East and Central African Journal of Pharmaceutical Sciences
Vol. 25 (2022) 54-63

Alcohol-Based Hand Sanitizers: Relevance of the Physicochemical Properties of Alcohol-Water Mixtures

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The use of alcohol-water mixtures as antimicrobial agents for hand-hygiene grew significantly in the year 2020 due to the global COVID-19 pandemic. Combining alcohols, such as ethanol or isopropanol, with water results in mixtures with a number of unusual characteristics with several solution properties deviating from ideal behavior. These characteristics are related to clustering or aggregation of the constituent molecules at the microscopic level. This paper reviews the physicochemical properties (polarity, density, viscosity, vapor pressure, surface tension) of alcohol-water mixtures and their relevance to alcohol-based hand sanitizers. The role of the quasi-surfactant characteristics (amphiphilism, surface and interfacial tension lowering) of alcohols in eliciting their antimicrobial effects is discussed.

Keywords: Alcohol-water mixtures, polarity, viscosity, vapor pressure, surface tension, disinfection, hand sanitizers

INTRODUCTION

Alcohol-water solutions have found applications in disinfection, ethanol-based beverages, mouthwashes and pharmaceuticals. Although alcohol-water mixtures have long been used as topical antiseptics, they gained enhanced worldwide attention during the COVID-19 pandemic.[1–3] Pharmaceutical applications also include their use as solvent systems for drug solubilization or extraction.[4–6] The key properties of alcohol-water mixtures include their density, viscosity, surface tension, vapor pressure and polarity. The relevance of these factors in various applications is summarized in Table 1.

The alcohols of interest in this review are ethanol and the propanol isomers, isopropanol and n-propanol which constitute the active ingredients in alcohol-based hand sanitizers. An interesting aspect of alcohol-water mixtures is the deviation of their physicochemical properties from ideal behavior.[7] An ideal solution is one in which there is no change in the properties of the mixed components other than dilution.[8] In ideal solutions the heat of mixing is zero and the properties of the mixture are weighted averages of those of the individual components.

It has been shown that while being macroscopically miscible, alcohol-water solutions exhibit molecular segregation and incomplete mixing at the microscopic level with the structural ordering of water and alcohol molecules around each other.[9–12] The molecular basis for these phenomena is that while water is a polar molecule, alcohols are amphiphilic being composed of both polar and non-polar moieties. Mixtures therefore involve a balance of hydrogen bonding (H-bonding) and hydrophobic interactions which determine the resultant composition-dependent liquid structures.

Although the properties of alcohol-water mixtures have been characterized in numerous studies, there has been limited work relating these properties to their applications as hand sanitizers or antiseptics.

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Table 1: Relevance of the Properties of Alcohol-Water Mixtures

Property	Relevance/Applications
Density	Measuring and dispensing of liquids
	Determines container fill volumes
	Used to modify the density of the continuous phase in emulsions
Viscosity	Influences liquid flow, pourability, handling, spreading on surfaces and diffusion rates
Surface tension	Influences wetting, spreading and adhesion on surfaces
	Mixing of immiscible liquids and polar/non-polar materials
Vapor pressure	Fractional distillation
	Evaporation/drying times in alcohol-based hand sanitizers
Polarity	Solute solubility
	Solute stability

Given the increased utilization in the year 2020 of these mixtures as alcohol-based hand sanitizers (ABHS), a review of their physical properties is valuable in understanding their behavior. Key factors in the performance of ABHS such as liquid flow, wetting and drying time are dependent on properties such as the viscosity, surface tension and the vapor pressure. Furthermore, an understanding of the properties of alcohol-water mixtures is also applicable to their pharmaceutical applications in the solubilization and extraction of therapeutic compounds.

PHYSICOCHEMICAL PROPERTIES

The utility and performance attributes of a material are determined by its physicochemical properties. Relevant properties of ethanol, isopropanol, n-propanol and water are listed in Table 2. The isomers, n-propanol and isopropanol, have fairly similar properties with the striking exception of their vapor pressures.
The vapor pressure of n-propanol is less than half that of isopropanol and more comparable to that of water. Consequently, ABHS with high levels of n-propanol will have longer drying times than the other two alcohols. The higher dielectric constant of ethanol relates to its higher polarity compared to the propanols. Figure 1 shows the general trends in variation of density, dielectric constant, viscosity and surface tension for alcohol-water mixtures.

