Unravelling the Enigma of Hand Sanitizer In COVID-19 – A Bibliometric Analysis of Related Publications Over the Year

Elvis Samuel
Karunya Institute of Technology and Sciences
Almi Babu
Karunya Institute of technology and Science: Karunya Institute of Technology and Sciences
Shanamitha Arjunan
Karunya Institute of Technology and Sciences
Biswanath Mahanty (bmahanty@karunya.edu)
Karunya Institute of Technology and Sciences https://orcid.org/0000-0002-5815-2440

Research Article

Keywords: ABHSs, Alcohol toxicity, Covid-19, Environmental hazard, Formulations, Hand sanitizer

Posted Date: May 21st, 2021

DOI: https://doi.org/10.21203/rs.3.rs-526772/v1

Abstract

Alcohol-based sand sanitizers (ABHSs) are effective in controlling the spread of COVID-19 and has been integrated to our daily life since the onset of the outbreak. However, the sudden and unprecedented global induction of ABHSs has not been smooth, as conflicting reports continued to pour into the public domain, not all for good reason. This review, therefore, attempts to identify the emerging aspects of ABHSs in the era of COVID-19. Articles indexed in Scopus and PubMed on “hand sanitizer” published between January 2020 and February 2021, were screened based on PRISMA guidelines, and classified into different thematic groups. Selected articles on hand sanitizers (101) primarily echo “health hazard” (40, 39.6%) associated with accidental/intentional exposure, methanol toxicity, or occupational irritant contact dermatitis. Articles on “formulations” (23, 22.8%) and “efficacy” (18, 17.8%) mainly refer to alcoholic preparations, though a small subset of formulations has been actually been tested against SARS-Cov-2. Articles on semi-alcoholic, non-alcoholic, or even ayurvedic preparations have been implicated without a standardized efficacy report. Quality concern (12, 11.9%), and shortage (8, 7.9%) have also been reflected in publications during the pandemic. However, this representation is somewhat overinflated given that 28% of total articles are of review, editorial, letters, and not actual case studies. Many potential studies designed in the pandemic might not have reached to publication stage. However, the implication from existing studies on the use of ABHSs can still be useful to build better public awareness, and prioritize interventional strategies among stakeholders.

1. Introduction

Coronavirus disease 2019 (COVID-19) outbreak attributed to a novel coronavirus [severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)], started in December 2019 in Wuhan, the capital of Hubei province in mainland China (Hui et al. 2020). Word health organization (WHO) declared the COVID-19 outbreak as a public health emergency of international concern on 30th January 2020, which have resulted in more than 90 million confirmed with 1.9 million death as of 14th January 2021 (https://covid19.who.int/). In absence of standardized medical treatment, interventional strategies such as wearing a mask, maintaining hand hygiene, and social distancing continued to be vital instruments not only to slow down the spread of COVID-19but to reduce the possibility of other respiratory infectious diseases(Chiu et al. 2020).

CDC’s recommendations on ABHSs are prescribed to prevent the spread of COVID-19 in hospitals and healthcare environments (Centers for Disease Control and Prevention (CDC) 2020; Lotfinejad et al. 2020).WHO has campaigned “Save Lives: Clean Your Hands” incorporating guidelines on the usage of hand rub, hand wash, and ‘My 5 Moments for Hand Hygiene’ to be adopted (World health Organization (WHO) 2020a; World health Organization 2020). Standard precaution and hand hygiene can protect health care workers (HCWs) from Covid-19 in a low-risk, outpatient clinic setting (Chung et al. 2020). Despite interventions and campaigns from national and international health authorities, hand hygiene has not been always satisfactory even in this time of health emergency (Stadler and Tschudin-Sutter 2020).

As people apprehend the necessity for hand hygiene, the sale of hand sanitizers shoots up in early March 2020 and went out of selves caused by unprecedented demand, and aggravated by stockpiling (Keane and Neal 2021). To establish normalcy, many regulatory authorities across the globe eased the licensing protocol, robing many non-government organizations and related industries for the production and sale of hand-sanitizer products (U.S Food and Drug Administration 2020). This relaxation though encouraged many enterprises, organizations to explore the sanitizer market with different formulations, also eased the entry of many sub-standard, low-quality counterfeit products containing hazardous ingredients, incomplete label information, ingredient lists, or cautionary warnings, escalating an ongoing safety concern (Dear et al. 2020; Welle et al. 2021). Many turned to stream media for instruction instead of guidelines for hand sanitizer production published by the WHO (Hakimi and Armstrong 2020). The availability of hand sanitizers containing high concentrations of ethanol or isopropanol has been a concern of substance abuse (Meehan and Wightman 2020). Cases of methanol poisoning and even death associated with ingestion of ABHSs are not unknown (Yip et al. 2020).

The undesirable attributes of sanitization products, ABHSs in particular, added startling newer dimensions in the scope of hand hygiene during this pandemic (Fig. 1). Though a very important to have protection against Covid-19 spread, improper or possible misuse of hand sanitizer has been an apprehension across all settings (i.e., home, offices, workplace) during this health emergency. Excessive use of sanitizers may not necessarily be equated to hand hygiene compliance, as also reflected in a large number of articles that appeared in the scientific domain within a span of just one year.

This review is undertaken to put a comprehensive perspectivity on unravelling dimensions of hand sanitizers (specially ABHSs) from literature, precisely in the context of this pandemic. Articles focusing on sanitizer formulation, their efficacy, pandemic crisis, short-/long-term health, and environmental hazards have been critically reviewed. An attempt has been made to untangle the actual reports, case studies from editorials, notes, opinions, and reviews which could have possibly over-inflated the ABHSs apprehension.

2. Literature Search And Selection Summary

2.1. Search strategy

The integrative review has been formulated to qualitatively analyze the different aspects of hand sanitizers as reflected in the peer-reviewed literature in past one year. A bibliographic search of PMC and Scopus database was undertaken (on 10/02/2021) with a formulated query of "hand sanitizer OR hand-sanitizer" in “Title, Abstract, and Keywords”. Lists of eligible studies were exported into Microsoft excel format, were manually screened for titles, followed by abstracts.

2.2. Selection criteria

Peer-reviewed research articles, case studies, notes, and editorials focusing on either formulation, toxicity, or health hazard published between 01/01/2020 and 10/02/2021 were included. Articles not written in

English or contextually not relevant were excluded. The detailed screening and eligibility conditions have been shown in the PRISMA flow diagram (Moher et al. 2009) (Fig. 2).

2.3. Data items and analysis

Due to the heterogeneity and limited information on the studies, a meta-analysis was not feasible; thus, the analysis is based on a qualitative narrative synthesis of the findings. After exporting all selected studies into Microsoft excel, each of the articles were classified into five thematic area, *i.e.,* formulation, efficacy, health hazard, quality, or shortage. Each of the articles with available full text were manually screened by independent reviewer for relevant information. In formulation subclass of articles, information on product type, product form, and concentrations data were extracted. The information on test microorganism, duration of sanitization, and log reduction of microbial load (if available) were noted for articles reporting efficacy of sanitizer. For classified reports on health hazard, information on the subject (age/sex), exposure route, long/short term consequences were recorded from the full text assessment.

2.4. Summary of information

Using the query as described earlier, and inclusion/exclusion criteria, a total of 101 papers were identified in the context of hand sanitizer. The findings from selected articles were collated to produce a summary of information (Fig. 3). The selected studies on hand sanitizer focus on health hazards (40), formulation (23), efficacy (18), quality concern (12), or shortage (8). Health hazards by far have been the major thematic area represented by a maximum number of research articles, letters, notes in comparison to others. However, most of the reviews, either by the number of proportions, are on the formulation aspect. None of the published reviews address sanitizer “quality” concern or “shortage” during this pandemic.

3. Hand Sanitizer In Covid-19 Perspective

3.1. Recommended Hand sanitization

Hand hygiene plays a vital role in reducing the transmission of infectious diseases like Covid-19 (Kantor et al. 2020; Roy et al. 2020). It is recommended to maintain hand hygiene by frequently washing using soap and water for at least 20 s-30 s (MacGibeny and Wassef, 2020; Manderson and Wahlberg, 2020; United Nations Economic Commission for Africa; 2020). Sanitizers can be of different variants, primarily based on active ingredients, such as soap containing natural fats, detergents, or alcohol-based (Table 1). Centers for Disease Control and Prevention (CDC) recommends the use of ABHSs as a first-line preventive measure against Covid-19 (Mahmood et al. 2020; D. Singh et al. 2020). World health organization (WHO) has endorsed the use of alcohol-based hand rub containing a minimum of 60% v/v alcohol for 20-30 seconds to maintain hand hygiene (World Health Organization (WHO), 2020a). Formulations either with 80% (v/v) ethanol or 75% (v/v) isopropyl alcohol each with glycerol 1.45% (v/v), hydrogen peroxide (H_2O_2) 0.125% (v/v) and sterile distilled or boiled cold water are recommended. Detailed review on hand sanitizer formulations, mechanisms of action, and efficacy against coronaviruses has been published

(Golin et al. 2020; D. Singh et al. 2020). Berardi et al (2020b) have reviewed on-hand sanitation approaches and products available on the market while guiding product development with standardized ingredients for interested commercial organizations. Effectiveness of available hand sanitizers as well as the formulation aspects, adverse effects have been reviewed (Jing et al. 2020) Health and environmental impact of alcoholic formulation and the possibility of greener alternative has been reviewed (Daverey and Dutta 2021).

