactions when exposed to the lungs, mouth, skin methanol should not be used in hand sanitizers [20]. Hand sanitizers based on alcohol are available in various dosage types, such as gels, liquid, foam, since each form has of its own characteristics, a research was carried out to understand the effect on sensory characteristics that can affect the quality of the product by the consumer and eventually affect the use of hand hygiene [21-23]. If soap and water were not readily available, hand sanitizers can be held easily and useful. As not all sanitizers are effective and the WHO has therefore advised the use of hand sanitizer alcohol based that can be readily produced for local manufacturing [24].WHO recommends two alcohol based formulations for local manufacturing facilities or in house that are 80% v/v ethanol,1.45 %v/v glycerol,0.125%v/v hydrogen peroxide for formulation A and 75 % v/v isopropyl alcohol,1.45 %v/v glycerol,0.125 %v/v hydrogen peroxide for formulation B [25]. Though the main component of hand sanitizers, H_2O_2 and alcohol are generally not externally harmful, there has been concern about skin degradation involved with improper use of hand sanitizers, which may help protect the skin from other microorganisms and viruses [26].

2.1 Alcohol and soap

CDC suggests hand washing with soap and water, it substantially reduces bacteria and dirt on surface of the skin[6]. Contrasted to soap and alcohol based hand sanitizers do not destroy all kinds of bacteria, germs like norovirus and clostridium difficle, common diarrhea that causes pathogens [27, 28]. Since they are useful most people tend to use hand sanitizers and assume that sanitizers might not be efficient as the germs that destroy soap, but people cannot use sufficient sanitizers to disinfect their hands [29, 30]. Around 2.5 – 3m L of liquid is dispersed on the palm and applied on the surfaces of both hands for 25 – 30s optimize the potency of the hand sanitizers [10].

3. Mechanism of action

Mechanism of action for the chemicals is as shown in the Table 1

Table-1: classification of chemicals disinfectants commonly used in hand sanitizers and their mechanism of action.

Chemical groups	Mechanism of action	Examples
Alcohol	Denaturation of proteins in the plasma membrane	**Ethanol** **Iso propanol**
Pyrogens	Free radical oxidation of essential cell components	**Hydrogen peroxide** **Peracetic acid**
Quaternary ammonium compounds	Lower surface tension Inactivates the enzymes Degradation of cell- protein	**Benzalkonium chlorides, including alkyl dimethyl benzyl ammonium chloride** **Didecyl dimethyl ammonium chloride**
Chlorine compounds	Oxidation/ Halogenatation of cellular proteins	**Chloride dioxide** **Hypochlorites** **Chloramines-t trihydrate**

3.1 Alcohol Mechanism against bacteria

Here the example of the mode of action of alcohol against bacteria is compound n- propanol [19], the exact mode of antimicrobial action of alcohol is not understood, but may be associated with inhibition and damage to the membrane or uncoupling of mRNA and protein synthesis by the actions of ribosome and RNA polymerase, as well as protein denaturation [19, 31]. At concentration between 60% and 90% , the optimum bactericidal effectiveness against bacteria is achieved[32]. The essential mechanism of protein denaturation is water [33]. If several are affected by alcohol, there is disruption to the membrane of essential metabolism and degradation of membrane integrity[19]. Alcohols however, demonstrate bactericidal action against vegetative bacteria, but against spores, which undergo metabolism and binary fission[34].

3.2 Alcohol Mechanism against viruses

Primarily viral targets for hand sanitizers dependent on alcohol are the viral membrane that is extracted by host lipids, if exists the protein containing and protecting the genetic material [19]. The viral life cycle has attachment, biosynthesis, penetration, maturation, lysis are important components and they are necessary for transfer to other host, the structure or function of each components above the virus would usually be made inactive [33]. While it is understood about the fundamental mechanism of alcohol agents against viruses relative to bacteria, it is known ethanol has greater and stronger virucidal effect to propanol. High concentrations of ethanol have proven particularly effective against virus- enveloped viruses [35]. By adding ethanol solutions, the potency against viruses which are high resistant to ethanol alone can be improved [8, 36]. Considering the possible combination of ethanol and acidity, it is also recognized most

sanitizers tend to be inactive towards the non-enveloped viruses [37].