Polarity

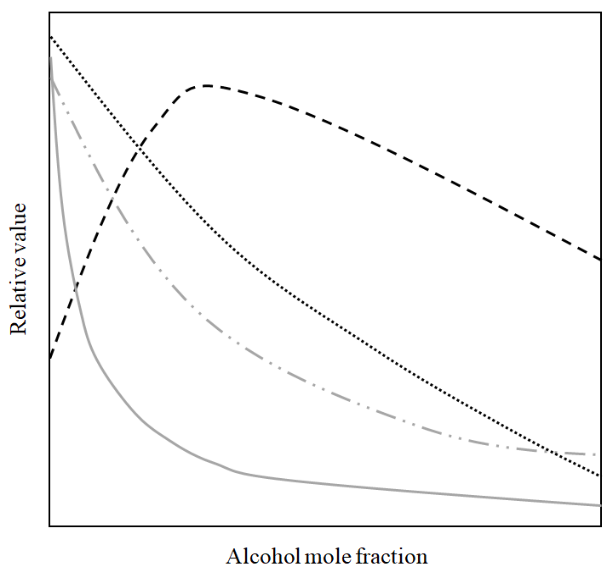
Water, alcohol and alcohol-water binary mixtures have distinct polarity differences that have informed their applications as solvents and antimicrobials. Mixing solvents with different dielectric constants is one means of varying their polarity in order to control solute dissolution and solubility. Ethanol, is used as a solvent or cosolvent for active ingredients in pharmaceutical preparations and as a preservative due to its antimicrobial properties.[15] Alcohols are the active ingredient of ABHS which act through denaturation of functional proteins in microbes. This interaction heavily depends on the polarity of the alcohol-water composition.

Table 2: Physical and thermodynamic properties of ABHS alcohols and water

Property	Ethanol	Isopropanol	n-Propanol	Water
Formula	C_2H_5OH	C_3H_7OH	C_3H_7OH	H_2O
Molecular weight	46.1	60.1	60.1	18.0
ρ (g/cm^3) at 20 °C †	0.789	0.786	0.804	0.997 ‡
η (mPa.s) at 25 °C ‡	1.04	2.04	1.95	0.89
σ (mN/m) at 25 °C ‡	21.9	20.9	23.4	72.1
ε at 20 °C ‡	25.3	20.2	20.8	80.1
Vapor pressure (kPa) at 25 °C †	7.58	5.87	2.67	3.17 ‡

ρ – density, η – Viscosity, σ – surface tension, ε - dielectric constant. † [13]; ‡ [14]

The miscibility of solvents is governed by similarities in polarity which can be expressed by the relative permittivity or dielectric constant (ε). Polarity influences intermolecular interactions through H-bonding in alcohol-water binary systems.



surface tension, viscosity, dielectric constant, density.

Figure 1: General schematic diagram of the relative variation of selected properties as a function of alcohol concentration.

The significant variables are the alcohol mole fraction and carbon-atom number which makes the lower monohydric homologs water-miscible. The ε values for the binary mixtures are additive but deviate from linear behavior.[16] The dielectric constants of methanol, ethanol and n-propanol were observed to decrease with increasing concentration of the alcohol or the carbon number.[16] Even though water and alcohol are considered miscible, mixtures exhibit molecular-level heterogeneity. At low concentrations, ethanol tends to exist as macromolecular aggregates dispersed in the aqueous medium while high alcohol content reverses this behavior forming water clusters in alcohol. Water polarity promotes self-association of alcohol molecules due to a balance of interactions.[9]

This non-monotonic behavior relies on H-bonding networks which influence the dominant intermolecular forces depending on the relative concentrations of either solvent. The resulting microscopic phase separation makes the two solvents undergo incomplete mixing with characteristic alcohol-rich and water-rich clusters in co-existence.[17] These effects result from the presence of both polar (hydroxyl) and non-polar (hydrocarbon) groups in alcohol molecules. Considering their amphiphilic nature and interface effects (e.g., surface tension lowering), alcohols can be considered quasisurfactants as pertains to their use in hand sanitizers.

The recommended alcohol concentration in ABHS is 60–95% (v/v).[18] This range possesses the optimum polarity which permits interaction with functional proteins through H-bonding hence exerting biocidal activity. Lower levels of alcohol do not provide adequate amounts for antimicrobial action while high concentrations cause membrane proteins to undergo precipitation. The insoluble precipitates thus formed prevent entry of alcohol into the cell which limits the resultant antimicrobial activity. In practice, alcohol concentrations of 70–80 % v/v are the most commonly utilized.

