WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 9, 18-30. Research Article ISSN 2277– 7105

REGULATORY COMPLIANCE OF HAND SANITIZERS IN IGBINEDION UNIVERSITY COMMUNITY IN THE FIGHT AGAINST COVID-19: A SURVEY

Nnabuike Didacus Nnamani[1†], Adesegun Jubril Kashimawo and Osarugue Uyi

[1†]Department of Pharmaceutics and Pharmaceutical Technology, College of Pharmacy, Igbinedion University Okada, Edo State, Nigeria.

[2]Department of Pharmaceutical and Medicinal Chemistry, Niger Delta University, Wilberforce Island, Bayelsa State, Nigeria.

[3]Department of Clinical Pharmacy and Pharmacy Practice, College of Pharmacy, Igbinedion University, Okada, Edo State, Nigeria.

Article Received on
05 May 2022,

Revised on 26 May 2022,
Accepted on 15 June 2022

DOI: 10.20959/wjpr20229-24555

***Corresponding Author**
Nnamani Nnabuike Didacus
Department of Pharmaceutics and Pharmaceutical Technology, College of Pharmacy, Igbinedion University Okada, Edo State, Nigeria.

ABSTRACT

Igbinedion University Community, Okada, is a gathering of people from different part of the World with increased risk of exposure and transmission of coronavirus-2019 disease. Hand sanitization is one of the multidimensional approach in curbing coronavirus-2019 disease. The compliance to regulatory recommendations of inclusion of 60 – 95 % alcohol, humecant glycerol, and sporicidal hydrogen peroxide, and labelling indications of hand sanitizers within Igbinedion University community was surveyed. All the hand sanitizer collected and sampled had manufacturing and expiring dates, and properly stated lists of ingredients on their labels. The samples were alcohol based with a mode of 70 % ethanol, and had average pH of 6.4. A 48 % of samples were registered with NAFDAC, and 99% were manufactured in Nigeria. Labelling inscriptions “For External Use” and “Kills 99% germ” were in 100 and 95 % of samples respectively. Warning inscriptions of “Flammable”, and “Keep out of reach of children” were in 90 and 99 % of the samples respectively. Sporicidal hydrogen peroxide was present in 14 % of the samples, while antimicrobial denaturant, chlorhexidine, was present in 14 % of the samples. Humecants, thickeners, and stabilizers were present in 62, 48 and 29 % of the samples respectively. The statistical 2^n manifold classification of attributes showed that 38 % of hand sanitizers available in the

community met regulatory recommendations for content, labelling and packaging, while 62 % of the samples met content and packaging guidelines. With the hand sanitizers available in Igbinedion University Community, Okada in compliant with regulatory recommendations, emphasis should be on its proper and regular usage.

KEYWORDS: Humecant, sporicidal, denaturant, antimicrobial.

INTRODUCTION

University community is a convergence of people of different ages, especially the vulnerable old academics, from different parts of the world. There is communal and interchangeable use of spaces, books, tools, sits, and other items amongst University staff, students, and the larger community. These unavoidable habit puts this community at a higher risk of exposure to coronavirus disease - 2019 (COVID-19). Severe-Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV 2) which causes COVID-19 is transmitted when people are physically close, through the respiratory droplets and aerosols from breathing, talking, singing, coughing, and sneezing of an infected person.[1,2] The SARS-CoV 2 can remain active for hours to days depending on the inoculum shed on inert surfaces, and be transmitted through these contaminated surfaces.[3,4,5] Curtailing the transmission, spread and infection of SARS-CoV 2 requires multicomponent intervention such as contact isolation, quarantine, avoiding crowded areas, social distancing, wearing of protective nose mask and face shield, keeping unwashed hand away from face, and other strict infection control methods such as maintaining hand hygiene.[5]

Hand hygiene can be maintained by thorough washing of the hand for 20 to 60 seconds with water and soap. When the hands are greasy, soiled, stained or contaminated with chemical and after communal activities like handling of food, gardening, sports, outdoor activities, or use of toilet, hand washing with water and soap is preferred, and is more effective than hand sanitizer.[6,7] Hand washing with water and soap is also more effective at removing visible stains, transient microbes, bacterial spores, viruses such as SARS-CoV 2 and non-envelop virus such as norovirus, and other bioburden which contaminate, colonize or infect the superficial layer of the skin.[8,9,10] But hand washing with water and soap is not effective in dislodging all pathogenic microbes.[11,12] Too much extensive and repetitive soap washing can deplete essential natural resident microbes in the skin, remove natural fatty acid of the skin, dry and crack the skin, and open pathway for entrance of pathogens.[13] To reduce the adverse effect of repetitive soap washing, hand sanitizer is used as a complementary tool for hand

hygiene. Unlike soap washing, most hand sanitizer types have lower efficiency in removing visible stains and dirts, no activity against bacteria spores, low activity against some non-envelop viruses such as norovirus, and may result in norovirus outbreak.[14]