3.3 Benzalkonium chloride mechanism of action

The example followed for the NABHS is benzalkonium chloride. The main component of NABHS is benzalkonium chloride and it is not effective towards non enveloped viruses [38, 39]. And a report demonstrates its potency against human coxsackie virus exception that it is not enveloped [40]. The lipid enveloped in both bacteria and viruses seems, given this exception, to be a vital structure for the effectiveness of benzalkonium chloride. The benzalkonium chloride cationic head group is gradually adsorbed in the lipid bilayer to phospholipids negatively charged phosphate heads, thereby increasing its concentration, contributing to decreased membrane fluidity and thus to the formation of hydrophilic membrane gaps [41]. The alkyl chains 'tail' portion of benzalkonium chloride further disrupts and disturbs the lipid bilayer by pervading the surface and disturbing the structural and functional characteristics [41]. Consequently, the activity of the protein is disrupted and the variation of the above effects results in the absorption of bilayer components into benzalkonium chloride or phosphor lipid micelles [41]. Benzalkonium chloride inhibits inter cellular targets and contradicts the transcriptional actions of DNA [42].

4. Toxicity of hand sanitizers

4.1 Toxicity of Iso propanol

Iso propyl alcohol poisoning arises mostly because of unintentional absorption of compounds and also because of rectal and tropical applications. 250ml and 160 -240 ml are known to be the fatal dosage of isopropyl alcohol [43, 44]. Several reports have documented that topical isopropyl alcohol administration contributes to unconsciousness [45-47]. According to Halloa enterprises, safety data sheet, impact the health toxicity occurs at LD 50 >2000 mg/kg (orally) and toxic effects due to dermal contamination, it will occur at LD 50 >2000 mg/kg and it expected to be LC50 >5 mg/l by inhalation. In fatal poisoning, the concentration of 1g/l of blood or more was reported(48). There have been no major health complications with low dosage use, while the ingestion of 20-30 ml (50 % iso propanol) indicates mild signs or symptoms [49]. Nearly 0.5 -1 ml/kg of 70 %hand sanitizer based on isopropyl is known to be hazardous dosage, although it can vary from person to other person based on the degree of human resistance [50]. The potential lethal dosage of iso propanol for adults is approximately 240ml(51),if orally consumed isopropyl alcohol is completely absorbed within 2 hours, as the liver metabolizes iso propanol into acetone and it is excreted by the kidney [52]. It is a Central Nervous System depressant, that is metabolized into acetone that can be contribute to chronic CNS depression, decrease respiratory drive and hypotension iso propyl alcohol often irritates the gastrointestinal mucosa lining and contributes to gastritis along with causing hypoglycemia of ketosis respiratory failure and serum creatinine increase [52-54]. Myocardial depression can be caused by a higher dose when it is long term use leads to acute renal failure, rhabdomyolysis, myoglobinuria [26]. Dermal absorption of the iso propanol can cause prolonged and regular skin and irritation. Skin rash, redness, dryness and itching results from exposure to isopropyl alcohol.

4.2 Toxicity of Hydrogen peroxide

The toxicity of H_2O_2 relies on its ingestion with concentration as a typical route of administration [55]. It has been accepted that low hydrogen peroxide content (3% solution) intake is not particularly detrimental to human health and responsible for mild health issues [56]. In some cases, moderate mucosal inflammation and portal vein metabolism, bowel dilation [57] vomiting have been identified as causing gastrointestinal problems [58]. Hydrogen peroxide is toxic due to formation of gases and local tissue inflammation, as tissue catalase reacts with it and decomposes into oxygen and water with 3% exposure to hydrogen peroxide. Concentration of hydrogen peroxide is correlated with the amount of oxygen released. At normal temperature and,1ml of 3% hydrogen peroxide is responsible for producing 10 ml of oxygen and gas emboli, gastric distension, gas emboli is responsible for pressure [26], due to the existence of abundant tissue catalase and H_2O_2 connection to the vascular system [56]. Dermal exposure with 3% hydrogen peroxide results in mild skin and mucosal membrane irritation.

