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## COVID-19 and frequent use of hand sanitizers; human health and environmental hazards by exposure pathways



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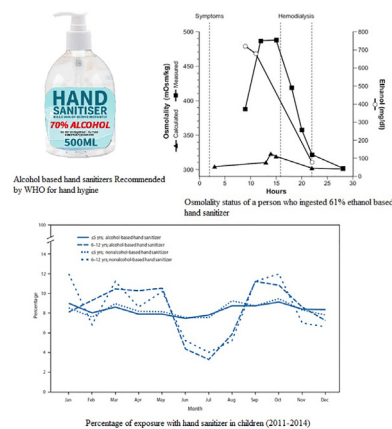
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### HIGHLIGHTS

- Alcohol based hand sanitizers are recommended by WHO as preventive measure of COVID-19.
- Till April 2020, 7593 hand sanitizer exposure cases of children were reported.
- Frequent usage of hand sanitizers results antimicrobial resistance.
- Frequent usage of hand sanitizers enhance the chance of other viral diseases.

### GRAPHICAL ABSTRACT



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### ABSTRACT

Till date no medication or vaccine is available to cope with the COVID-19 infection and infection rate is increasing drastically across the globe. Only preventive measures and healthy life style with efficient immune system have been suggested by WHO to fight and stay safe from COVID-19. WHO recommended alcohol based hand sanitizers for frequent hand hygiene, which are mainly made up from ethanol, isopropyl alcohols, hydrogen peroxides in different combinations. These preparations may become toxic to human health and environment when misused. These chemicals have known toxic and hazardous impact on environment when released by evaporation. In early five months of 2020, American Association of Poison Control Center reported 9504 alcoholic hand sanitizer exposure cases in children under the age of 12 years and recognized that even a small amount of alcohol can cause alcohol poisoning in children that is responsible for confusion, vomiting and drowsiness, and in severe cases, respiratory arrest and death. Furthermore, frequent usage of said hand sanitizers has reported increased chance of antimicrobial resistance and chance of other viral diseases. Current review is designed with main objective to highlight the toxic and serious health risks to human health and environment by frequent using hand hygiene products with alcohols based formulations.

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## 1. Introduction

COVID-19 (Coronavirus disease-2019), the novel and new disease spreads through recent coronavirus 2 (SARS-CoV-2) from Wuhan, China (Huang et al., 2020). This disease is characterized by acute respiratory disorder, pneumonia, dry cough, fever and body pain with high rate of mortality, particularly in older people or those with underlying health conditions (Lai et al., 2020). COVID-19 has been declared as pandemic by World Health Organization (WHO) in March 11, 2020 and till June 25, 2020 confirmed infections are 9,110,186 with 473,061 deaths across 216 countries (WHO, 2020). Humans are main transmission source of SARS-CoV-2 through human to human interactions; in case, any infected person with mild or even no symptoms come in contact with healthy person (Kratzel et al., 2020). So far, no medication or vaccine is available to cope with this novel coronavirus and infection rate is increasing drastically across the globe. In current scenario preventive measures and healthy life style with efficient immune system have been suggested by WHO to fight and stay safe from COVID-19. Adaptation of effective hand hygiene is vital, where one of the best advices by WHO is to wash or sanitize your hands frequently with soap or >60% alcoholic hand sanitizer, respectively. WHO suggested two alcohols based formulations for hands hygiene in healthcare to sensitize the hands and to reduce the spread and infectivity of coronavirus (WHO, 2020). These recommendations are based on fast, effective and broad spectrum antimicrobial activity combined with easy availability and considered safety.