Alcohol Based Hand Sanitizer (ABHS) is effective against SARS-CoV 2, MERS-CoV 2 (Middle East Respiratory Syndrome-Related Coronavirus), other clinically relevant viruses, vegetative bacteria, multidrug resistant bacteria and some other pathogens.[2,15,16,17,18,19] The application of adequate amount, up to or over 2 ml, and concentration of ABHS properly all over the hand for 20 – 30 seconds can rapidly and effectively inactivate and destroy many pathogenic microbes and some viruses including SARS-CoV 2.[15,16,20] Lipid solvents component of ABHS such as 60 – 80 % ethanol, 60 – 80 % n-propanol, 60 – 80 % isopropanol, 75 % ether and other denaturants such as chlorine, chloroform, benzethonium chloride, mercurochrome, thiomersal, and chloroazodine helps in deactivating microbes.[21,22] The drawbacks to ABHS use includes its flammability, volatility, risk of fire, low viscosity / high fluidity and attendant risk of accidental discharge, poisoning on ingestion and absorption, ease of contamination with bacteria spores, ineffectiveness against non-envelop viruses and some other pathogens, and compliance problem due to skin discomfort.[13,23,2425,26,27]

To counter some drawbacks of ABHS, modifications are made to its formulation, direction for use, storage conditions, packaging, and labelling instructions. Modification to ABHS formulation includes addition of higher concentration of alcohol, hydrogen peroxide and denaturants to improve antiseptic activity, eradicate contaminating bacteria spores, and increase its efficacy against viruses and other pathogens that are resistant to alcohol alone.[28,29] Other ABHS formulation modification may include addition of buffers, pH stabilizers, chelating agents, humectant glycerol and water miscible non-toxic hypoallergenic emollient to reduce corrosiveness, ameliorate skin irritation, improve skin condition, and improve acceptability / compliance.[29,30,31,32] Modification on ‘direction for use’ ABHS includes instruction to allow more contact time between ABHS and hand during sanitization as a way of improving its effectiveness against non-envelope viruses.[2,29,33] Additional instruction may include advice to moisturize the hand immediately after ABHS sterilizing, with lotion or water based antiseptic lotion such as antiviral and anti-inflammatory benzethonium chloride.[23] Labelling instructions include indication as poison, warnings of accidental discharge and advice on accidental intake.[29]

To prevent long term skin damage from ABHS, it is recommended that hand sanitizer be used only when soap and water are not easily available or where there is scarcity of water, or in certain situations such as hospital settings where quick sanitization is required and better tolerated.[9,34] The types, and compliance to official labelling and production guidelines of ABHS available in University Community, Okada, was surveyed and analysed.

Table 1: WHO Standard Formulation Guideline for Production of 10,000ml Hand Sanitizer.[35]

	Formulation 1	**Formulation 2**
Ingredient (% Strength)	**Volume (ml)**	**Volume (ml)**
Ethanol (96%)	8,333	-
Isopropyl Alcohol (99.8%)	-	7515
Glycerol (98%)	145	145
Hydrogen Peroxide (3%)	417	417
Distilled Water to	**10,000**	**10,000**

MATERIALS

The hand sanitizer collected within Igbinedion University are: Nature care, Tetmosol, 1st Aid Antimicrobial Hand Gel, Igbinedion University Hand Sanitizer, Gelly Cologne, A Morison, Nature's Gentle Touch, Cussion Carex, Efficacy, Vineyard, 2 Sure, Coguard, NCP, Astonish, Evree, Purit, East Jielin, Dawn, Feli Jays, Zenon, and Louis Cardin Instant Hand Sanitizer. Equipment for pH determination; pH Meter (pH-S25 EC/ORC, China). LvDv 1+ (Brookfield) viscometer. Microsoft excel spread sheet.

METHOD

Points of Collection of Hand Sanitizers

The points of collection of samples where supermarkets, pharmacies, patent medicine stores and open market kiosks.