Table 1. Major ingredients and efficacy of different hand sanitizer formulations reported in the literature

Product formulation	Product form	Concentration	Contact time(s)	Log 10 Reduction	Reference
	Alcoholic formulations				
Alcohol[a]	Solution	60.5-95% (w/w)	10-15 s	≥ 3.25-4.01	(Mukherjee et al. 2021)
Ethanol[a]	Gel	70%	30 s	≥3.22	(Leslie et al. 2020)
Ethanol[a]	Foam	70%	30 s	≥3.10	(Leslie et al. 2020)
Ethanol[b]	Solution	70%	15 s	>1.8	(Prince-Guerra et al. 2020)
Ethanol[c]	Solution	56%	30 s	>5	(Ciotti et al. 2021)
Ethanol[d]	Solution	90%	20-30 s	>1.22	(Anitha et al. 2020)
Ethanol[a]	Solution	60-95 %	45 s	-	(Samara et al. 2020)
Ethanol[a,*]	Solution	80% (v/v)	30 s	≥3.8-≥5.9	(Kratzel et al. 2020)
2-propanol[a,**]	Solution	75% (v/v)	30 s	≥3.8-≥5.9	(Kratzel et al. 2020)
Ethanol	Gel	75% (w/w)	15 s	>3	(Fu et al. 2020)
	Non-alcoholic formulations				
Cleanser[a]	Liquid surfactant (10-19% w/w)	50%	10-20 s	≥ 3.01-3.42	(Mukherjee et al. 2021)
Benzalkonium chloride [a]	Solution	<0.12 %	300 s	-	(Samara et al. 2020)

Qimei[a]	Wipes	100%	15-30 s	-	(Ogilvie et al. 2021)
Benzalkonium chloride[a]	Foam /Wipes	0.025-0.13%	25s/60s	≥ 2.97-≥ 5.0	(Ijaz et al. 2020)
Salicylic acid[a]	Foam/ Gel	0.023-0.025% (w/w)	60s	≥ 3.6	(Ijaz et al. 2020)
	Herbal or Semi-herbal formulation				
Germix® [f]	Liquid	n.a.	-	-	(Balkrishna et al. 2020)
Ethanol, Snow mushroom extract	Gel	66.5% (EtOH), 10% SM extract	-	0.94	(Lourith et al. 2021)
Ayurvedic formulation	Gel	n.a.	-	-	(Azim et al. 2020)

The reported efficiency against [a] - SARS-CoV-2, [b] – coliform, [c] - *Pseudomonas aeruginosa,* [d] – CFU, [e] - *Candida auris*; [f] formulation consisting of isopropyl alcohol, *A. indica*, *O. sanctum,* and *Aloe arbadensis* and tested against S*. epidermidis* and *S. aureus,* n.a. – data not available

* - Original and modified WHO formulation I, ** - Original and modified WHO formulation II,

3.2 Alcohol-Based Hand Sanitizers (ABHSs)

3.2.1. Ethanol-based formulation

Ethanol-based hand sanitizers play a vital role in inactivating enveloped viruses such as strains of COVID-19 (Kantor et al. 2020; Kratzel et al. 2020). Most of the published studies on ABHSs formulation differ on either the alcohol concentration or efficacy. Only a few studies verified the efficacy of commercial ABHSs formulations at different dilutions on SARS-CoV-2 suspension culture, where log reduction of SARS-CoV-2 titre varies between 3 and 5, depending on alcohol content or dilution tested (49%- 95% w/w) and exposure time (>15 s to 1 min) (Ijaz et al. 2020; Leslie et al. 2020; Mukherjee et al. 2021). Though liquid-based hand sanitizers are likely to be more effective than gels due to their prolonged application time, the difference in acceptance and compliance can be confounded (Tan et al. 2020). Both gel or foam-based hand sanitizers with equivalent ethanol (70%) shows >3 log reductions in SARS-CoV-2 suspension culture within 30 s contact (Leslie et al. 2020). However, a survey conducted among HCWs indicates the

possibility of suboptimal use of ABHSs, as a significant proportion HCWs considers WHO recommended ABHSs dose and drying time (1.5-2.25 mL with of 20-30 seconds) as unreasonably high (Kenters et al. 2020).

Several research studies report the effectiveness of ABHSs formulation in laboratory conditions, but not in context with SARS-CoV-2. Researchers have studied hydroalcoholic sanitizer gel containing ethanol (71.9%) and essential oils (Lemon, Lavandar, and Tea tree) against antibiotic-resistant *Pseudomonas aeruginosa* at 8-80% dilution, resulting in 1.8 to >5 log reduction in 30 s (Ciotti et al. 2021). The ethanol-based sanitizer has been effective in reducing human norovirus infection risk by 85%, following 60-second exposure (Wilson et al. 2020). However, the effectiveness against human norovirus remains dubious, as others (Escudero-Abarca et al. 2020) have observed <1 log reduction in genome equivalent copies when exposed to standard ethanolic formulation regardless of contact time (30 or 60s). In real-world studies ethanol-based, gel/ solution is useful in eradicating the *Candida auris* colonization (3.00 log10 CFU) (Fu et al. 2020), microbial load in hand swab of dental student in clinical settings (Anitha et al. 2020), or coliform concentrations in farmworker hands (Prince-Guerra et al. 2020). A recent study reports the adoption of Ghanaian local beverage in sanitizer with 63.70% ethanol and carbopol® 940 against *vibrio cholera* (Osei-Asare et al. 2020). The market demand for hand sanitizers has increased drastically in the pandemic, few studies offer detailed methodology on the preparation of hand sanitizer (Ahmed and Goh 2020; Bussey 2020; C. F. Goh and Ahmed 2020).

3.2.2 Isopropyl based formulation

Isopropyl alcohol content in WHO suggested formulations varies between 60 to 90% and exhibits significant anti-bacterial, anti-viral, anti-fungal activities (World health Organization (WHO) 2020b). Isopropanol in a concentration range between 62% to 80% can inactivate high titer of human coronavirus dried on solid surfaces within 15-s contact time (Meyers et al. 2021). The observed efficiency of isopropyl-based hand sanitizers against the novel coronavirus can be improved while adding other active ingredients, such as anionic surfactants (Jahromi et al. 2020). However, a recent review suggests significant skin barrier damage from repeated exposure to isopropanol gets aggravated in presence of detergents (Tasar et al. 2021). Development of contact leukoderma on rigorous hand hygiene using an isopropanol-based hand rub has also been reported (Inder and Kumar 2020). ABHSs formulation with methanol or 1-propanol is not recommended due to potential toxicity (Berardi, Cenci-Goga, et al. 2020).

3.3 Non-Alcohol Based Hand Sanitizer

Soap and synthetic detergent are some of the used disinfectants against the spread of coronavirus (Gammon and Hunt 2019; Lotfinejad et al. 2020). Quaternary ammonium compound-based sanitizers on such as Cavicide® and Qimei® can deactivate SARS-CoV-2 within 15 s (Ogilvie et al. 2021). Commercially available benzalkonium chloride (0.12%) hand sanitizer offers better protection in HCWs against *Staphylococcus aureus* transient skin contamination when compared to 70% ethanol-based hand sanitizer (Bondurant et al. 2020). Though benzalkonium chloride is included in the EPA-approved list for its use against SARS-CoV-2 (Environmental Protection Agency (EPA) 2020), CDC does not recommend

benzalkonium chloride-based formulations for poor efficacy against coronavirus (Centers for Disease Control 2020; Kampf et al. 2020). For non-alcoholic preparation, Aaride AGT-1 possesses high antibacterial activity against pathogenic bacteria including MRSA, where 6 log reduction is possible within 30 s (Jindal et al. 2020).

Hand sanitizer gel containing 66.5% ethanol and 10% of snow mushroom (*Tremella fuciformis*) extract offers significantly better skin hydration and slightly improved sanitizing efficacy than the controlled formulation (Lourith et al. 2021). Semi-ayurvedic isopropyl alcohol-based formulation blended with medicinal herbs like *Azadirachta indica*, *Ocimum sanctum,* and *Aloe barbadensis* shows better antimicrobial potency against *S. epidermidis* and *S. aureus* (Balkrishna et al. 2020).

Reports on the use of alcohol-free hand sanitizers have been either rare or very preliminary without rigorous validation on efficacy. Alcohol-free α-pinene and turpentine oil gel preparation have been implicated against *Staphylococcus aureus* and *E. coli* when tested using standard disc diffusion assay (Wijayati et al. 2020). Ayurvedic hand sanitizer formulation with *A. indica*, O. *sanctum,* and *Citrus limon* has also been suggested, though the effectiveness of those preparations remains unverified (Azim et al. 2020). Use of polyherbal preparation is implicated for use of ready-made herbal hand sanitizer considering the antiviral, antibacterial, antimicrobial, antifungal effects reported for herbs (Pargaonkar et al. 2020).

4. Hand Sanitizer Scarcity

In the early month of the pandemic, there has been an acute shortage of hand sanitization products all over the world as reflected in few studies. An online survey administered in March 2020 to all members of the “Association for Professionals in Infection Control and Epidemiology” in the US suggests that >70 % of respondents have an insufficient supply of hand sanitizers (Rebmann et al. 2021). During the 1st week of March 2020, sales of disinfectants were 7.5-fold higher than usual and dropped to half the normal sales in the subsequent weeks stock depleted (Opatz et al. 2020). A cross-sectional survey in community pharmacies working in Egypt in April 2020 reveals the infrequent availability of hand sanitizers (62.1%) (Bahlol and Dewey 2021). Uncertainty about possessing a COVID-19 risk has been an important factor, that promoted the increased purchase of preparatory health and safety products (Clemens et al. 2020). Attempt to address the shortage of sanitizer by using handmade sanitizer has received criticism from the medical fraternity (Bhattacharya et al. 2020).

5. Hand Sanitizer Associated Toxicity And Health Hazards

5.1 Alcohol Toxicity due to accidental exposure or abuse

A subset of published articles correlates the accidental use or misuse of ABHSs to misleading information in popular do-it-yourself YouTube video contents on hand sanitizer (Erikainen and Stewart 2020; Hakimi and Armstrong 2020). Many instances such media contents fail to provide information on

labelling, storage, or even promoted the use of colouring agents to make it attractive for children. The deceptive hand-sanitizer packaging in containers resembling food or drinks can be dangerous, particularly in children (Voelker 2020). Mandating manufacturers to display clear warning labels, lockable dispensers, supervised usage in children are few recommendations that can be implemented for intentional or unintentional consumption-related poisoning (Richards 2020).