WHO recommended alcohol based hand sanitizers are mainly made up from ethanol, isopropyl alcohols, hydrogen peroxides in different combinations (WHO, 2020). These preparations may become toxic to human health and environment when misused. These chemicals have known toxic and hazardous impact on environment when released by evaporation (Slaughter et al., 2014). It is recognized that ingestion of low concentration of hydrogen peroxide (3% solution) is responsible for minor gastrointestinal tract irritation (Moon et al., 2006) and in few cases it is also responsible for portal vein embolism (Sung et al., 2018) and mild mucosal irritating and vomiting (ATSDR, 2014). Ingestion of isopropyl alcohol accidentally or deliberately leads to severe respiratory or central nervous system depression (Slaughter et al., 2014). Toxicological reviews of methanol published by public health England showed oral and dermal toxicity of methanol with observation not to use in hand hygiene products (Public Health England, 2015). Ethanol toxicity is also associated with respiratory depression which results into respiratory arrest, hypothermia, cardiac dysrhythmias with possible cardiac arrest, hypoglycemia, ketoacidosis and hypotension (Gormley et al., 2012).

Current review was designed with main objective to highlight the toxic and serious health risks to human health and environment by frequent using hand hygiene products with alcohols based formulations. Increased use of hand rubs as preventive measures of COVID-19 are not environmental friendly and hazardous for human health. It is advised to wash hands with antimicrobial soap after frequent intervals to get rid of possible infection by this pandemic.

## 2. Composition of commercial hand sanitizers

The active reagents of alcohol based hand sanitizers are ethanol or isopropyl alcohol at 60–95% concentration (Barrett and Babl, 2015). Langer et al. (2004) reported alcohol based solutions with ethanol, 2-propanol and distilled water (Softasept®) and disinfectant with octenidine dihydrochloride and phenoxyethanol as the vital reagents (Octenisept®). They also considered Lavasept® with hexamethylenbiguanide (Langer et al., 2004). The most popular hand sanitizers such as Dettol® contains Alcohol Denat and Purell® includes ethyl alcohol 70% v/v, isopropyl alcohol and aminomethyl propanol.

Coronavirus pandemic has brought a shortage of hand sanitizers all around the world (Suthivarakom, 2020). World Health Organization

(WHO) has directed the local manufacturers regarding the preparation of hand sanitizers. WHO suggested two formulations for lesser volume production; one with ethanol (96%) and the other with isopropyl alcohol (99.8%). Final product concentration suggested by WHO for household or local production is ethanol (80%) v/v, hydrogen peroxide (0.125%) v/v and glycerol (1.45%) v/v for formulation A and isopropyl alcohol (75%) v/v, hydrogen peroxide (0.125%) v/v and glycerol (1.45%) v/v for formulation B (SI Tables 1–2).

## 3. Hazardous impact of hand sanitizers on human health

Hand sanitizer results toxicity that leads to fatal, attributed by accidental ingestion (Santos et al., 2017) absorption through dermal contact (Leeper et al., 2000) and suicidal ingestion (Zaman et al., 2002).

### 3.1. Ethanol toxicity

Ethanol has its widespread use as disinfectant along with oral consumption as alcoholic beverages. Its potential to cause skin cancer through skin absorption and carcinogenicity is still unclear due to lack of up to date research (Lachenmeier, 2008). Ingestion or dermal contact with ethanol based hand sanitizer is associated to minimal systematic toxicity (Ellis-Caleo and Burstein, 2017). Different people exhibit different reaction and tolerance level to ethanol that resulted difficulties to determine the degree of toxic dose of ethanol based hand rub. According to Kirschner et al. (2007), the dermal uptake of ethanol with detection limit of 0.5 mg/l were considered insignificant as the serum ethanol concentration was in the range of 1.0–1.5 mg/l after applying 74.1% ethanol-based disinfectant for 10 min. In a study conducted by Kramer et al. (2007), 12 volunteers were given hand sanitizers containing 95% (w/w), 85% (w/w) or 55% (w/w) ethanol. 4 ml was applied for 30 s over 20 min with a minute break in between. 20.95 mg/l, 11.45 mg/l and 6.9 mg/l, respectively were found to be the maximum average absorptions. The amount of absorbed ethanol was 1365 mg (2.3%), 630 mg (1.1%), and 358 mg (0.9%), correspondingly. Furthermore, blood acetaldehyde was observed, its peak median was found to be 0.57 mg/l. This study supported the fact that acute exposure is not toxic, however an impaired performance is expected if blood ethanol concentrations reach 200–300 mg/l and above (Gerchow, 2005). According to Lachenmeier (2008), the concentrations of above-mentioned hand rubs studied by Kirschner et al. (2007) and Kramer et al. (2007) depicted that achieved values are far less than the values acquired for acute toxicity, however chronic toxicity must be accounted for the continuous application of sanitizers in the safety evaluation.