4.3 Toxicity of Ethanol

Ethanol is commonly used as a disinfectant. Due to this lack of up to date research, its capability to cause skin cancer through absorbing skin carcinogenicity remains uncertain[59]. Specific toxicity related to ingestion or dermal contact with hand sanitizer based on ethanol can be appropriate. People have different levels of ethanol response and resistance leading to difficulties in determining the degree of hand rub dose dependent on toxic ethanol. The serum ethanol concentration was determined to be negligible after administering 74.1 % ethanol based disinfectant with a concentration level0.5 mg/l for 10 minutes in 1.0 to 1.5 mg/l range, depending mostly on dermal absorption of ethanol [60]. Hand sanitizers comprising between 95%(w/w),85%(w/w) and 55%(w/w) of ethanol were provided in a study conducted by 12 participants [61]. The highest average absorption was observed with a break for minute between 20.95mg/l,11.45mg/l, and 6.9 mg/l, 4ml for 30s for 2o minutes. The volume of ethanol ingested was 1365mg (2.3%), 630 mg (1.1%), and 358mg (0.9), respectively. Moreover, blood acetaldehyde was detected and 0.57 mg/l was estimated to be its median peak. The acute exposure is not harmful was reported in this study, but decreased efficiency is predicted when blood ethanol levels

exceed 200 -300mg/l and above. Based on the concentrations of the afore mentioned hand rubs tested and demonstrated that the values obtained are much lower than those obtained for acute toxicity, however, the persistent use of sanitizers in the safety assessment must be compensated by chronic toxicity [59-61]. Dermal ethanol exposure causes skin and eye irritation and allergic condition when repeated use results in skin dry skin or cracking with peeling redness or scratching. Severe alcohol toxicity occurs by oral ingestion of any house hold alcohol containing substance, like hand sanitizers based on alcohol , mouth washing [62]. A 360ml of hand sanitizer based on ethanol can trigger life threatening conditions in an adult. Lethal ethanol dosage of around 400 ml/dl, while 400ml(80 % ethanol based solution) could be fatal in an abnormal individual exposure [63, 64]. Ethanol poisoning is correlated with respiratory failure, resulting to hypothermia respiratory arrest, cardiac arrest ketoacidosis, hypotension, hypoglycemia [65]. Acute liver damage, myoglobinuria, hypomagnesaemia, hypokalemia, hypocalcaemia, hyophosphatemia [66] and water dieresis [67] can be associated with ethanol exposure. Concluding the discussion, the repeated and extended use of hand sanitizer based on ethanol will contribute to health risks. If anyone uses hand rub based on ethanol for months and many times a day, dermal absorption ca escalate to a toxic level as this is currently occurring as a result of the prevention step of COVID-19. Carelessness or misuse in the consumption of such product, as reflected in different studies, can cause severe health problems [65, 67, 68].

5. Adverse effects

Allergic Contact Dermatitis and Irritant Contact Dermatitis are the most frequently reported skin reaction to the use of alcohol based hand sanitizers [69, 70]. ICD symptoms can vary from mild to weakening, if serious with symptoms such as dryness, pruritus, erythema and bleeding. Following ACD, symptoms may be moderate and localized or extreme and common, with the most serious signs and symptoms, ACD is characterized by respiratory failure or other symptoms of anaphylaxis [71, 72]. products for hand hygiene like sanitizers, soaps can damage to the skin by several mechanisms; denaturation of the protein of the stratum corneum, modification of lipid bilayer, decrease of cohesion in corneocytes and reduction of the water binding potential of the stratum corneum [73, 74]. Ethanol has the least irritants to skin among the alcohol based hand formulations, related to n-propanol and iso propanol property [75]. Hand sanitizers based on alcohol have a drying effect on the hands that may further cause the skin to peel or crack [76-78]. Individuals with alcohol based allergic disorders can have a true allergy to alcohol or impurity allergies, metabolites of aldehydes or excipients such as parabens, benzalkonium chloride, benzyl alcohol [23, 79, 80].