Health hazards associated with ABHSs can be either acute ethanol toxicity, methanol poising, or chronic skin irritation, or contact dermatitis (Table 2). Hand sanitizers mostly contain ethanol and isopropyl alcohol as their main ingredient can be considered as a common cause of acute intoxication in children (Patidar et al. 2020), particularly when repeatedly ingested (Hanna et al. 2020). Children are at greater risk for developing hypoglycaemia, toxicity even at a small amount of alcohol dose (Chen and Haber 2021). Accidental ingestion at a residential setting has been the primary exposure route in a large number of US children (<5 years), though with minor/minimal medical consequences (McCulley et al. 2021). The reported cases of hand sanitizer exposure in 2020 from children (<12 years age) alone (24,802) surpass the annual average of total cases (>21,000) over the years between 2012 and 2019 (Fig. 4) (Mahmood et al. 2020). Croatian Poison Control Centre reported about a nine times increase in sanitizer exposure cases in the first half of 2020, where preschool children have been the most vulnerable group (Babić et al. 2020). Apart from oral ingestion, ABHS-related ocular exposures in children have increased in comparison with the earlier year (Martin et al. 2021), though without long-term sequelae (Yangzes et al. 2021). Accidental splitting of alcohol-based hand rub gel can cause corneal epithelial defect even in adults and require surgical intervention (Sunny 2020). Aerosol from frequent use of ABHS spray can cause episodic redness, irritation in adults in a closed environment (Shetty et al. 2020).

Intentional consumption of ABHSs can lead to acute poisoning and even death (Kuehn 2020). The toxicity of ABHSs consumption can be aggravated in patients on anti-depressant prescription (Richards 2020). Surprisingly, suicidal or accidental ingestion of ABHSs has also been reported in hospital settings for patients undergoing treatment for different medical conditions (Jorge et al. 2020; Lim 2020; Stevens and Hix 2020). Caution must be exercised with ABHSs usage in patients on disulfiram getting treated for their “alcohol use disorders”. Inhalation of alcoholic vapor from hand sanitizers and cutaneous alcohol absorption could be sufficient to cause a disulfiram-ethanol reaction (Brewer and Streel 2020). Disulfiram adherent patients using alcohol-based sanitizer have a clinical manifestation of disulfiram ethanol reaction (Ghosh et al. 2021), aggravated by excessive hand sanitizing zeal (De Sousa 2020). Long-term dermal absorption of isopropyl alcohol from a topical application can cause multiple unexplained cardiac and neurological deficits in adults (Leeper et al. 2000).

Table 2. Case studies reporting on exposure of ABHSs and their short or long-term consequences

Subject	Product	Exposure type	Consequences	Reference
	Accidental or intentional exposure			
Woman in their 30's	Ethanol/Propanol based ABHS	Intentional – Mental health facility	Death due to venlafaxine and alcohol	(Richards 2020)a
Unclassified reports from New Maxico and Arizona	ABHS containing methanol	Intentional ingestion	Death and vison loss	(Kuehn 2020)
Female in their 40’s (psychiatric)	isopropanol-based ABHSs	Intentional and suicidal	consciousness and oxygen saturation -	(Stevens and Hix 2020)
Female, inpatient psychiatric unit	ABHSs	Intentional	unresponsive with faint pulses	(Jorge et al. 2020)
Man in their 60’s with spondylitis	ABHSs	Accidental	restlessness and disorientation	(Lim 2020)
Middle-aged men adherent to disulfiram	Sanitizers	Skin/Inhalation	Disulfiram-Ethanol reaction	(Ghosh et al. 2021)
3 subjects – undisclosed age/sex	ABHSs	Skin/Inhalation	Disulfiram-Ethanol reaction	(Brewer and Streel 2020)
Child <10	ABHS	Intentional -	Poisoning/	(Hanna et

years in Australia		habitual	recovered	al. 2020)
Children ≤5 years National Poison Data System data	Ethanol ABHS	Unintentional ingestion	Ocular, gastrointestinal	(McCulley et al. 2021)
Croatian Poison Control Centre	Sanitizer ethanol/isopropyl alcohol	Accidental ingestion/inhalation	Mild/ asymptomatic	(Babić et al. 2020)
Women in early 30's	ABHSs	Accidental Ocular exposures	Temporary corneal defect - treated	(Sunny 2020)
Children data from French poison control	ABHSs	Accidental Ocular exposures	Corneal lesions	(Martin et al. 2021)
Female in mid-20's	ABHSs	hand sanitizer spray – aerosol exposure	Episodic redness, irritation, and a burning	(Shetty et al. 2020)
4–5-year-old child	ABHSs	Accidental ocular exposure	conjunctival congestion	(Yangzes et al. 2021)
	Long-term dermal exposure			
School children, Denmark	Hand sanitizer	Increased Hand sanitization	irritant contact dermatitis	(Borch et al. 2020)

HCWs from an Irish hospital	ABHSs	Increased Hand sanitization	Dry skin, ICD	(Kiely et al. 2021)
HCWs hospital	ABHSs	Increased use	Dryness of skin	(Altunisik Toplu et al. 2020)
HCWs - 15-year survey – Geneva Hospital	ABHSs (isopropanolol)	Hand-hygiene - long-term	irritant contact dermatitis (66%)	(Quenan and Piletta 2020)
	Ingestion of methanol contaminated ABHSs			
Women in mid-20's	tetrahydroxypropyl ethylenediamine - sanitizer	Occupational exposure	allergic contact dermatitis	(Antelmi et al. 2020)
Man in mid-20's	Methanol contaminated ABHS	Intentional – addictive ingestion	Death	(Overbeek et al. 2021)
15 cases (age between 21-65 years)	Methanol contaminated ABHS	Ingestion	4 death	(Yip et al. 2020)
Alcoholic male in late 50's	Methanol contaminated ABHS	Ingestion	bilateral loss of vision	(Kochgaway et al. 2020)
797 cases	Sanitizer, Alcohol	Ingestion	Toxicity, death	(Sefidbakht et al. 2020)
5000 people	Sanitizer, Alcohol	Ingestion	Toxicity, death	(Shokoohi

a – Old case of 2013 reported in the publication

5.2. Hazards due to methanol mixing or counterfeit products

A significant number of study reports flourishing market of substandard or counterfeit ABHSs which either have undisclosed methanol content or with an alcohol content below 60% cause a different dimension of health hazard (Jairoun et al. 2021). A probe in Addis Ababa market reveals that 70% of hand sanitizers had alcohol strength below the WHO recommended limit and all products failed to meet the hydrogen peroxide (H_2O_2) content limit (Selam 2020). Though the proportion of substandard products may vary, the situation has been perilous either in Italy (Berardi, Cenci-Goga, et al. 2020), Turkey (Berkkan and Ulutas 2020), or Dubai (Jairoun et al. 2021). Development and validation of a scale to identify falsified hand sanitizer (Jairoun et al. 2020) or availability of low-cost portable instrument for monitoring ethanol content (Pasquini et al. 2020) or on-site methanol screening (Güntner et al. 2021) with enforcement authorities can be instigated to curb such counterfeit products. Consumer awareness on tell-tale signs for the identification of fraudulent ABHSs can be created (Aschenbrenner 2020).

Relaxed legislation in several countries to meet the unprecedented demand of ABHRs has also fuelled the potential risk of ‘methylated spirits’ substitution for ethanol or isopropyl alcohol (Dear et al. 2020). Methanol in formulations when inhaled or even exposed to human skin gets into the blood through dermal absorption if used very frequently (Mojica et al. 2020). Ingestion or transdermal absorption of ABHRs with undisclosed methanol content has been reported to cause acute bilateral loss of vision (Kochgaway et al. 2020) or even death (Overbeek et al. 2021; Yip et al. 2020). CDC released an advisory on a specific methanol-based hand sanitizer manufactured in Mexico, due to the potential presence of methanol (CDC 2020). A dramatic increase in methanol poisoning-related morbidity and mortality from consumption of sanitizers, alcohol on belief to prevent COVID-19 infection has been reported in Iran during the early phase of the pandemic (Sefidbakht et al. 2020; Shokoohi et al. 2020).

5.3. Health hazards due to accompanying ingredients

The various combinations of ingredients present in ethanol, isopropyl alcohol-based hand-sanitizer formulations may be toxic to human health when misused. A recent review suggests significant skin damage on repeated exposure to isopropanol-based formulations, possibly due to the synergistic effect of combined irritants such as sodium lauryl sulfate (Tasar et al. 2021). Intake of the chemical in a lower concentration of hydrogen peroxide (3% solution) leads to minor gastrointestinal tract irritation (Alhasson et al. 2020). Active ingredients in disinfectant products such as hydrogen peroxide, sodium hypochlorite peroxyacetic acid, alcohols can cause skin irritation in prolonged usage (Choon Fu Goh et al. 2020). Sanitizer formulation containing tetrahydroxypropyl ethylenediamine has been known to be connected with occupational allergic contact dermatitis (Antelmi et al. 2020). A study in the early phase of Covid-19

reveals episodic experiences one or other form of side effects on frequent hand washing and sanitization such as skin dryness, obsession, skin itching, coughing, and eye irritation (Dindarloo et al. 2020).

5.4. Adverse effects on long-term use

Healthcare workers require frequent handwashing to maintain HHC during the pandemic. However, evidence now suggests that such practices are damaging their skin integrity. The majority of health workers frequently report symptoms of irritant contact dermatitis (ICD) during this pandemic (Kiely et al. 2021), though the same observation has been reported from decade long survey in tertiary care institutions (Quenan and Piletta 2020). The problem of hand-skin dryness has a statistically significant association with the use of alcohol-based hand sanitizers (Altunisik Toplu et al. 2020). Though most common in health workers, none the less increasing proportion of school children are also now facing the same ICD due to increased frequency of hand washing (Borch et al. 2020). American contact dermatitis Society expects an increase in hand dermatitis due to repeated use of detergents or ABHSs containing preservatives, surfactants, and antimicrobial agents (Rundle et al. 2020). Moisturizer blended ABHSs is recommended to minimize sensitizing and irritancy potential.