Sample Evaluation

Using the method of Nyamweya and Abuga,[36] the samples were evaluated for packaging, and labelling instructions and content specification. The labels were observed for manufacturing and expiring dates, NAFDAC registration number, content and ingredient indications, and warnings such as "Flammable", "For External Use Only", and "Keep out of Reach of Children". The content specifications noted include per cent alcohol, and presence

of sporicide, humecant, thickener, and denaturants. The results from these observation were analysed and discussed.

pH Determination

A pH-S25 EC/ORC (China) pH meter was used to determine the pH of all the sample hand sanitizers. The electrode of the pH meter was immersed into hand sanitizer meter cylinder. The pH was read after 2 min., repeated thrice, recorded and the average calculated.

Viscosity Determination

The spindle of LvDv 1+ (Brookfield) viscometer was immersed mid-way inside a 50 ml cylinder containing 40 ml sample hand sanitizer. The spindle was set and operated at 100 r.p.m and the viscometer readings taken. The test for each sample was conducted in triplicate, and the average noted as the viscosity of the sample.

Statistical analysis

The data on the ABHS samples were statistically analysed using 2^n manifold classification of Kothari and Garg.[37] The "n" attributes considered for the ABHS are compliance to regulatory recommendations of content and labelling instructions. The presence of the "n" attributes of content and labelling instructions are denoted as A and B respectively. Absence of the "n" attributes of content and labelling instructions are denoted as a and b respectively. Therefore, the classes of final order are AB, Ab, aB and ab.

Table 2: Table of Statistics of Attributes of Compliance to Regulatory Recommendations.

Manifold Classification	Result
AB	38 %
Ab	62 %
aB	70 %
Ab	0 %

Key:

AB = Compliance to regulation of content and labelling inscription

Ab = Compliance to regulation of content

aB = Compliance to regulation of labelling inscription

ab = Non-compliance to regulation of content and labelling inscription

RESULTS

All the hand sanitizers sampled were alcohol-based and had manufacturing and expiring dates, list of ingredients, and warning "For External Use Only" (Figure 1). Microsoft excel data spread sheet was used to generate the recommended chats in figures 1 and 2. The mode of concentration of alcohol in the hand sanitizers is 70% ethanol (Figure 2). Glycerol and propylene glycol humecants were present in 38 and 24% of the samples respectively. Thickeners were present in 48 % of the sample, with carbomers consisting of 43 % and polyacrylic acid 5 %. Sample with combination of glycerine, propylene glycol and carbomer had the highest viscosity of 1411.71 mPa. The 43% sample without either glycerol or propylene glycol had viscosities within 100 and 200 mPa (Figure 4). Extra-functional excipients such as sodium hydroxide, triethanolamine, chlorhexidine, disodium EDTA, aloe vera, and essential oils were used in some ABHS. The average pH of the samples was pH 6.4. The full pH range of the samples was pH 4 – 7.35, and 48 % of the samples had pH 4.5 – 6.5 (Figure 3). The price range for 200 ml of the samples ranged from 400 – 600 naira (Figure 5). The result showed that of the hand sanitizers available in Okada met 38 % met regulatory guideline on content and labelling, 70 % met regulation on content, 62 % met regulation on labelling, while zero was non-compliant of any regulation (Table 2).