6. CONCLUSION

Proper hand hygiene prevents several diseases from spreading, include COVID -19. The use of hand sanitizers and hand washing with soap and water to clean hands changed tremendously during COVID- 19. Usage of ABHS is increasing more prevalent due to their quick action and effectiveness in killing microorganisms, particularly when hand washing with soap and water is not effective. Increased and repeated use of hand sanitizer results in toxicity and fatal, it can be contributed by unintentional ingestion, absorption though dermal contact and suicidal ingestion. Prolonged exposure of antibiotics and genotoxic chemicals to microbes tends to cause mutations through natural process that make them resistant to survive from repeated use of hand sanitizers.

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REFERENCES

1. Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., ... & Cao, B. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The lancet*, *395*(10223), 497-506.
2. Lai, C. C., Shih, T. P., Ko, W. C., Tang, H. J., & Hsueh, P. R. (2020). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. *International journal of antimicrobial agents*, *55*(3), 105924.
3. Organization, W. H. (2020). Coronavirus Disease (COVID-19)-events as they happen. Website: https://www who int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen [accessed 17April 2020].
4. Jairoun, A. A., Al-Hemyari, S. S., & Shahwan, M. (2021). The pandemic of COVID-19 and its implications for the purity and authenticity of alcohol-based hand sanitizers: The health risks associated with falsified sanitizers and recommendations for regulatory and public health bodies. *Research in Social and Administrative Pharmacy*, *17*(1), 2050-2051.
5. Almaghaslah, D., Kandasamy, G., Almanasef, M., Vasudevan, R., & Chandramohan, S. (2020). Review on the coronavirus disease (COVID-19) pandemic: its outbreak and current status. *International journal of clinical practice*, *74*(11), e13637.
6. Jing, J. L. J., Pei Yi, T., Bose, R. J., McCarthy, J. R., Tharmalingam, N., & Madheswaran, T. (2020). Hand sanitizers: a review on formulation aspects, adverse effects, and regulations. *International journal of environmental research and public health*, *17*(9), 3326.