Though ABHSs is recommended for lipolysis-based germicidal action of alcohol, they have a minimal effect on non-enveloped viruses, such as noroviruses (Sato et al. 2020). A recent study reported less than one log10 reduction in human norovirus genome equivalent copies when treated with 60% ethanol, regardless of contact time (30 or 60s) (Escudero-Abarca et al. 2020). When the “alcohol-based and other hand sanitizers effectiveness against norovirus are contentious” the possibility of a new norovirus epidemic may pop up, though CDC observes no definitive proof by all stretch and “use” could be more reasonable to avoid infections (Vogel 2011). Although antimicrobial resistance (AMR) is already a challenge in clinical practice, the discussion has resurfaced in the face of the pandemic (Metsemakers et al. 2021) may boost up the antimicrobial resistance in humans (Rezasoltani et al. 2020). The continual usage of hand sanitizers will increase biocides or antimicrobials load in receiving water bodies leading to the selection of AMR bacteria (Murray 2020). The recent report on the development of alcohol resistance *Enterococcus faecium* and vancomycin-resistant strains can be collateral damage to microbiomes “wiping” several commensals in various niches and possibly creating “mines” for newer threats (A. Singh 2020).

6. Environments Hazards Of Hand Sanitization Products

Very few articles published during this pandemic have actually implicated environmental hazards associated with sand sanitizer. However, ABHSs with high alcohol content certainly possess a flammability risk (Atolani et al. 2020), and must be viewed as a safety concern in a fire-related work environment. Disinfectants, hand sanitizer preparations including the so-called green variants may contain a number of hazardous fragrances or may emit potentially hazardous volatile chemicals not disclosed on the product label or safety data sheet (Steinemann et al. 2021). Large-scale use of disinfectants, surfactants without proper disposal protocol is likely to cause environmental pollution, and

impacts at a different hierarchy of ecosystems (Saadat et al. 2020). The presence of ethanol, isopropyl alcohol, and hydrogen peroxide in sanitizer formulation may cause depletion of oxygen in water bodies (Mahmood et al. 2020) impacting microbial dynamics and other invertebrates. Though not directly linked with sanitizer formulation itself, management of plastic hand sanitizer bottles as medical waste can be a challenge in urban coastal areas or commercial hubs (Hellewell et al. 2020).

7. Conclusions

The use of hand sanitizer, ABHSs in particular, remains a front-line defence against the spread of Covid-19. From the systematic review on “hand sanitizer” during the ongoing pandemic, the following conclusions can be made.

- A significant number of publications on ABHSs are review, editorial, commentary in nature
- Variation in ethanol content in ABHSs related formulation is evident, only a few studies relate their efficacy on SARS-Cov-2. The efficacy of semi-alcoholic, ayurvedic formulations are either inexistent or poorly described.
- Most reports of accidental ethanol exposure from ABHSs are in children, without serious consequences. Few scattered reports are there on intentional ingestion, methanol poisoning from counterfeit sanitizers, and death. Short-term over sanitization-related skin dermatitis in children and healthcare workers have been reported.

Though the ABHSs misuse could have been resolved through a better awareness program, campaign, and close monitoring, the flourishing market of fake/spurious products needs to be curbed by enforcement authorities.

Declarations

Acknowledgments

This work is supported by Karunya Institute of Technology and Sciences. Standard ethical and professional conduct have been followed. There are no conflicts of interest (financial or otherwise) associated with this publication.

Conflict of interest: None

Financial support: None

Credit Author statement

BM conceived the project work and drafted the outline of the manuscript. ES, AB, SA performed a literature review on different aspects of the review. BM revised the manuscript, added necessary components, breadth, and depth of analysis. ES in consultation with BM prepared the artwork for

manuscript submission. All the authors cross-checked the content, updated and edited the manuscript. All the author agrees for the submission.

References

Ahmed, A. H. M., & Goh, C. F. (2020). How to make hand sanitiser/hand rub. *Community Eye Health*, *33*(109), 24–25.

Alhasson, H., Salama, A., & Alweis, R. (2020). The Dangers of Ingesting Antiseptics: Hydrogen Peroxide-Induced Chemical Colitis. *The American Journal of Medicine*. https://doi.org/10.1016/j.amjmed.2020.06.027

Altunisik Toplu, S., Altunisik, N., Turkmen, D., & Ersoy, Y. (2020). Relationship between hand hygiene and cutaneous findings during COVID-19 pandemic. *Journal of Cosmetic Dermatology*, *19*(10), 2468–2473. https://doi.org/10.1111/jocd.13656

Anitha, G., Khairnar, M. R., Dalvi, T. M., Kalghatgi, S., Datar, U. V, Wadgave, U., et al. (2020). Comparative Efficacy of Hand Disinfection Potential of Hand Sanitizer and Liquid Soap among Dental Students: A Randomized Controlled Trial. *Indian Journal of Critical Care Medicine*, *24*(5), 336–339. https://doi.org/10.5005/jp-journals-10071-23420

Antelmi, A., Hopkins, K., Svedman, C., & Dahlin, J. (2020). Occupational allergic contact dermatitis to tetrahydroxypropyl ethylenediamine in hand sanitizers. *Contact Dermatitis*, *83*(3), 220–221. https://doi.org/10.1111/cod.13552

Aschenbrenner, D. S. (2020). Is that Hand Sanitizer Safe? *AJN, American Journal of Nursing*, *120*(10), 23–23. https://doi.org/10.1097/01.NAJ.0000718612.75996.e3

Atolani, O., Baker, M. T., Adeyemi, O. S., Olanrewaju, I. R., Hamid, A. A., Ameen, O. M., et al. (2020). Covid-19: Critical discussion on the applications and implications of chemicals in sanitizers and disinfectants. *EXCLI Journal*, *19*, 785–799. https://doi.org/10.17179/excli2020-1386

Azim, A. A. S., Rajput, D., Ashiya A S Azim, & Dhirajsingh Rajput. (2020). Drugs For Ayurvedic Hand Sanitizer And Nasal Spray And Its Method Of Preparation. *International Journal of Research in Pharmaceutical Sciences*, *11*(SPL1), 310–316. https://doi.org/10.26452/ijrps.v11iSPL1.2718

Babić, Ž., Turk, R., & Macan, J. (2020). Toxicological aspects of increased use of surface and hand disinfectants in Croatia during the COVID-19 pandemic: a preliminary report. *Archives of Industrial Hygiene and Toxicology*, *71*(3), 261–264. https://doi.org/10.2478/aiht-2020-71-3470

Bahlol, M., & Dewey, R. S. (2021). Pandemic preparedness of community pharmacies for COVID-19. *Research in Social and Administrative Pharmacy*, *17*(1), 1888–1896. https://doi.org/10.1016/j.sapharm.2020.05.009

Balkrishna, A., Singh, K., Singh, H., Haldar, S., & Varshney, A. (2020). GermiX: A skin friendly hand sanitizer with prolonged effectivity against pathogenic bacteria. *AMB Express*, *10*(1), 210. https://doi.org/10.1186/s13568-020-01151-y

Berardi, A., Cenci-Goga, B., Grispoldi, L., Cossignani, L., & Perinelli, D. R. (2020). Analysis of Commercial Hand Sanitisers amid CoViD-19: Are We Getting the Products that We Need? *AAPS PharmSciTech*, *21*(7), 286. https://doi.org/10.1208/s12249-020-01818-6

Berardi, A., Perinelli, D. R., Merchant, H. A., Bisharat, L., Basheti, I. A., Bonacucina, G., et al. (2020). Hand sanitisers amid CoViD-19: A critical review of alcohol-based products on the market and formulation approaches to respond to increasing demand. *International Journal of Pharmaceutics*, *584*, 119431. https://doi.org/10.1016/j.ijpharm.2020.119431

Berkkan, A., & Ulutas, O. K. (2020). Evaluation of Alcohol Content of Cologne Products in the Turkish Market Amid the COVID-19 Pandemic. *Gazi Medical Journal*, *31*(3A), 513–517. https://doi.org/10.12996/gmj.2020.121

Bhattacharya, S., Mahbub Hossain, M., & Singh, A. (2020). Addressing the shortage of personal protective equipment during the COVID-19 pandemic in India-A public health perspective. *AIMS Public Health*, *7*(2), 223–227. https://doi.org/10.3934/publichealth.2020019

Bondurant, S., McKinney, T., Bondurant, L., & Fitzpatrick, L. (2020). Evaluation of a benzalkonium chloride hand sanitizer in reducing transient Staphylococcus aureus bacterial skin contamination in health care workers. *American Journal of Infection Control*, *48*(5), 522–526. https://doi.org/10.1016/j.ajic.2019.08.030

Borch, L., Thorsteinsson, K., Warner, T. C., Mikkelsen, C. S., Bjerring, P., Lundbye-Christensen, S., et al. (2020). COVID-19 reopening causes high risk of irritant contact dermatitis in children. *Danish Medical Journal*, *67*(9), A05200357.

Brewer, C., & Streel, E. (2020). Is Alcohol in Hand Sanitizers Absorbed Through the Skin or Lungs? Implications for Disulfiram Treatment. *Alcohol and Alcoholism*, *55*(4), 354–356. https://doi.org/10.1093/alcalc/agaa045

Bussey, R. (2020). Taking the first steps in hand sanitiser production. *Cleanroom Technology*, *28*(10), 39–41.

CDC. (2020). *HAN: Serious Adverse Health Events Associated with Methanol-based Hand Sanitizers*. *CDC Health Alert Network*.

Centers for Disease Control. (2020). CDC Hand Hygiene Guidelines for COVID-19.

Centers for Disease Control and Prevention (CDC). Guidance for Healthcare Providers about Hand Hygiene and COVID-19 (2020).