Density

The density variation of water-alcohol mixtures is relatively linear with the mole fractions irrespective of temperature differences.[19] At 20 °C the curve extends from the densities of the pure solvents of 1.00 g/cm^3 for water to 0.79 g/cm^3 for ethanol. Nonetheless, there is a slight negative deviation from ideal linearity attributable to volume contraction in alcohol-water mixtures.[20,21] In liquid mixtures containing dispersed or emulsified lipids, varying the density of the dispersion medium can be used to prevent phase separation due to gravity (creaming).

The density-concentration relationship of water-alcohol solutions forms the basis for use of alcoholmeters for the determination of alcohol content of spirit beverages and alcohol-based hand sanitizers.[22] However, this technique is non-specific for the type of alcohol and hence would not detect adulteration with toxic non-permitted alcohols such as methanol whose densities approximate that of ethanol.

Viscosity

Viscosity is an important determinant of flow properties influencing factors such as liquid pourability, surface application, spreading and sensory characteristics. Additionally, viscosity affects diffusion related processes such as ABHS drying times after application. Conversely, viscosity may undermine ABHS efficacy as it has been reported that gel-based ABHS do not act as rapidly as lower viscosity liquids.[23,24]

The viscosities of alcohol-water mixtures are unusual with intermediate compositions having higher viscosities than either of the pure liquids. The highest viscosities are observed at alcohol mole fractions of 0.25 - 0.3 and are associated with the regions of maximum volume contraction.[20]

The viscosities of alcohol-water mixtures are however rather low for application of ABHS to the skin. Consequently, in many consumer ABHS products polymers such as carbomers are added to increase the viscosity to the point where the applied product is easier to handle and does not run-off after application.[25]

Surface tension

The surface tension influences the wetting properties of a liquid and interfacial interactions with other materials. Alcohols have much lower surface tension values than water and in mixtures display a predominant effect with surface tension dropping sharply with the addition of small amounts of alcohol (Figure 1). Khattab *et al.* reported that at an ethanol concentration of 62.7%, v/v, aqueous solutions had a surface tension of about 29 mN/m at 20 °C.[19] Similar results have been reported in other studies with surface tension values of 26.7, 24.9 and 24.1 mN/m reported for 60% (w/w) solutions of ethanol, n-propanol and isopropanol, respectively (at 20 °C).[26] Interestingly, these values approached the surface tensions of the pure alcohols which were 22.3, 23.7 and 21.7 mN/m for pure ethanol, n-propanol and isopropanol, respectively.[26] Notably, the surface tension values of alcohol-water mixtures at these levels (i.e., the range of ≥ 60% alcohol, v/v used in ABHS) are comparable to those of some surfactants. For example, the widely used surfactant polysorbate 80 in aqueous solution yields a surface tension of about 38 mN/m at its critical micellar concentration (at 22 °C).[27] The effects of alcohols on the lowering of interfacial tension at hydrophobic surfaces follows a similar trend to that of surface tension.[12] Interfacial tension is especially important in the application of ABHS as the alcohol-water mixture encounters or acts at interfaces (such as skin surface or microbial membranes) prior to exerting antimicrobial action.

Vapor pressure

The vapor pressure is the pressure exerted by molecules above the surface of a liquid. It is driven by the escaping tendency of the molecules in the liquid and is dependent on temperature, pressure and composition. Vapor pressure is relevant to liquid-gas transition (evaporation) driven processes such as drying, boiling and distillation. It is also the basis for the flashpoints of volatile solvents which are important in their safe usage and handling.

The total vapor pressure resulting when two liquids are mixed may exhibit ideal or non-ideal behavior. Non-ideal behavior is observed when the intermolecular interactions between the two species are either stronger or weaker than those of the pure substances. Vapor pressure curves of ethanol-water mixtures as function of alcohol concentration show a positive deviation from ideal behavior[28], indicating that ethanol-water interactions are weaker than the intermolecular forces in the pure components. With regards to ABHS, the key reason for the utility of alcohols other than their antimicrobial action is their ability to evaporate rapidly due to their relatively high vapor pressures (volatility). This facilitates their use as 'leave-on' products which have the advantage of eliminating the need for rinsing with water.