7. Gold, N.A., Avva, U. (2018). Alcohol Sanitizer. StatPearls [Internet]: StatPearls Publishing.
8. Kampf, G. (2018). Efficacy of ethanol against viruses in hand disinfection. *Journal of Hospital Infection*, *98*(4), 331-338.
9. Kampf, G., Todt, D., Pfaender, S., & Steinmann, E. (2020). Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. *Journal of hospital infection*, *104*(3), 246-251.
10. Pittet, D., Allegranzi, B., Boyce, J., & World Health Organization World Alliance for Patient Safety First Global Patient Safety Challenge Core Group of Experts. (2009). The World Health Organization guidelines on hand hygiene in health care and their consensus recommendations. *Infection Control & Hospital Epidemiology*, *30*(7), 611-622.
11. Cohen, S. H., Gerding, D. N., Johnson, S., Kelly, C. P., Loo, V. G., McDonald, L. C., ... & Wilcox, M. H. (2010). Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the infectious diseases society of America (IDSA). *Infection Control & Hospital Epidemiology*, *31*(5), 431-455.
12. Hayat, A., & Munnawar, F. (2016). Antibacterial effectiveness of commercially available hand sanitizers. *Int J Biol Biotech*, *13*(3), 427-431.
13. Seto, W. H., Tsang, D., Yung, R. W. H., Ching, T. Y., Ng, T. K., Ho, M., ... & Advisors of Expert SARS group of Hospital Authority. (2003). Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *The lancet*, *361*(9368), 1519-1520.
14. Manocha, S., Walley, K. R., & Russell, J. A. (2003). Severe acute respiratory distress syndrome (SARS): a critical care perspective. *Critical care medicine*, *31*(11), 2684-2692.
15. Fendler, E., & Groziak, P. (2002). Efficacy of alcohol-based hand sanitizers against fungi and viruses. *Infection Control & Hospital Epidemiology*, *23*(2), 61-62.
16. Oluwatuyi, S. V., Agbele, A. T., Ogunrinde, M. E., Ayo, A. T. V., Ayo, A. M., Fayoke, A. B., ... & Deborah, A. A. (2020). Alcohol-Based Hand Sanitizers: Review of Efficacy and Adverse Effect. *Alcohol*, *81*.
17. Ansari, S. A., Springthorpe, V. S., Sattar, S. A., Rivard, S., & Rahman, M. (1991). Potential role of hands in the spread of respiratory viral infections: studies with human parainfluenza virus 3 and rhinovirus 14. *Journal of clinical microbiology*, *29*(10), 2115-2119.
18. Sattar, S. A. (2004). Microbicides and the environmental control of nosocomial viral infections. *Journal of Hospital infection*, *56*, 64-69.
19. McDonnell, G., & Russell, A. D. (1999). Antiseptics and disinfectants: activity, action, and resistance. *Clinical microbiology reviews*, *12*(1), 147-179.
20. Chan, A. P., & Chan, T. Y. (2018). Methanol as an unlisted ingredient in supposedly alcohol-based hand rub can pose serious health risk. *International journal of environmental research and public health*, *15*(7), 1440.
21. Visscher, M., Davis, J., & Wickett, R. (2009). Effect of topical treatments on irritant hand dermatitis in health care workers. *American journal of infection control*, *37*(10), 842-e1.
22. Pittet, D. (2001). Compliance with hand disinfection and its impact on hospital-acquired infections. *Journal of Hospital Infection*, *48*, S40-S46.
23. Winnefeld, M. A., Richard, M. A., Drancourt, M., & Grob, J. J. (2000). Skin tolerance and effectiveness of two hand decontamination procedures in everyday hospital use. *British Journal of Dermatology*, *143*(3), 546-550.
24. Daverey, A., & Dutta, K. (2021). COVID-19: Eco-friendly hand hygiene for human and environmental safety. *Journal of environmental chemical engineering*, *9*(2), 104754.
25. World Health Organization. (2010). *Guide to local production: WHO-recommended handrub formulations* (No. WHO/IER/PSP/2010.5). World Health Organization.
26. Mahmood, A., Eqan, M., Pervez, S., Alghamdi, H. A., Tabinda, A. B., Yasar, A., ... & Pugazhendhi, A. (2020). COVID-19 and frequent use of hand sanitizers; human health and environmental hazards by exposure pathways. *Science of the Total Environment*, *742*, 140561.
27. Blaney, D. D., Daly, E. R., Kirkland, K. B., Tongren, J. E., Kelso, P. T., & Talbot, E. A. (2011). 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. *American journal of infection control*, *39*(4), 296-301.
28. Oughton, M. T., Loo, V. G., Dendukuri, N., Fenn, S., & Libman, M. D. (2009). Hand hygiene with soap and water is superior to alcohol rub and antiseptic wipes for removal of Clostridium difficile. *Infection Control & Hospital Epidemiology*, *30*(10), 939-944.
29. Kampf, G., Marschall, S., Eggerstedt, S., & Ostermeyer, C. (2010). Efficacy of ethanol-based hand foams using clinically relevant amounts: a cross-over controlled study among healthy volunteers. *BMC Infectious Diseases*, *10*(1), 1-5.
30. Stebbins, S., Cummings, D. A., Stark, J. H., Vukotich, C., Mitruka, K., Thompson, W., ... & Burke, D. S. (2011). Reduction in the incidence of influenza A but not influenza B associated with use of hand sanitizer and cough hygiene in schools: a randomized controlled trial. *The Pediatric infectious disease journal*, *30*(11), 921.