Chen, G., & Haber, P. S. (2021). Gastrointestinal Disorders Related to Alcohol and Other Drug Use. In *Textbook of Addiction Treatment* (pp. 1077–1097). Cham: Springer International Publishing. https://doi.org/10.1007/978-3-030-36391-8_76

Chiu, N.-C., Chi, H., Tai, Y.-L., Peng, C.-C., Tseng, C.-Y., Chen, C.-C., et al. (2020). Impact of Wearing Masks, Hand Hygiene, and Social Distancing on Influenza, Enterovirus, and All-Cause Pneumonia During the Coronavirus Pandemic: Retrospective National Epidemiological Surveillance Study. *Journal of Medical Internet Research*, *22*(8), e21257. https://doi.org/10.2196/21257

Chung, H., Kim, E. O., Kim, S.-H., & Jung, J. (2020). Risk of COVID-19 Transmission from Infected Outpatients to Healthcare Workers in an Outpatient Clinic. *Journal of Korean Medical Science*, *35*(50). https://doi.org/10.3346/jkms.2020.35.e431

Ciotti, C., Ferrao, B., Garrigues, I., & Nérome, S. (2021). Bacteria which are highly resistant to antibiotics are not resistant hydro-alcoholic products. *Infectious Diseases Now*, *51*(1), 77–80. https://doi.org/10.1016/j.medmal.2020.10.002

Clemens, K. S., Matkovic, J., Faasse, K., & Geers, A. L. (2020). Determinants of safety-focused product purchasing in the United States at the beginning of the global COVID-19 pandemic. *Safety Science*, *130*, 104894. https://doi.org/10.1016/j.ssci.2020.104894

Daverey, A., & Dutta, K. (2021). COVID-19: Eco-friendly hand hygiene for human and environmental safety. *Journal of Environmental Chemical Engineering*, *9*(2), 104754. https://doi.org/10.1016/j.jece.2020.104754

De Sousa, A. (2020). Disulfiram Ethanol Reaction in a Patient Abstinent from Alcohol Caused by Hand Sanitizing. *Alcohol and Alcoholism*, *55*(4), 349–349. https://doi.org/10.1093/alcalc/agaa038

Dear, K., Grayson, L., & Nixon, R. (2020). Potential methanol toxicity and the importance of using a standardised alcohol-based hand rub formulation in the era of COVID-19. *Antimicrobial Resistance & Infection Control*, *9*(1), 129. https://doi.org/10.1186/s13756-020-00788-5

Dindarloo, K., Aghamolaei, T., Ghanbarnejad, A., Turki, H., Hoseinvandtabar, S., Pasalari, H., & Ghaffari, H. R. (2020). Pattern of disinfectants use and their adverse effects on the consumers after COVID-19 outbreak. *Journal of Environmental Health Science and Engineering*, *18*(2), 1301–1310. https://doi.org/10.1007/s40201-020-00548-y

Environmental Protection Agency (EPA). (2020). Disinfectants for Use Against SARS-CoV-2.

Erikainen, S., & Stewart, E. (2020). Credibility Contests: Media Debates on Do-It-Yourself Coronavirus Responses and the Role of Citizens in Health Crises. *Frontiers in Sociology*, *5*. https://doi.org/10.3389/fsoc.2020.592666

Escudero-Abarca, B. I., Goulter, R. M., Arbogast, J. W., Leslie, R. A., Green, K., & Jaykus, L. -A. (2020). Efficacy of alcohol-based hand sanitizers against human norovirus using RNase-RT-qPCR with validation by human intestinal enteroid replication. *Letters in Applied Microbiology*, *71*(6), 605–610. https://doi.org/10.1111/lam.13393

Fu, L., Le, T., Liu, Z., Wang, L., Guo, H., Yang, J., et al. (2020). Different efficacies of common disinfection methods against candida auris and other candida species. *Journal of Infection and Public Health*, *13*(5), 730–736. https://doi.org/10.1016/j.jiph.2020.01.008

Gammon, J., & Hunt, J. (2019). The neglected element of hand hygiene - significance of hand drying, efficiency of different methods and clinical implication: A review. *Journal of Infection Prevention*, *20*(2), 66–74. https://doi.org/10.1177/1757177418815549

Ghosh, A., Mahintamani, T., Balhara, Y. P. S., Roub, F. E., Basu, D., BN, S., et al. (2021). Disulfiram Ethanol Reaction with Alcohol-Based Hand Sanitizer: An Exploratory Study. *Alcohol and Alcoholism*, *56*(1), 42–46. https://doi.org/10.1093/alcalc/agaa096

Goh, C. F., & Ahmed, A. (2020). How to make hand sanitiser gel. *Community Eye Health*, *33*(109), 26.

Goh, Choon Fu, Ming, L. C., & Wong, L. C. (2020). Dermatologic reactions to disinfectant use during the COVID-19 pandemic. *Clinics in Dermatology*. https://doi.org/10.1016/j.clindermatol.2020.09.005

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. https://doi.org/10.1016/j.ajic.2020.06.182

Güntner, A. T., Magro, L., van den Broek, J., & Pratsinis, S. E. (2021). Detecting methanol in hand sanitizers. *iScience*, *24*(2), 102050. https://doi.org/10.1016/j.isci.2021.102050

Hakimi, A. A., & Armstrong, W. B. (2020). Hand Sanitizer in a Pandemic: Wrong Formulations in the Wrong Hands. *The Journal of Emergency Medicine*, *59*(5), 668–672. https://doi.org/10.1016/j.jemermed.2020.07.018

Hanna, S., Zwi, K., & Tzioumi, D. (2020). Morbidity in the COVID-19 era: Ethanol intoxication secondary to hand sanitiser ingestion. *Journal of Paediatrics and Child Health*, jpc.15017. https://doi.org/10.1111/jpc.15017

Hellewell, J., Abbott, S., Gimma, A., Bosse, N. I., Jarvis, C. I., Russell, T. W., et al. (2020). Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. *The Lancet Global Health*, *8*(4), e488–e496. https://doi.org/10.1016/S2214-109X(20)30074-7

Hui, D. S., I Azhar, E., Madani, T. A., Ntoumi, F., Kock, R., Dar, O., et al. (2020). The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health — The latest 2019 novel coronavirus outbreak in

Wuhan, China. *International Journal of Infectious Diseases*, *91*, 264–266. https://doi.org/10.1016/j.ijid.2020.01.009

Ijaz, M. K., Whitehead, K., Srinivasan, V., McKinney, J., Rubino, J. R., Ripley, M., et al. (2020). Microbicidal actives with virucidal efficacy against SARS-CoV-2. *American Journal of Infection Control*, *48*(8), 972–973. https://doi.org/10.1016/j.ajic.2020.05.015

Inder, D., & Kumar, P. (2020). Isopropyl Alcohol (70%)-Based Hand Sanitizer-Induced Contact Dermatitis: A Case Report Amid Covid-19. *Indian Journal of Case Reports*, *6*(7), 403–405. https://doi.org/10.32677/IJCR.2020.v06.i07.017

Jahromi, R., Mogharab, V., Jahromi, H., & Avazpour, A. (2020). Synergistic effects of anionic surfactants on coronavirus (SARS-CoV-2) virucidal efficiency of sanitizing fluids to fight COVID-19. *Food and Chemical Toxicology*, *145*, 111702. https://doi.org/10.1016/j.fct.2020.111702

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. https://doi.org/10.1016/j.sapharm.2020.04.014

Jairoun, A. A., Al-Hemyari, S. S., Shahwan, M., El-Dahiyat, F., & Jamshed, S. (2020). Scale validation for the identification of falsified hand sanitizer: public and regulatory authorities perspectives from United Arab Emirates. *BMC Public Health*, *20*(1), 1595. https://doi.org/10.1186/s12889-020-09707-0

Jindal, H., Chandramathi, S., Sekaran, S., & Suresh, K. (2020). Evaluation of bactericidal and virucidal activity of novel disinfectant Aaride AGT-1 compared to other commercially available disinfectants against hospital-acquired infections (HAIs). *Tropical Biomedicine*, *37*(3), 626–636. https://doi.org/10.47665/tb.37.3.626

Jing, J. L. J., Pei Yi, T., Bose, R. J. C., 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. https://doi.org/10.3390/ijerph17093326

Jorge, V., Curet, K., Aly, R., Gupta, S. S., Gupta, S. S., & Hares, H. (2020). Safety of Alcohol-Based Hand Sanitizers in Behavioral Health Facilities. *American Journal of Medical Quality*, 106286062095638. https://doi.org/10.1177/1062860620956381

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. https://doi.org/10.1016/j.jhin.2020.01.022

Kantor, J., Philadelphia, M., & Augustine, S. (2020). Behavioral considerations and impact on personal protective equipment use: Early lessons from the coronavirus (COVID-19) pandemic. *Journal of the*

American Academy of Dermatology, *82*(5), 1087–1088. https://doi.org/10.1016/j.jaad.2020.03.013

Keane, M., & Neal, T. (2021). Consumer panic in the COVID-19 pandemic. *Journal of Econometrics*, *220*(1), 86–105. https://doi.org/10.1016/j.jeconom.2020.07.045

Kenters, N., Eikelenboom-Boskamp, A., Hines, J., McGeer, A., Huijskens, E. G. W., & Voss, A. (2020). Product dose considerations for real-world hand sanitiser efficacy. *American Journal of Infection Control*, *48*(5), 503–506. https://doi.org/10.1016/j.ajic.2019.12.001

Kiely, L. F., Moloney, E., O'Sullivan, G., Eustace, J. A., Gallagher, J., & Bourke, J. F. (2021). Irritant contact dermatitis in healthcare workers as a result of the COVID-19 pandemic: a cross-sectional study. *Clinical and Experimental Dermatology*, *46*(1), 142–144. https://doi.org/10.1111/ced.14397

Kochgaway, L., Nair, A., Mitra, A., Bhargava, S., & Singh, M. (2020). COVID casualty: Bilateral blindness due to ingestion of spurious sanitizer. *Oman Journal of Ophthalmology*, *13*(3), 164. https://doi.org/10.4103/ojo.OJO_277_2020

Kratzel, A., Todt, D., V'kovski, P., Steiner, S., Gultom, M., Thao, T. T. N., et al. (2020). Inactivation of Severe Acute Respiratory Syndrome Coronavirus 2 by WHO-Recommended Hand Rub Formulations and Alcohols. *Emerging Infectious Diseases*, *26*(7), 1592–1595. https://doi.org/10.3201/eid2607.200915

Kuehn, B. M. (2020). Hand Sanitizer Poisoning and Deaths Reported in 2 States. *JAMA*, *324*(12), 1130. https://doi.org/10.1001/jama.2020.16614

Leeper, S. C., Almatari, A. L., Ingram, J. D., & Ferslew, K. E. (2000). Topical absorption of isopropyl alcohol induced cardiac and neurologic- deficits in an adult female-with intact skin. *Veterinary and Human Toxicology*.