The influence of alcohol concentration on droplet evaporation of aqueous solutions is illustrated in Figure 2. In addition to a faster rate of evaporation, a lower contact angle, increased spreading and surface wetting (due to reduced surface tension) are observed with increased ethanol concentration. The evaporation of both liquid and gel ABHS has been observed to follow first-order kinetics.[29,30]

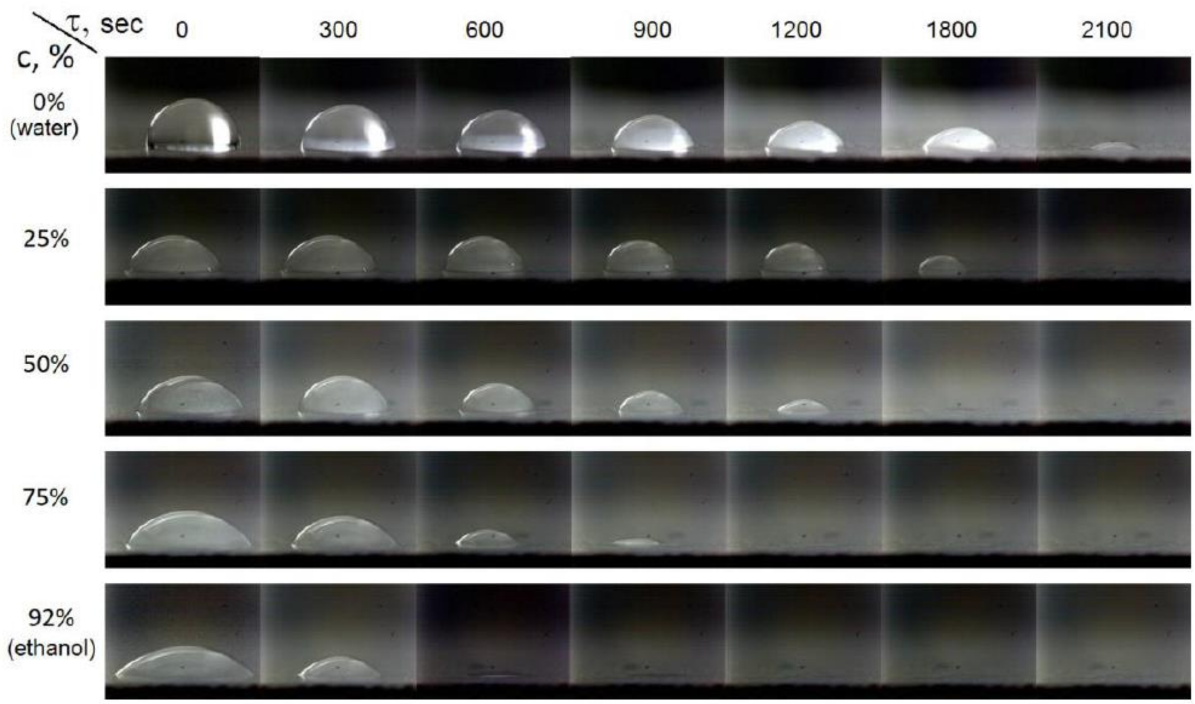


Figure 2: Photographs of 5 µl droplets of water-ethanol mixtures evaporating from a Teflon substrate at different time-points.

(From Sterlyagov *et al.*, 2018 [31] under the terms of Creative Commons Attribution 3.0 license CC BY 3.0).

DISCUSSION

Despite the extensive use of ABHS as antiseptics and disinfectants, their mechanism of antimicrobial action is not well understood.[32] The two most common mechanisms that have been reported in the literature are protein denaturation and cell membrane damage.[33,34] Ingram also suggested that ethanol may exert antimicrobial action by altering the dielectric constant (around the surface and within the cell membrane), replacing water in hydrogen bonding and weakening hydrophobic interactions.[35]

Considering the properties of alcohol-water mixtures that have been reviewed in this work, there appears to be a basis for the amphiphilic nature and surface tension lowering effect of alcohols playing a contributing role in antimicrobial action. Earlier work by Herman *et al.* reported a correlation between reduced surface tension and antimicrobial activity at low concentrations (5%) for several short-chain alcohols.[36] The authors suggested that antimicrobial action may be related in part to the ability of alcohol molecules to align at lipid-water interfaces and interfere with membrane function. The antimicrobial activity of alcohol solutions was found to increase with alcohol chain length which corresponded to reductions in surface tension.