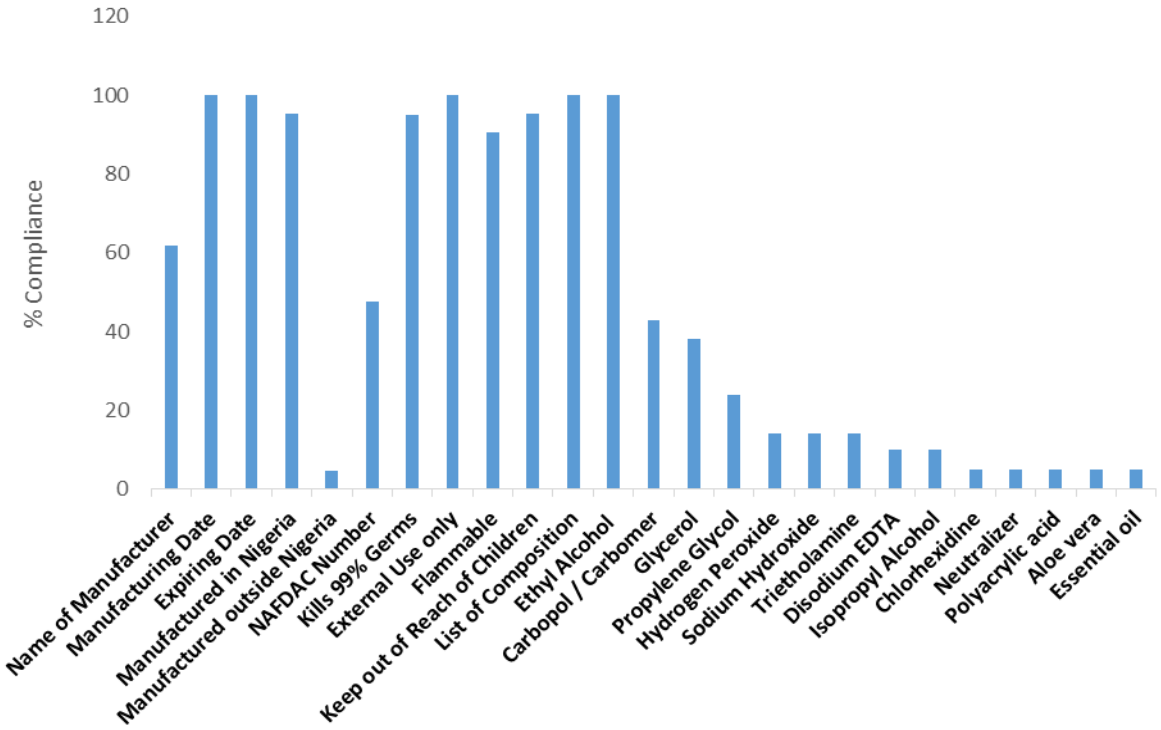

Figure 1: Bar Chart of Per Cent Hand Sanitizer Compliance to Stated Labelling and Content Parameters.

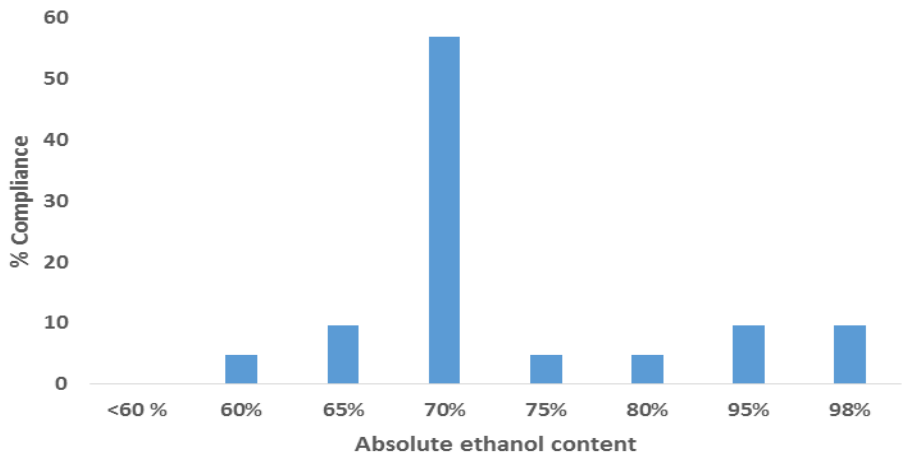

Figure 2: Bar Chart of the Concentration of Alcohol in Hand Sanitizers.

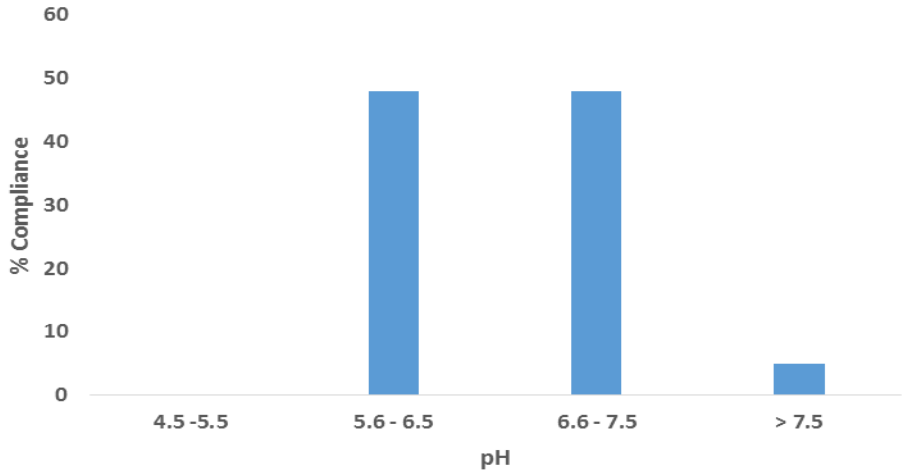

Figure 3: Bar Chart of pH Ranges of Hand Sanitizers.