Leslie, R. A., Zhou, S. S., & Macinga, D. R. (2020). Inactivation of SARS-CoV-2 by commercially available alcohol-based hand sanitizers. *American Journal of Infection Control*. https://doi.org/10.1016/j.ajic.2020.08.020

Lim, D.-J. (2020). Intoxication by hand sanitizer due to delirium after infectious spondylitis surgery during the COVID-19 pandemic: A case report and literature review. *International Journal of Surgery Case Reports*, *77*, 76–79. https://doi.org/10.1016/j.ijscr.2020.10.086

Lotfinejad, N., Peters, A., & Pittet, D. (2020). Hand hygiene and the novel coronavirus pandemic: the role of healthcare workers. *Journal of Hospital Infection*, *105*(4), 776–777. https://doi.org/10.1016/j.jhin.2020.03.017

Lourith, N., Pungprom, S., & Kanlayavattanakul, M. (2021). Formulation and efficacy evaluation of the safe and efficient moisturizing snow mushroom hand sanitizer. *Journal of Cosmetic Dermatology*, *20*(2), 554–560. https://doi.org/10.1111/jocd.13543

MacGibeny, M. A., & Wassef, C. (2020). Preventing adverse cutaneous reactions from amplified hygiene practices during the COVID-19 pandemic: how dermatologists can help through anticipatory guidance. *Archives of Dermatological Research*. https://doi.org/10.1007/s00403-020-02086-x

Mahmood, A., Eqan, M., Pervez, S., Alghamdi, H. A., Tabinda, A. B., Yasar, A., et al. (2020). COVID-19 and frequent use of hand sanitizers; human health and environmental hazards by exposure pathways. *Science of The Total Environment*, *742*, 140561. https://doi.org/10.1016/j.scitotenv.2020.140561

Manderson, L., & Wahlberg, A. (2020). Chronic Living in a Communicable World. *Medical Anthropology*, *39*(5), 428–439. https://doi.org/10.1080/01459740.2020.1761352

Martin, G. C., Le Roux, G., Guindolet, D., Boulanger, E., Hasle, D., Morin, E., et al. (2021). Pediatric Eye Injuries by Hydroalcoholic Gel in the Context of the Coronavirus Disease 2019 Pandemic. *JAMA Ophthalmology*, *139*(3), 348. https://doi.org/10.1001/jamaophthalmol.2020.6346

McCulley, L., Cheng, C., Mentari, E., Diak, I.-L., & Michele, T. (2021). Alcohol-based hand sanitizer exposures and effects on young children in the U.S. during the COVID-19 pandemic. *Clinical Toxicology*, *59*(4), 355–356. https://doi.org/10.1080/15563650.2020.1811298

Meehan, C. P., & Wightman, R. S. (2020). A Case Report of Isopropanol Ingestion During the SARS-CoV-2 Pandemic. *Journal of Addiction Medicine*, *14*(5), e264–e266. https://doi.org/10.1097/ADM.0000000000000728

Metsemakers, W.-J., Zalavras, C., Schwarz, E. M., Chen, A. F., Trampuz, A., & Moriarty, T. F. (2021). Antimicrobial Resistance, the COVID-19 Pandemic, and Lessons for the Orthopaedic Community. *Journal of Bone and Joint Surgery*, *103*(1), 4–9. https://doi.org/10.2106/JBJS.20.01214

Meyers, C., Kass, R., Goldenberg, D., Milici, J., Alam, S., & Robison, R. (2021). Ethanol and isopropanol inactivation of human coronavirus on hard surfaces. *Journal of Hospital Infection*, *107*, 45–49. https://doi.org/10.1016/j.jhin.2020.09.026

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Medicine*, *6*(7), e1000097. https://doi.org/10.1371/journal.pmed.1000097

Mojica, C. V., Pasol, E. A., Dizon, M. L., Kiat, W. A., Lim, T. R. U., Dominguez, J. C., et al. (2020). Chronic methanol toxicity through topical and inhalational routes presenting as vision loss and restricted diffusion of the optic nerves on MRI: A case report and literature review. *eNeurologicalSci*, *20*, 100258. https://doi.org/10.1016/j.ensci.2020.100258

Mukherjee, S., Vincent, C. K., Jayasekera, H. W., & Yekhe, A. S. (2021). Antiviral efficacy of personal care formulations against Severe Acute Respiratory Syndrome Coronavirus 2. *Infection, Disease & Health*, *26*(1), 63–66. https://doi.org/10.1016/j.idh.2020.09.003

Murray, A. K. (2020). The Novel Coronavirus COVID-19 Outbreak: Global Implications for Antimicrobial Resistance. *Frontiers in Microbiology*, *11*. https://doi.org/10.3389/fmicb.2020.01020

Ogilvie, B. H., Solis-Leal, A., Lopez, J. B., Poole, B. D., Robison, R. A., & Berges, B. K. (2021). Alcohol-free hand sanitizer and other quaternary ammonium disinfectants quickly and effectively inactivate SARS-CoV-2. *Journal of Hospital Infection*, *108*, 142–145. https://doi.org/10.1016/j.jhin.2020.11.023

Opatz, T., Senn-Bilfinger, J., & Richert, C. (2020). Thoughts on What Chemists Can Contribute to Fighting SARS-CoV-2 – A Short Note on Hand Sanitizers, Drug Candidates and Outreach. *Angewandte Chemie International Edition*, *59*(24), 9236–9240. https://doi.org/10.1002/anie.202004721

Osei-Asare, C., Eshun Oppong, E., Apenteng, J. A., Adi-Dako, O., Kumadoh, D., Akosua, A. A., & Ohemeng, K. A. (2020). Managing Vibrio cholerae with a local beverage: preparation of an affordable ethanol based hand sanitizer. *Heliyon*, *6*(1), e03105. https://doi.org/10.1016/j.heliyon.2019.e03105

Overbeek, D. L., Watson, C. J., Castañeda, N. R., & Ganetsky, M. (2021). A Geographically Distinct Case of Fatal Methanol Toxicity from Ingestion of a Contaminated Hand Sanitizer Product During the COVID-19 Pandemic. *Journal of Medical Toxicology*. https://doi.org/10.1007/s13181-021-00824-9

Pargaonkar, A. S., Jibkate, B. R., & Umate, P. (2020). Review on utility of preferred drugs from Dashanga lepa as herbal hand sanitizer intended for pandemic COVID 19. *International Journal of Research in Pharmaceutical Sciences*, *11*(SPL1), 1356–1364. https://doi.org/10.26452/ijrps.v11iSPL1.3640

Pasquini, C., Hespanhol, M. C., Cruz, K. A. M. L., & Pereira, A. F. (2020). Monitoring the quality of ethanol-based hand sanitizers by low-cost near-infrared spectroscopy. *Microchemical Journal*, *159*, 105421. https://doi.org/10.1016/j.microc.2020.105421

Patidar, N. J., Juengling, A., Narayanan, M., & Spencer, J. (2020). COVID -19 pandemic danger: Acute alcohol intoxication in a 5-year-old following ingestion of an ethyl-alcohol-based hand sanitiser. *Journal of Paediatrics and Child Health*, jpc.15144. https://doi.org/10.1111/jpc.15144

Prince-Guerra, J. L., Nace, M. E., Lyles, R. H., Fabiszewski de Aceituno, A. M., Bartz, F. E., Arbogast, J. W., et al. (2020). Both Handwashing and an Alcohol-Based Hand Sanitizer Intervention Reduce Soil and Microbial Contamination on Farmworker Hands during Harvest, but Produce Type Matters. *Applied and Environmental Microbiology*, *86*(18). https://doi.org/10.1128/AEM.00780-20

Quenan, S., & Piletta, P. (2020). Hand dermatitis in healthcare workers: 15-years experience with hand sanitizer solutions. *Contact Dermatitis*, cod.13738. https://doi.org/10.1111/cod.13738

Rebmann, T., Vassallo, A., & Holdsworth, J. E. (2021). Availability of personal protective equipment and infection prevention supplies during the first month of the COVID-19 pandemic: A national study by the APIC COVID-19 task force. *American Journal of Infection Control*, *49*(4), 434–437. https://doi.org/10.1016/j.ajic.2020.08.029

Rezasoltani, S., Yadegar, A., Hatami, B., Asadzadeh Aghdaei, H., & Zali, M. R. (2020). Antimicrobial Resistance as a Hidden Menace Lurking Behind the COVID-19 Outbreak: The Global Impacts of Too Much Hygiene on AMR. *Frontiers in Microbiology*, *11*. https://doi.org/10.3389/fmicb.2020.590683

Richards, G. C. (2020). Alcohol-based hand sanitisers: a warning to mitigate future poisonings and deaths. *BMJ Evidence-Based Medicine*, bmjebm-2020-111568. https://doi.org/10.1136/bmjebm-2020-111568

Roy, A., Parida, S. P., & Bhatia, V. (2020). Role of disinfection and hand hygiene: a COVID-19 perspective. *International Journal Of Community Medicine And Public Health*, *7*(7), 2845. https://doi.org/10.18203/2394-6040.ijcmph20203025