Additionally, it is notable that while alcohols may generally not be suitable solvents for oils, ethanol can solubilize more polar lipids such as certain phospholipids[37] and triglycerides.[38] Cell membranes are made up of phospholipid bilayers and are present in most microorganisms, with some exceptions such as non-enveloped viruses. Alcohols have been reported to reduce interfacial tension, mechanical moduli and membrane thickness in lipid bilayers[39] as well as decrease bilayer lipid orientational order and increase permeability in membrane models.[40] Therefore, given both the surface activity and polar lipid solubilization capability effects, it is reasonable to consider that these factors may contribute to the antimicrobial action of alcohols, especially by membrane destabilization mechanisms. Coincidentally, ABHS are not as effective against non-enveloped viruses which lack the lipid bilayer. From the foregoing, a model for the sequence of events leading to microbial inactivation by ABHS based on alcohol surface tension lowering and microbial membrane destabilization effects is illustrated in Figure 3.

CONCLUSION

The physicochemical properties of alcohol-water mixtures are important in understanding and characterizing their application in alcohol-based hand sanitizers. The confluence of hydrogen bonding, hydration and hydrophobic interactions in these systems leads to several unique characteristics. Further research on the influence of the physicochemical and surface-active properties of alcohol-water mixtures on their antimicrobial activity is needed. This review highlights the importance of establishing relationships between material properties and product performance.