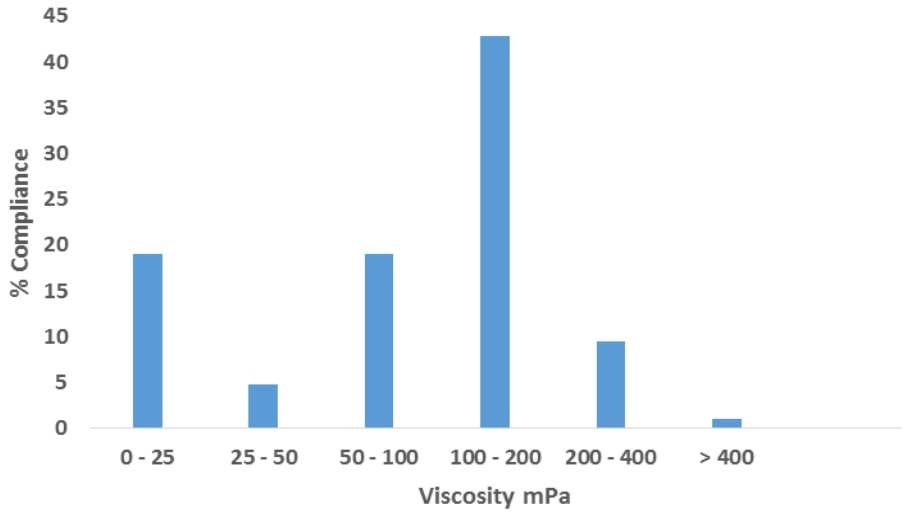

Figure 4: Viscosity Ranges of Hand Sanitizers,

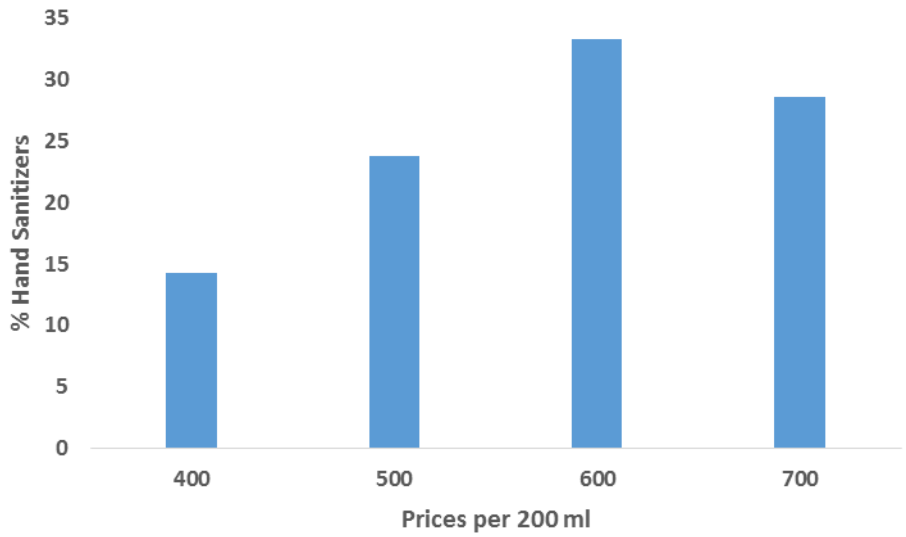

Figure 5: Bar Chart of Prices of Hand Sanitizers.