Rundle, C. W., Presley, C. L., Militello, M., Barber, C., Powell, D. L., Jacob, S. E., et al. (2020). Hand hygiene during COVID-19: Recommendations from the American Contact Dermatitis Society. *Journal of the American Academy of Dermatology*, *83*(6), 1730–1737. https://doi.org/10.1016/j.jaad.2020.07.057

Saadat, S., Rawtani, D., & Hussain, C. M. (2020). Environmental perspective of COVID-19. *Science of The Total Environment*, *728*, 138870. https://doi.org/10.1016/j.scitotenv.2020.138870

Samara, F., Badran, R., & Dalibalta, S. (2020). Are Disinfectants for the Prevention and Control of COVID-19 Safe? *Health Security*, *18*(6), 496–498. https://doi.org/10.1089/hs.2020.0104

Sato, S., Matsumoto, N., Hisaie, K., & Uematsu, S. (2020). Alcohol abrogates human norovirus infectivity in a pH-dependent manner. *Scientific Reports*, *10*(1), 15878. https://doi.org/10.1038/s41598-020-72609-z

Sefidbakht, S., Lotfi, M., Jalli, R., Moghadami, M., Sabetian, G., & Iranpour, P. (2020). Methanol toxicity outbreak: when fear of COVID-19 goes viral. *Emergency Medicine Journal*, *37*(7), 416–416. https://doi.org/10.1136/emermed-2020-209886

Selam, M. N. (2020). Hand Sanitizers Marketed in the Streets of Addis Ababa, Ethiopia, in the Era of COVID-19: A Quality Concern. *Risk Management and Healthcare Policy*, *Volume 13*, 2483–2487. https://doi.org/10.2147/RMHP.S284007

Shetty, R., Chaitra, J., Chabra, A., Maheshwari, S., Sharon, D., Khamar, P., et al. (2020). Sanitizer aerosol-driven ocular surface disease (SADOSD)—A COVID-19 repercussion? *Current Ophthalmology*, *68*(6), 981–983.

Shokoohi, M., Nasiri, N., Sharifi, H., Baral, S., & Stranges, S. (2020). A syndemic of COVID-19 and methanol poisoning in Iran: Time for Iran to consider alcohol use as a public health challenge? *Alcohol*, *87*, 25–27. https://doi.org/10.1016/j.alcohol.2020.05.006

Singh, A. (2020). Covid-19: disinfectants and sanitisers are changing microbiomes. *BMJ*, m2795. https://doi.org/10.1136/bmj.m2795

Singh, D., Joshi, K., Samuel, A., Patra, J., & Mahindroo, N. (2020). Alcohol-based hand sanitisers as first line of defence against SARS-CoV-2: a review of biology, chemistry and formulations. *Epidemiology and Infection*, *148*, e229. https://doi.org/10.1017/S0950268820002319

Stadler, R. N., & Tschudin-Sutter, S. (2020). What is new with hand hygiene? *Current Opinion in Infectious Diseases*, *33*(4), 327–332. https://doi.org/10.1097/QCO.0000000000000654

Steinemann, A., Nematollahi, N., Rismanchi, B., Goodman, N., & Kolev, S. D. (2021). Pandemic products and volatile chemical emissions. *Air Quality, Atmosphere & Health*, *14*(1), 47–53. https://doi.org/10.1007/s11869-020-00912-9

Stevens, D. L., & Hix, M. (2020). Intentional ingestion of hand sanitizer in an adult psychiatric unit. *Mental Health Clinician*, *10*(2), 60–63. https://doi.org/10.9740/mhc.2020.03.060

Sunny, C. L. A. (2020). Hand sanitizer associated ocular chemical injury: A mini-review on its rise under COVID-19. *Visual Journal of Emergency Medicine*, *21*, 100881. https://doi.org/10.1016/j.visj.2020.100881

Tan, J. B. X., de Kraker, M. E. A., Pires, D., Soule, H., & Pittet, D. (2020). Handrubbing with sprayed alcohol-based hand rub: an alternative method for effective hand hygiene. *Journal of Hospital Infection*, *104*(4), 430–434. https://doi.org/10.1016/j.jhin.2020.02.008

Tasar, R., Wiegand, C., & Elsner, P. (2021). How irritant are n-propanol and isopropanol? – A systematic review. *Contact Dermatitis*, *84*(1), 1–14. https://doi.org/10.1111/cod.13722

U.S Food and Drug Administration. (2020). Guidance for industry: temporary policy for preparation of certain alcohol-based hand sanitizer products during the public health emergency (COVID-19). https://www.fda.gov/media/136289/download. Accessed 24 January 2021

United Nations Economic Commission for Africa; (2020). *COVID-19 in Africa - Protecting Lives and Economies*. UN. https://doi.org/10.18356/77f486e5-en

Voelker, R. (2020). Deceptive Hand Sanitizer Packaging. *JAMA*, *324*(13), 1277. https://doi.org/10.1001/jama.2020.18727

Vogel, L. (2011). Hand sanitizers may increase norovirus risk. *Canadian Medical Association Journal*, *183*(12), E799–E800. https://doi.org/10.1503/cmaj.109-3922

Welle, L., Medoro, A., & Warrick, B. (2021). Tainted Hand Sanitizer Leads to Outbreak of Methanol Toxicity During SARS-CoV-2 Pandemic. *Annals of Emergency Medicine*, *77*(1), 131–132. https://doi.org/10.1016/j.annemergmed.2020.07.011

Wijayati, N., Widiyastuti, A., Mursiti, S., & Rakainsa, S. K. (2020). Formulation of Hand Sanitizer Gel of A-Pinene Isolated from Turpentine Oil and its Antibacterial Activity. *IOP Conference Series: Materials*

Science and Engineering, *846*, 012069. https://doi.org/10.1088/1757-899X/846/1/012069

Wilson, A. M., Reynolds, K. A., Jaykus, L.-A., Escudero-Abarca, B., & Gerba, C. P. (2020). Comparison of estimated norovirus infection risk reductions for a single fomite contact scenario with residual and nonresidual hand sanitizers. *American Journal of Infection Control*, *48*(5), 538–544. https://doi.org/10.1016/j.ajic.2019.09.010

World health Organization. WHO Guidelines on Hand Hygiene in Health Care (2020).

World health Organization (WHO). (2020a). *Hand Hygiene: Why, How & When? WHO Save Lives: Clean Your Hands*.

World health Organization (WHO). (2020b). *Water, sanitation, hygiene, and waste management for the COVID-19 virus*. https://doi.org/WHO/2019-nCoV/IPC_WASH/2020.4

Yangzes, S., Grewal, S., Gailson, T., & Grewal, S. P. S. (2021). Hand Sanitizer–Induced Ocular Injury. *JAMA Ophthalmology*, *139*(3), 362. https://doi.org/10.1001/jamaophthalmol.2020.6351

Yip, L., Bixler, D., Brooks, D. E., Clarke, K. R., Datta, S. D., Dudley, S., et al. (2020). Serious Adverse Health Events, Including Death, Associated with Ingesting Alcohol-Based Hand Sanitizers Containing Methanol — Arizona and New Mexico, May–June 2020. *MMWR. Morbidity and Mortality Weekly Report*, *69*(32), 1070–1073. https://doi.org/10.15585/mmwr.mm6932e1

Figures

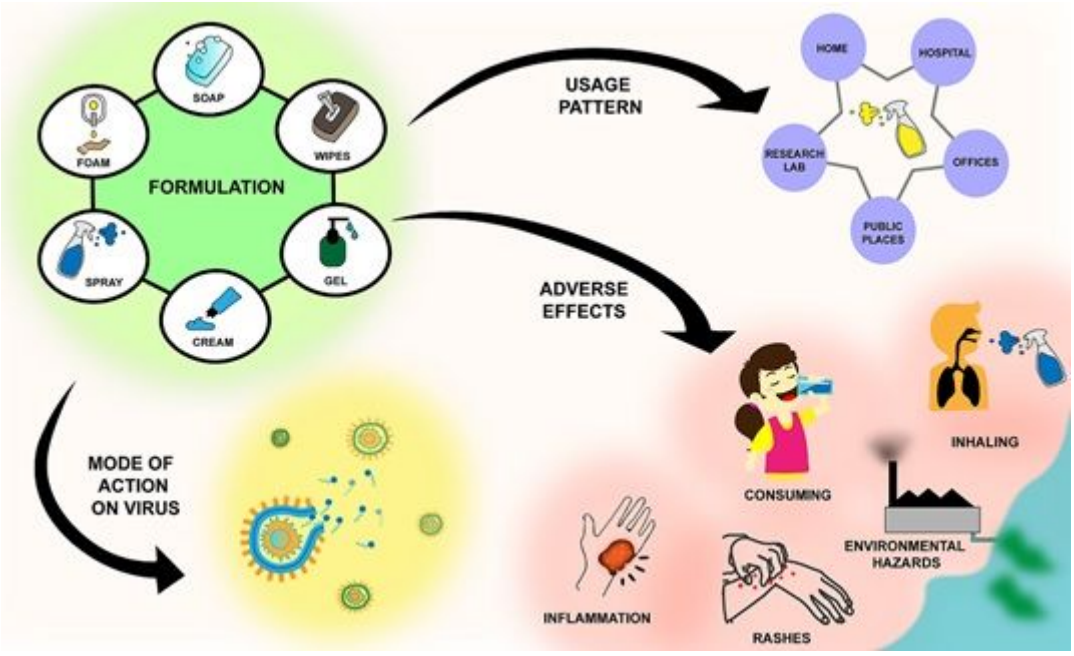

Figure 1

The different dimensions of hand sanitizers unfolding in hand hygiene practices during the Covid-19.