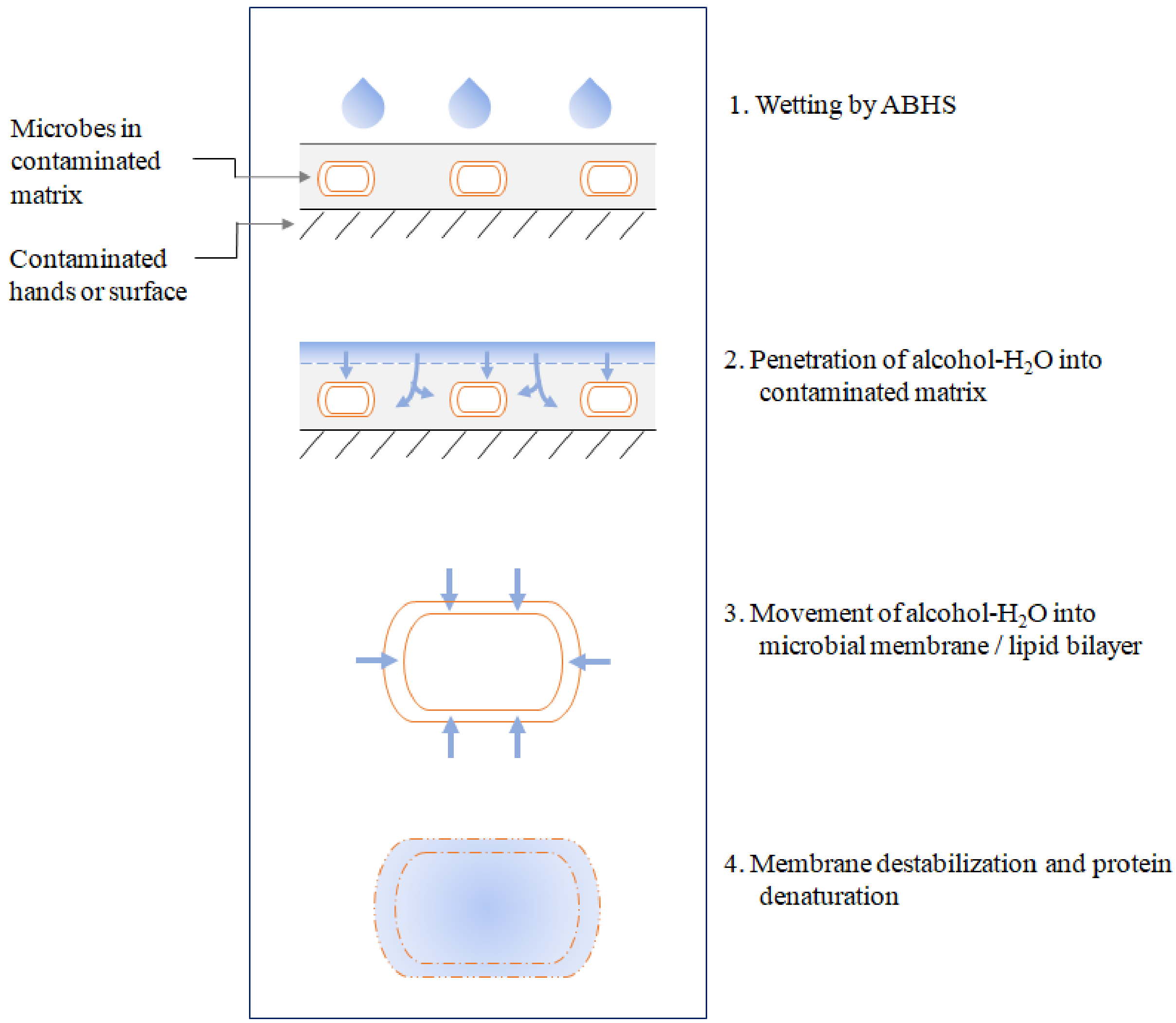


Figure 3: Proposed model of events leading to microbial inactivation by ABHS.

1) and 2) - low surface tension facilitates wetting and interaction with contaminated organic matter and surfaces, especially if hydrophobic; 3) - low surface and interfacial tension facilitates interaction of alcohol-water mixture with microbial membranes leading to 4) lipid bilayer damage and protein denaturation.

References

(1) Berardi, A.; Perinelli, D. R.; Merchant, H. A.; Bisharat, L.; Basheti, I. A.; Bonacucina, G.; Cespi, M.; Palmieri, G. F. Hand Sanitisers amid CoViD-19: A Critical Review of Alcohol-Based Products on the Market and Formulation Approaches to Respond to Increasing Demand. *Int. J. Pharm.* **2020**, *584*, 119431. https://doi.org/10.1016/j.ijpharm.2020.119431.

(2) Nyamweya, N.; Abuga, K. A Survey of Alcohol-Based Hand Sanitizers in Nairobi: Packaging, Labelling and Regulatory Compliance. *East Cent. Afr. J. Pharm. Sci.* **2020**, *23* (2), 72–76.

(3) Abuga, K.; Nyamweya, N. Alcohol-Based Hand Sanitizers in COVID-19 Prevention: A Multidimensional Perspective. *Pharmacy* **2021**, *9* (1), 64. https://doi.org/10.3390/pharmacy9010064.

(4) Li, A.; Yalkowsky, S. H. Solubility of Organic Solutes in Ethanol/Water Mixtures. *J. Pharm. Sci.* **1994**, *83* (12), 1735–1740. https://doi.org/10.1002/jps.2600831217.

(5) Quinn, M. E. Alcohol. In *Handbook of Pharmaceutical Excipients*, 6th ed.; Rowe, R. C., Sheskey, P. J., Quinn, M. E., Eds.; American Pharmaceutical Association: Washington, 2009; pp 17–19.

(6) Waszkowiak, K.; Gliszczyńska-Świgło, A. Binary Ethanol–Water Solvents Affect Phenolic Profile and Antioxidant Capacity of Flaxseed Extracts. *Eur. Food Res. Technol.* **2016**, *242* (5), 777–786. https://doi.org/10.1007/s00217-015-2585-9.

(7) Franks, F.; Ives, D. J. G. The Structural Properties of Alcohol–Water Mixtures. *Q. Rev. Chem. Soc.* **1966**, *20* (1), 1–44. https://doi.org/10.1039/QR9662000001.

(8) Sinko, P. J. *Martin's Physical Pharmacy and Pharmaceutical Sciences*, 5th ed.; Lippincott Williams & Wilkins: Baltimore, 2006.

(9) Li, R.; D'Agostino, C.; McGregor, J.; Mantle, M. D.; Zeitler, J. A.; Gladden, L. F. Mesoscopic Structuring and Dynamics of Alcohol/Water Solutions Probed by Terahertz Time-Domain Spectroscopy and Pulsed Field Gradient Nuclear Magnetic Resonance. *J. Phys. Chem. B* **2014**, *118* (34), 10156–10166. https://doi.org/10.1021/jp502799x.

(10) Karlsson, B. C. G.; Friedman, R. Dilution of Whisky – the Molecular Perspective. *Sci. Rep.* **2017**, *7* (1), 6489. https://doi.org/10.1038/s41598-017-06423-5.

(11) Stehle, S.; Braeuer, A. S. Hydrogen Bond Networks in Binary Mixtures of Water and Organic Solvents. *J. Phys. Chem. B* **2019**, acs.jpcb.9b02829. https://doi.org/10.1021/acs.jpcb.9b02829.