DISCUSSION

The hand sanitizers had 60 – 95 % alcohol ethanol with a mode of 70 % ethanol. This 60 – 95 % alcohol concentration range is effective for antiseptic purposes than the lower or higher concentration of this range.[38] Hydrogen peroxide (3 %) was present in the sanitizers at risk of contamination with bacterial spores, as indicated by WHO.[29] Hydrogen peroxide is corrosive, toxicity and difficult to procure. To avoid the need of hydrogen peroxide, majority of the formulations (86 %) used distilled water and adequate sterilization to remove microorganisms including bacterial spores from production water and environment.[29] Glycerol or propylene glycol that function as humecant and emollient in reducing drying and irritation of skin was present in over half of the samples, but in low concentration to reduce stickiness of the formulation.[39] Carbomer, carbopol, and polyacrylic acid polymers and others like xanthan gum and polyethylene glycol excipients, are used as thickenening, suspending and dispersing agents, and viscosity enhancers in cosmetic.[39] Ethylenediaminetetraacetic acid (EDTA), triethanolamine and unspecified neutralizer were present in 10, 14 and 5 % samples respectively as stabilizers. Trietholamine is used as oil surfactant, and pH and buffer stabilizer, and EDTA is used as buffer, chelating and stabilizing agent, and permeability enhancer, with extra antimicrobial activity, in formulations.[32,40,41] Chlorhexidine was present in some formulations as denaturant against Gram positive bacteria and moderate activity against Gram-negative bacterial, SARS-CoV 2 and envelope viruses as expressed by Larson, (1995), and Ison and Beattie (2002).[13,42] The average pH of the hand sanitizer was pH 6.4. This pH is within the range pH 4.5 – 7 recommended range for body

and hand cleansers.[31,43] The average price of 576 naira (about a dollar) for 200 ml ABHS in the Community is affordable, using the estimations of Greenaway *et al*. and Pittet *et al.*[20,44]

CONCLUSION

The hand sanitizers found within Igbinedion University Community had passable qualities and complied with regulatory and safety indications. The concentration of 60 – 95 % alcohol present in the hand sanitizers is the effective level for sanitization. The presence of sporocides, denaturants, humecants, thickening, emollient, permeability, chelating, sporicides, and buffer, pH and stability agents in different mix and concentration in the hand sanitizers minimizes risks and increases acceptability and compliance. The cost of the hand sanitizers meet the economics from cost recommendation. The University Community has essential and effective hand sanitizers in her armour in the fight against coronavirus disease 2019.

AKNOWLEDGMENT

I acknowledge the cooperation of staff, students and members of Igbinedion University in answering questions concerning the use of hand sanitisers during Covid-19 pandemic.

RECOMMENDATION

Extra due diligence, monitoring and compliance to guidelines, such as that of Presidential Task Force (PTF) and World Health Organization (WHO) on COVID-19, is important in preventing the infection and transmission of COVID-19. The provision of water and soap at crucial spots, and of hand sanitizer for quick sanitization between activities is essential to maintaining proper hand hygiene recommendations, as the additional fool proof carriage, use and ease of replacement of personal hand sanitizer.

REFERENCES

1. Seto WH, Tsang D, Yung RWH, Ching TY, Ng TK, Ho M, Ho LM, Peiris JSM. Advisors of expert SARS group of hospital authority effectiveness of precautions against droplets and contact in preventing of nosocomical transmaission of severe acute respiratory syndrome (SARS). LancetI, 2003; 361: 1519 – 1520.
2. Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronavirus on inanimate surfaces and their inactivation with biocidal agents. Journal of Hospital Infection, 2020; 104: 246-251.