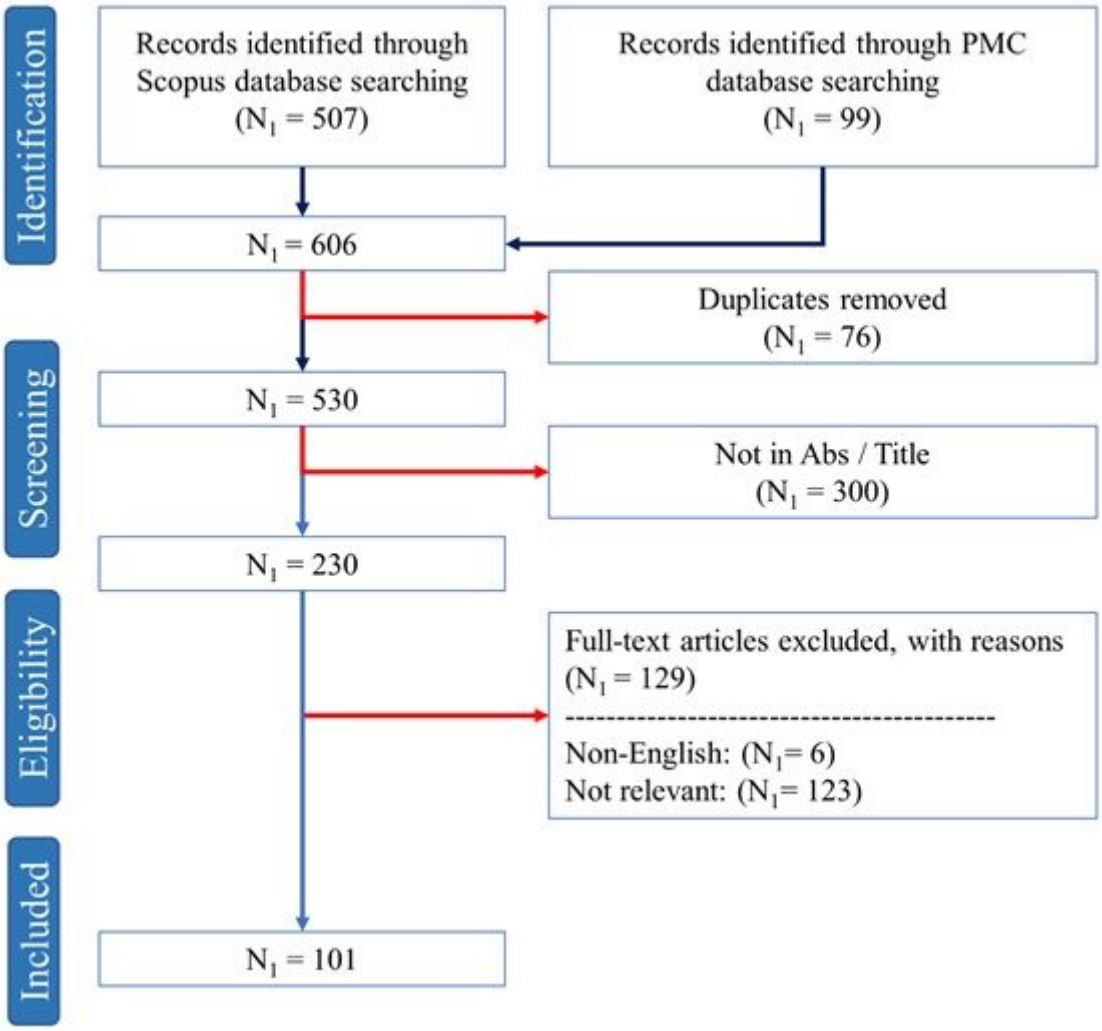

Figure 2

Flow chart diagram showing the selection of relevant studies pertinent to this review.

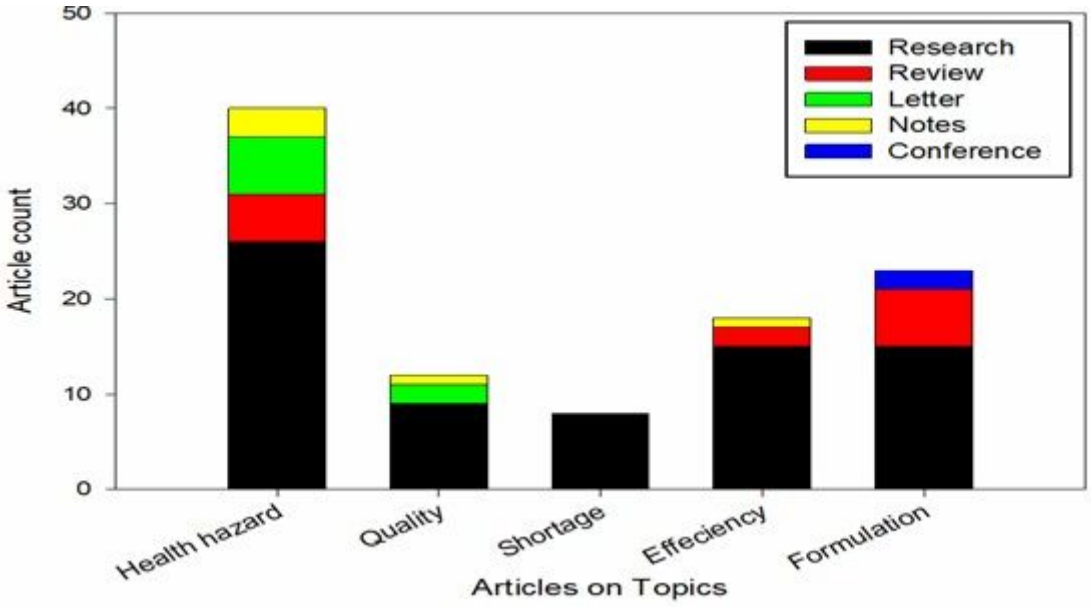

Figure 3

Classification of hand sanitizer related publications, based on article type and thematic area, indexed in Scopus® and PMC databases and published in 2020-2021 (10/02/2021).

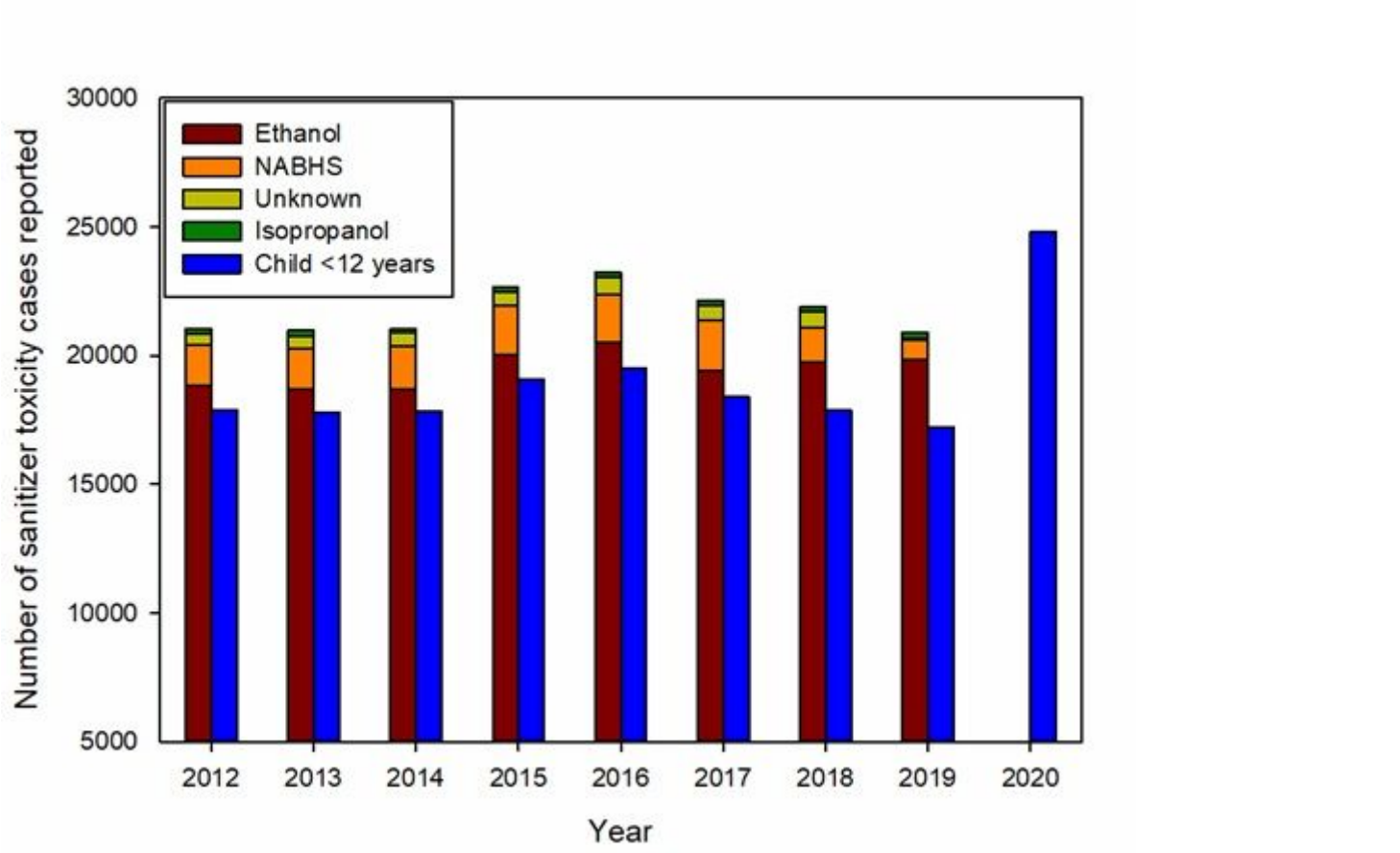

Figure 4

Number of different hand-sanitizer-related toxicity cases (total) reported to AAPCC over the years (left-aligned stacked bar) and the subset with children less than 12 years old (right-aligned bar). The number of total reported cases in 2020 is not available. Retrieved from: https://aapcc.org/track/hand-sanitizer