(12) Ballal, D.; Chapman, W. G. Hydrophobic and Hydrophilic Interactions in Aqueous Mixtures of Alcohols at a Hydrophobic Surface. *J. Chem. Phys.* **2013**, *139* (11), 114706. https://doi.org/10.1063/1.4821604.

(13) Mackay, D.; Shiu, W.-Y.; Ma, K.-C.; Lee, S. C. *Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals*, 2nd ed.; CRC Press: Boca Raton, 2006. https://doi.org/10.1201/9781420044393.

(14) Lide, D. R. *CRC Handbook of Chemistry and Physics*, 85th ed.; CRC Press: Boca Raton, 2004.

(15) European Medicines Agency. European Medicines Agency, Information For The Package Leaflet Regarding Ethanol Used As An Excipient In Medicinal Products For Human Use. 2019. https://www.ema.europa.eu/en/documents/scientific-guideline/information-package-leaflet-regarding-ethanol-used-excipient-medicinal-products-human-use_en.pdf (accessed accessed 2021-03-30).

(16) Yilmaz, H. Excess Properties of Alcohol-Water Systems at 298.15 K. *Turk. J. Phys.* **2002**, *26*, 243–246.

(17) Wakisaka, A.; Matsuura, K. Microheterogeneity of Ethanol–Water Binary Mixtures Observed at the Cluster Level. *J. Mol. Liq.* **2006**, *129* (1–2), 25–32. https://doi.org/10.1016/j.molliq.2006.08.010.

(18) Gold, N. A.; Mirza, T. M.; Avva, U. Alcohol Sanitizer. StatPearls. http://www.ncbi.nlm.nih.gov/books/NBK513254/ (accessed 2021-03-30).

(19) Khattab, I. S.; Bandarkar, F.; Fakhree, M. A. A.; Jouyban, A. Density, Viscosity, and Surface Tension of Water+ethanol Mixtures from 293 to 323K. *Korean J. Chem. Eng.* **2012**, *29* (6), 812–817. https://doi.org/10.1007/s11814-011-0239-6.

(20) Kuchuk, V. I.; Shirokova, I. Yu.; Golikova, E. V. Physicochemical Properties of Water-Alcohol Mixtures of a Homological Series of Lower Aliphatic Alcohols. *Glass Phys. Chem.* **2012**, *38* (5), 460–465. https://doi.org/10.1134/S1087659612050057.

(21) Lee, I.; Park, K.; Lee, J. Precision Density and Volume Contraction Measurements of Ethanol–Water Binary Mixtures Using Suspended Microchannel Resonators. *Sens. Actuators A: Phys.* **2013**, *194*, 62–66. https://doi.org/10.1016/j.sna.2013.01.046.

(22) WHO. Guide to Local Production: WHO-Recommended Handrub Formulations. 2010. https://www.who.int/gpsc/5may/Guide_to_Local_Production.pdf?ua=1. (accessed 2021-03-30).

(23) Kramer, A.; Rudolph, P.; Kampf, G.; Pittet, D. Limited Efficacy of Alcohol-Based Hand Gels. *Lancet* **2002**, *359* (9316), 1489–1490. https://doi.org/10.1016/S0140-6736(02)08426-X.

(24) do Prado, M. F.; Coelho, A. C. C.; de Brito, J. P. B.; Ferreira, D. O.; Junior, A. W.; da Silva Menecucci, C.; de Queiroz, A. B.; Garcia, L. B.; Cardoso, C. L.; Tognim, M. C. B. Antimicrobial Efficacy of Alcohol-Based Hand Gels with a 30-s Application: Alcohol-Based Hand Rubs. *Lett. Appl. Microbiol.* **2012**, *54* (6), 564–567. https://doi.org/10.1111/j.1472-765X.2012.03240.x.

(25) Nyamweya, N.; Lumb, P.; Mujyarugamba, J.-C.; Abuga, K. Inactive Ingredients Used In Alcohol-Based Hand Sanitizers Marketed In The Nairobi Metropolitan Area. *Pharm. J. Kenya* **2021**, *25* (1), 17–20.

(26) Vazquez, G.; Alvarez, E.; Navaza, J. M. Surface Tension of Alcohol Water + Water from 20 to 50 °C. *J. Chem. Eng. Data* **1995**, *40* (3), 611–614. https://doi.org/10.1021/je00019a016.