3. Van-Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, Tamin A, Harcourt JL, Thornburg NJ, Gerber SI. Aerosol and surface stability of SARS-CoV 2 as compared with SARS-CoV 1. N. English Journal of Medicine, 2020; 382: 1564-1567.
4. Peeri NC, Shrestha N, Rahman MS. The SARS, MERS and novel coronavirus (COVID-19) epidemics, the newest and biggest global health threats: what lessons have we learned? International Journal of Epidemiology, 2020; 49: 717 – 726.
5. Thomas Y, Bosquete-Suter P, Koch D, Pittet D, Kaiser L. Survival of influenza virus on human fingers. Clinical Microbiology Infection, 2014; 20: O58-064.
6. Alzyood M, Jackson D, Aveyard H, Brooke J. COVID-19 reinforces the importance of handwashing. Journal of Clinical Nursing, 2020; 1-2. doi:10.1111/jocn.15313.
7. Centres for Disease Control and Prevention (2020). Coronavirus Disease 2019 (COVID-19): FAQ on Hand Hygiene. 2020. Retrieved from https://www.cdc.gov/coronavirus/2019-ncov/infection-control/hcp-hand-hygiene-faq.html
8. Jian VM, Karibasappa GN, Dodamani AS, Prashanth VK, Mali GV. Comparative assessment of antimicrobial efficacy of different hand sanitizers: an in vitro study. Dental Research Journal, 2016; 13: 424-431.
9. Foddai ACG, Grant IR, Dean M. Efficacy of instant hand sanitizers against foodborne pathogens compared with hand washing with soap and water in food preparation settings: a systemic review. International Association for Food Protection. Journal of Food Protection, 2006; 79: 1040-1054.
10. De-Witt H, Greenland K, Schnidt WP, Curtis V. Exploring the potential of antimicrobial hand hygiene products in reducing the infectious burden in low-income countries: an integrative review. American Journal of Infection Control, 2016; 44(7): 746-771.
11. Tuladhar E, Hazeleger WC, Koopmans M, Zwietering MH, Duizer E, Beumer RR. Reducing viral contamination from finger pads: handwashing is more effective than alcohol-based hand disinfectants. Joutnal of Hospital Infection, 2015; 90: 226-234.
12. Tambekar DH, Shirsat SD, Suradkar SB, Rajankar PN, Banginwar YS. Prevention of transmission of infectious disease: studies on hand hygiene in health-care among students. Cont Journal of Biomedical Sciences, 2007; 1: 6-10.
13. Larson EL, Norton Hughes CA, Pyrek JD, Sparks SM, Cagatay EU, Bartkus JM. Changes in bacterial flora associated with skin damage on hands of healthcare personnel. American Journal of Infection Control, 1998; 26: 513-521.

14. 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. American Journal of Infection Control, 2011; 39: 296-301.
15. Bore E, Hebraud M, Chafsey I. Adapted tolerance to benzalkonium chloride in Escherichia coli k-12 studied by transcriptome and proteome analysis. Microbiology, 2007; 153: 935-946.
16. Islam R, Cicek N, Sparling R, Levin D. Influence of initial cellulose concentration on carbon flow distribution during batch fermentation by Clostridium thermocellum ATCC 27405. Application of Microbiology Biotechnology, 2009; 82: 141-148.
17. Siddharta A, Pfaender S, Vielle NJ, Dijkman R, Friesland M, Becker B, Yang J, Engelmann M, Todt D, Windisch MP. Virucidal activity of World Health Organization-recommended formulation against enveloped viruses, including Zika, Ebola, and emerging coronaviruses. Journal of infectious Diseases, 2017; 215: 902-906.
18. Steinmann J, Becker B, Bischoff B. Virucidal activity of 2 alcohol-based formulations proposed as hand rubs by the World Health Organization. American Journal OF Infection Control, 2010; 38: 66-68.
19. Steinmann J, Paulmann D, Becker B, Bischorff B, Steinmann E. Comparison of virucidal activity of alcohol-based hand sanitizers versus antimicrobial hand soaps in vitro and in vivo. Journal of Hospital Infection, 2012; 82: 277-280.
20. Greenaway RE, Ormandy K, Fellows C, Hollowood T. Impact of hands sanitizer format (gel / foam / liquid) and dose amount on its sensory properties and acceptability for improving hand hygiene compliance. Journal of Hospital Infection, 2018; 100: 195-201.
21. Goldsmith CS, Tatti KM, Ksaizek TG, Rollin PE, Corner JA, Lee WW, Rota PA, Bnakamp B, Bellini WJ, Zaki SR. Ultrastructural characterization of SAR coronavirus. Emergency Infectious Disease, 2004; 10: 320-326.
22. Chatwal GR. Antiseptics In Arora M (ed.) Synthetic Grugs. Himalaya Publishing House, Mumbai, 2nd ed.: 2009; 21: 1-18.
23. Wilhelm KP. Prevention of surfactant-induced irritant contact dermatitis. In. Current Problems in Dermatology; Karger Publishers, London, UK: 1996, Volume 25, pp. 78-85.
24. Ale IS, Maibach HI. Irritant contact dermatitis. Review on Environmenta Health, 2014; 29: 195-206.
25. Podda M, Zollner T, Grundmann-Kollmann M, Kaufmann R, Boehbcke WH. Allergic contact dermatitis from benzyl alcohol during topical animycotic treatment. Contact Dermatology, 1999; 41: 302-303.