31. Haft, R. J., Keating, D. H., Schwaegler, T., Schwalbach, M. S., Vinokur, J., Tremaine, M., ... & Landick, R. (2014). Correcting direct effects of ethanol on translation and transcription machinery confers ethanol tolerance in bacteria. *Proceedings of the National Academy of Sciences*, *111*(25), E2576-E2585.
32. Morton, H. E. (1950). The relationship of concentration and germicidal efficiency of ethyl alcohol. *Annals of the New York Academy of Sciences*, *53*(1), 191-196.
33. Golin, A. P., Choi, D., & Ghahary, A. (2020). Hand sanitizers: A review of ingredients, mechanisms of action, modes of delivery, and efficacy against coronaviruses. *American journal of infection control*, *48*(9), 1062-1067.
34. Thomas, P. (2012). Long-term survival of Bacillus spores in alcohol and identification of 90% ethanol as relatively more spori/bactericidal. *Current microbiology*, *64*(2), 130-139.
35. Kampf, G., & Kramer, A. (2004). Epidemiologic background of hand hygiene and evaluation of the most important agents for scrubs and rubs. *Clinical microbiology reviews*, *17*(4), 863-893.
36. Park, G. W., Barclay, L., Macinga, D., Charbonneau, D., Pettigrew, C. A., & Vinjé, J. (2010). Comparative efficacy of seven hand sanitizers against murine norovirus, feline calicivirus, and GII. 4 norovirus. *Journal of food protection*, *73*(12), 2232-2238.
37. Dastider, D., Jyoti Sen, D., Kumar Mandal, S., Bose, S., Ray, S., & Mahanti, B. (2020). Hand sanitizers bid farewell to germs on surface area of hands. *Eur J Pharm Med Res*, *7*, 648-656.
38. Resnick, L., Veren, K., Salahuddin, S. Z., Tondreau, S., & Markham, P. D. (1986). Stability and inactivation of HTLV-III/LAV under clinical and laboratory environments. *Jama*, *255*(14), 1887-1891.
39. Springthorpe, V. S., Grenier, J. L., Lloyd-Evans, N., & Sattar, S. A. (1986). Chemical disinfection of human rotaviruses: efficacy of commercially-available products in suspension tests. *Epidemiology & Infection*, *97*(1), 139-161.
40. Wood, A., & Payne, D. (1998). The action of three antiseptics/disinfectants against enveloped and non-enveloped viruses. *Journal of Hospital Infection*, *38*(4), 283-295.
41. Wessels, S., & Ingmer, H. (2013). Modes of action of three disinfectant active substances: a review. *Regulatory toxicology and pharmacology*, *67*(3), 456-467.
42. Zinchenko, A. A., Sergeyev, V. G., Yamabe, K., Murata, S., & Yoshikawa, K. (2004). DNA compaction by divalent cations: structural specificity revealed by the potentiality of designed quaternary diammonium salts. *ChemBioChem*, *5*(3), 360-368.