(27) Pogorzelski, S.; Watrobska-Swietlikowska, D.; Sznitowska, M. Surface Tensometry Studies on Formulations of Surfactants with Preservatives as a Tool for Antimicrobial Drug Protection Characterization. *J. Biophys. Chem.* **2012**, *3* (4), 324–333. https://doi.org/10.4236/jbpc.2012.34040.

(28) O'Hare, K. D.; Spedding, P. L. Evaporation of a Binary Liquid Mixture. *Chem. Eng. J.* **1992**, *48* (1), 1–9. https://doi.org/10.1016/0300-9467(92)85001-P.

(29) Pinhas, A. R. A Kinetic Study Using Evaporation of Different Types of Hand-Rub Sanitizers. *J. Chem. Educ.* **2010**, *87* (9), 950–951. https://doi.org/10.1021/ed1003492.

(30) Felton, D. E.; Moberly, J. G.; Ederer, M. M.; Hartzell, P. L.; Waynant, K. V. Expanding Evaporation Rate Model Determination of Hand-Rub Sanitizers to the General Freshman and Engineering Chemistry Undergraduate Laboratory: Inquiry-Based Formulations, Viscosity Measurements, and Qualitative Biological Evaluations. *J. Chem. Educ.* **2018**, *95* (7), 1226–1229. https://doi.org/10.1021/acs.jchemed.7b00969.

(31) Sterlyagov, A. N.; Letushko, V. N.; Nizovtsev, M. I.; Borodulin, V. Y. Experimental Study of Evaporation of Sessile Droplets of the Water-Ethanol Solution with Different Concentrations. *J. Phys.: Conf. Ser.* **2018**, *1105*, 012068. https://doi.org/10.1088/1742-6596/1105/1/012068.

(32) Golin, A. P.; Choi, D.; Ghahary, A. Hand Sanitizers: A Review of Ingredients, Mechanisms of Action, Modes of Delivery, and Efficacy against Coronaviruses. *Am. J. Infect. Control* **2020**, *48* (9), 1062–1067. https://doi.org/10.1016/j.ajic.2020.06.182.

(33) McDonnell, G.; Russell, A. D. Antiseptics and disinfectants: activity, action, and resistance. *Clin. Microbiol. Rev* **1999**, *12*

(1), 147–179. https://doi.org/10.1128/CMR.12.1.147.

(34) Jing, J.; Pei Yi, T.; Bose, R.; McCarthy, J. R.; Tharmalingam, N.; Madheswaran, T. Hand Sanitizers: A Review on Formulation Aspects, Adverse Effects, and Regulations. *Int. J. Environ. Res. Public Health* **2020**, *17* (9), 3326. https://doi.org/10.3390/ijerph17093326.

(35) Ingram, L. O. Ethanol Tolerance in Bacteria. *Crit. Rev. Biotechnol.* **1989**, *9* (4), 305–319. https://doi.org/10.3109/07388558909036741.

(36) Herman, E. B.; Haas, G. J.; Crosby, W. H.; Cante, C. J. Antimicrobial Action of Short Chain Alcohols and Glycols. *J. Food Safety* **1980**, *2* (3), 131–139. https://doi.org/10.1111/j.1745-4565.1980.tb00391.x.

(37) Daicheng, L.; Ma, F. Soybean Phospholipids. In *Recent Trends for Enhancing the Diversity and Quality of Soybean Products*; Krezhova, D., Ed.; IntechOpen: Rijeka, 2011; p Ch. 22. https://doi.org/10.5772/20986.

(38) Moss, G. Medium-Chain Triglycerides. In *Handbook of Pharmaceutical Excipients*, 6th ed; Rowe, R. C., Sheskey, P. J., Quinn, M. E., Eds.; American Pharmaceutical Association: Washington, 2009; pp 429–431.

(39) Ly, H. V.; Longo, M. L. The Influence of Short-Chain Alcohols on Interfacial Tension, Mechanical Properties, Area/Molecule, and Permeability of Fluid Lipid Bilayers. *Biophys. J.* **2004**, *87* (2), 1013–1033. https://doi.org/10.1529/biophysj.103.034280.

(40) Eslami, H.; Das, S.; Zhou, T.; Müller-Plathe, F. How Alcoholic Disinfectants Affect Coronavirus Model Membranes: Membrane Fluidity, Permeability, and Disintegration. *J. Phys. Chem. B* **2020**, *124* (46), 10374–10385. https://doi.org/10.1021/acs.jpcb.0c08296.