26. Graham M, Nixon R, Burell LJ, Bolger C, Johnson PDR, Grayson ML. Low rates of cutaneous advers reactions to alcohol-based hand solution during prolonged use in a large teaching hospital. Antimicrobial Agents Chemotherapy, 2005; 49: 4404-4405.
27. Loffer H, Kampf G, Schmermund D, Maibach HI. How irritant is alcohol? Brazilian Journal of Dermatology, 2007; 157: 74-81.
28. Park GW, Barclay L, Maclnga D, Charbonneau D, Pettigre CA, Vinje J. Hand hygiene with efficacy of seven hand sanitizers against murine norovirus, feline calicivirus, and GII.4 norovirus. Journal of Food Protection, 2010; 73: 2232-2238.
29. World Health Organization. Guide to Local Production: WHO-recommended handrub formulations. World Health Organization. 2010, WHO/IER/PSP/2010.5. https://apps.who.int/iris/handle/10665/332005.
30. Lauharanta J, Ojajarvi J, Sarna S, Makela P. Prevention of dryness and eczema of the hands of hospital staff by emulsion cleansing instead of washing with soap. Journal of Hospital Infection, 1991; 17: 207-215.
31. Alli SM, Yosipovitch G. Skin pH: from basic science to basic skin care. Advances in Dermatology and Venereology, 2013; 93(3): 261-267. doi: 10.2340/0015555-153.
32. Hella N, Fernandes I, Heleno S, Costa P, Boucherit-Otmani Z, Boucherit K, Rodrigues R, Ferreira ICFR, Barreiro MF. Cosmetics preservation: a review on present strategies. Molecules, 2018; 23: 1571. doi:10.3390/molecules23071571.
33. Sattar SA, Abebe M, Bueti AJ, Jampani H, Newman J, Hua S. Activity of an alcoholbased hand gel against human adeno-, rhino-, and rotaviruses using the fingerpad method. Infection Control Hospital Epidemiology, 2000; 21: 516-519.
34. Pittet D, Allegranzi B, Boyce J. The World Health Organization guidelines on hand hygiene in health care and their consensus recommendations. Infection Control in Hospital Epidemiology, 2009; 30: 611-622.
35. Compounding Expert Committee. Compounding Alcohol-Based Hand Sanitizer during COVID-10 Pandemic: 2020, https://www.usp.org/sites/default/files/usp/documents/about/public-policy/usp-covid19-handrub.pdf.
36. Nyamweya NN, Abuga K. A survey of alcohol-based hand sanitizers in Nairobi: packaging, labelling and regulatory compliance. East and Central African Journal of Pharmaceutical Sciences, 2020; 23: 72-76.

37. Kothari CR, Garg G. Data preparation In Research Methodology: Methods and Techniques. Chapter 7. New Age International (P) Limited Publishers, New Delhi; 3rd edn. 2014, Chapter 7. pp 114 – 128.
38. Bonnabry P, Voss A. Hand Hygiene Agents in Pittet D, Boyce JM, Allegranzi B (eds.) Hand Hygiene: A Handbook of Medical Professionals. John Wiley & Sons: 2007; 935-946.
39. Carlisie BJ, Craft G, Harmon JP, Ijkevjitch A, Nicoghosian J, Sheyner I, Stewart JT. PEG and thicheners: a critical interaction between polyethylene glycol laxative and starch based thickeners. Journal of America Medical Directors Association, 2016; 17(9): 860-861. doi: 10.1016/j.amda.2016.01.024.
40. Varvaresou A, Papageorgiou S, Tsirivas E, Protopapa E, Kintziou H, Kefala V, Demetzos C. Self-preserving cosmetics. International Journal of Cosmetics Sciences, 2009; 31: 163-175.
41. Siegert W. Boosting the antimicrobial efficiency of multifunctional additives by chelating agents. International Journal of Applied Sciences, 2014; 140: 1-6.
42. Ison S, Beattie M. Book review: Disinfection, sterilization and preservation (5th ed). Seymour S Block (Ed.), Lippioncott Williams and Wilkins, Philadelphia, Australian Infection Control, 2002; 7(2): 74. https://doi.org/10.1071/H102074.
43. Jing JLJ, Yi TP, Bose RJC, McCarthy JR, Tharmalingam N, Madheswaran T. Hand sanitizers: a review on formulation aspects, adverse effects, and regulations. International Journal of Environmental Research and Public Health, 2020; 17(9): 3326. Doi:10.3390/ijerph17093326.
44. Pittet D, Sax H, Hugonnet S, Harbart S. Cost implications of successful hand hygiene promotion. Infection Control and Hospital Epidemiology, 2004; 25: 264-266. DOI: 10.1086/502389.