43. McBay, A. J. (1973). Toxicological findings in fatal poisonings. *Clinical chemistry*, *19*(4), 361-365.
44. Ashkar, F. S., & Miller, R. O. B. E. R. T. (1971). Hospital ketosis in the alcoholic diabetic: a syndrome due to isopropyl alcohol intoxication. *Southern medical journal*, *64*(11), 1409-1411.
45. McFadden, S. W., & Haddow, J. E. (1969). Coma produced by topical application of isopropanol. *Pediatrics*, *43*(4), 622-623.
46. Moss, M. H. (1970). Alcohol-induced hypoglycemia and coma caused by alcohol sponging. *Pediatrics*, *46*(3), 445-447.
47. Jones, A. E., & Summers, R. L. (2000). Detection of isopropyl alcohol in a patient with diabetic ketoacidosis. *The Journal of emergency medicine*, *19*(2), 165-168.
48. Adelson, L. (1962). Fatal intoxication with isopropyl alcohol (rubbing alcohol). *American journal of clinical pathology*, *38*(2), 144-151.
49. Fuller, H. C., & Hunter, O. B. (1927). Isopropyl alcohol–an investigation of its physiologic properties. *J. Lab. Clin. Med*, *12*, 326-349.
50. Olson, K. R., Anderson, I. B., Benowitz, N. L., Blanc, P. D., Clark, R. F., Kearney, T. E., ... & Wu, A. H. (Eds.). (2007). *Poisoning & drug overdose* (Vol. 13). Lange Medical Books/McGraw-Hill.
51. Gosselin, R. E., Smith, R. P., Hodge, H. C., & Braddock, J. E. (1984). *Clinical toxicology of commercial products* (Vol. 1085). Baltimore: Williams & Wilkins.
52. Zaman, F., Pervez, A., & Abreo, K. (2002). Isopropyl alcohol intoxication: a diagnostic challenge. *American Journal of Kidney Diseases*, *40*(3), e12-1.
53. Trummel, J., Ford, M., & Austin, P. (1996). Ingestion of an unknown alcohol. *Annals of emergency medicine*, *27*(3), 368-374.
54. Slaughter, R. J., Mason, R. W., Beasley, D. M. G., Vale, J. A., & Schep, L. J. (2014). Isopropanol poisoning. *Clinical toxicology*, *52*(5), 470-478.
55. Food and Drug Administration. (1988). Oral health care drug products for over-the-counter human use: tentative final monograph: notice of proposed rulemaking. *Federal Register*, *53*, 2436-2461.
56. Moon, J. M., Chun, B. J., & Min, Y. I. (2006). Hemorrhagic gastritis and gas emboli after ingesting 3% hydrogen peroxide. *The Journal of emergency medicine*, *30*(4), 403-406.
57. Watt, B. E., Proudfoot, A. T., & Vale, J. A. (2004). Hydrogen peroxide poisoning. *Toxicological reviews*, *23*(1), 51-57.
58. Sung, J., Cossarini, F., Palaiodimos, L., Benson, B., & Meholli, M. (2018). Extra oxygen leads to bubble trouble: portal vein gas embolism from 3% hydrogen peroxide ingestion. *Cureus*, *10*(2).
59. Lachenmeier, D. W. (2008). Safety evaluation of topical applications of ethanol on the skin and

inside the oral cavity. *Journal of Occupational Medicine and Toxicology*, *3*(1), 1-16.
60. Kirschner, M. H., Lang, R. A., Breuer, B., Breuer, M., Gronover, C. S., Zwingers, T., ... & Fauteck, J. D. (2009). Transdermal resorption of an ethanol- and 2-propanol-containing skin disinfectant. *Langenbeck's archives of surgery*, *394*(1), 151-157.
61. Kramer, A., Below, H., Bieber, N., Kampf, G., Toma, C. D., Huebner, N. O., & Assadian, O. (2007). Quantity of ethanol absorption after excessive hand disinfection using three commercially available hand rubs is minimal and below toxic levels for humans. *BMC Infectious Diseases*, *7*(1), 1-12.
62. Vonghia, L., Leggio, L., Ferrulli, A., Bertini, M., Gasbarrini, G., Addolorato, G., & Alcoholism Treatment Study Group. (2008). Acute alcohol intoxication. *European Journal of Internal Medicine*, *19*(8), 561-567.
63. Archer, J. R., Wood, D. M., Tizzard, Z., Jones, A. L., & Dargan, P. I. (2007). Alcohol hand rubs: hygiene and hazard. *Bmj*, *335*(7630), 1154-1155.
64. Sanap, M., & Chapman, M. J. (2003). Severe ethanol poisoning: a case report and brief review. *Critical Care and Resuscitation*, *5*(2).
65. Gormley, N. J., Bronstein, A. C., Rasimas, J. J., Pao, M., Wratney, A. T., Sun, J., ... & Suffredini, A. F. (2012). The rising incidence of intentional ingestion of ethanol-containing hand sanitizers. *Critical care medicine*, *40*(1), 290.
66. Wilson, M. E., Guru, P. K., & Park, J. G. (2015). Recurrent lactic acidosis secondary to hand sanitizer ingestion. *Indian journal of nephrology*, *25*(1), 57.
67. Bouthoorn, S. H., Van der Ploeg, T., Van Erkel, N. E., & Van der Lely, N. (2011). Alcohol intoxication among Dutch adolescents: acute medical complications in the years 2000-2010. *Clinical pediatrics*, *50*(3), 244-251.
68. Salomone, A., Bozzo, A., Di Corcia, D., Gerace, E., & Vincenti, M. (2018). Occupational exposure to alcohol-based hand sanitizers: the diagnostic role of alcohol biomarkers in hair. *Journal of analytical toxicology*, *42*(3), 157-162.
69. Wilhelm, K. P. (1996). Prevention of surfactant-induced irritant contact dermatitis. *Prevention of Contact Dermatitis*, *25*, 78-85.
70. Ale, I. S., & Maibach, H. I. (2014). Irritant contact dermatitis. *Reviews on environmental health*, *29*(3), 195-206.
71. Misteli, H., Weber, W. P., Reck, S., Rosenthal, R., Zwahlen, M., Fueglistaler, P., ... & Marti, W. R. (2009). Surgical glove perforation and the risk of surgical site infection. *Archives of surgery*, *144*(6), 553-558.
72. Larson, E. L., Hughes, C. A. N., Pyrek, J. D., Sparks, S. M., Cagatay, E. U., & Bartkus, J. M. (1998). Changes in bacterial flora associated with skin damage on hands of health care personnel. *American journal of infection control*, *26*(5), 513-521.
73. Löffler, H., Kampf, G., Schmermund, D., & Maibach, H. I. (2007). How irritant is alcohol?. *British Journal of Dermatology*, *157*(1), 74-81.
74. Graham, M. A., Nixon, R., Burrell, L. J., Bolger, C., Johnson, P. D., & Grayson, M. L. (2005). Low rates of cutaneous adverse reactions to alcohol-based hand hygiene solution during prolonged use in a large teaching hospital. *Antimicrobial Agents and Chemotherapy*, *49*(10), 4404-4405.
75. Erasmus, V., Daha, T. J., Brug, H., Richardus, J. H., Behrendt, M. D., Vos, M. C., & van Beeck, E. F. (2010). Systematic review of studies on compliance with hand hygiene guidelines in hospital care. *Infection Control & Hospital Epidemiology*, *31*(3), 283-294.
76. Guin, J. D., & Goodman, J. (2001). Contact urticaria from benzyl alcohol presenting as intolerance to saline soaks. *Contact Dermatitis*, *45*(3), 182-183.
77. de Groot, A. C. (1987). Contact allergy to cosmetics: causative ingredients. *Contact dermatitis*, *17*(1), 26-34.
78. Podda, M., Zollner, T., Grundmann-Kollmann, M., Kaufmann, R., & Boehncke, W. H. (1999). Allergic contact dermatitis from benzyl alcohol during topical antimycotic treatment. *Contact Dermatitis*, *41*(5), 302-303.
79. Larson, E., Leyden, J. J., McGinley, K. J., Grove, G. L., & Talbot, G. H. (1986). Physiologic and microbiologic changes in skin related to frequent handwashing. *Infection Control & Hospital Epidemiology*, *7*(2), 59-63.
80. Larson, E. L., Aiello, A. E., Bastyr, J., Lyle, C., Stahl, J., Cronquist, A., ... & Della-Latta, P. (2001). Assessment of two hand hygiene regimens for intensive care unit personnel. *Critical care medicine*, *29*(5), 944-951.