Jones and Rajs (1997) reported a human case with a 33% damaged skin had absorption of 70% (v/v) ethanol through skin. A blood-ethanol concentration was found to be 0.046 g/100 ml which corresponds to 30 ml absorption of surgical spirit. In addition to this, exposure of ethanol to immature skin can lead to reactions and systematic toxicity (Mancini, 2004). Giménez et al. (1968) studied ethanol intoxication due to percutaneous absorption in 28 children all under 33 months of age. This type of fatal intoxication was also defined by Niggemeyer and Zoepffel (1964). Skin necrosis and risen blood alcohol level have been noticed in pre-term infants, whose skins are ineffective for toxic compounds such as alcohol (Harpin and Rutter, 1982; Al-Jawad, 1983). Ethanol is not recommended to use on damaged skin and not even in cosmetics (Lachenmeier, 2008).

Dermal contact of ethanol cause irritation and allergic condition of skin and eyes while prolonged exposure results dryness or cracking of skin with peeling redness or itching (NJH, 2016b). A German study reported that regular use of ethanol is responsible for skin irritation or contact dermatitis (Lachenmeier, 2008). A recent study published in 2018 reported that consistent use of ethanol based hand sanitizer influence the concentration of urinary ethyl glucuronide whereas its production level was observed higher than in normal conditions (without use of ethanol hand rub) and lead to positive analytical results (Salomone

et al., 2018). On the other hand, despite of various published studies indicating health threats by ethanol based hand sanitizer, [Kramer et al., 2007](#) reported that ethanol-based hand-rubs is safe to use. This study was conducted to evaluate ethanol dermal absorption during hygienic and surgical hand disinfection, and to quantify absorption levels in humans. Results above stated publication indicated that dermal absorption was below the toxic level in humans and can be considered safe.

Acute alcohol toxicity may occur via oral consumption of any household product such as alcohol based hand sanitizers (ABHS), mouthwash, cosmetics etc. that contain alcohol ([Vonghia et al., 2008](#)). The clinical symptoms express themselves at a particular blood alcohol concentration as shown in [Table 1](#). A 360 ml of ethanol based hand sanitizer may cause life-threatening conditions in an adult. Lethal dose of ethanol is >400 ml/dl while in an unhabituated individual exposure of 400 ml (80% ethanol based solution) may be lethal ([Archer et al., 2007](#); [Sanap and Chapman, 2003](#)). Absorption occurs mainly in proximal intestinal track, followed by stomach (70%) and duodenum (25%) while small percentage remains in small intestine. About 90% of ingested ethanol metabolized in acetaldehyde and further metabolize into acetyl CO-A ([Ellis-Caleo and Burstein, 2017](#)). Symptoms of ingested ethanol based hand sanitizer appear within 1 to 2 h. [Fig. 1](#) exhibited that symptoms started to appear in one hour after ingestion by an hospitalized patient, where hemodialysis was started after (16–22 h) the peak osmolality was measured. Common symptoms that appear after ingestion are; nausea, vomiting, epigastria pain, and varying degrees of central nervous system depression ([Archer et al., 2007](#)). Ethanol toxicity is also associated with respiratory depression which results into respiratory arrest hypothermia, cardiac dysrhythmias with possible cardiac arrest, hypoglycemia, ketoacidosis and hypotension ([Gormley et al., 2012](#)). A 300 mg/dl ethanol level in serum may lead towards increased risk of respiratory depression and arrest while a  $\geq 500$  mg/dl level might be responsible for cardiac arrest and death ([Vonghia et al., 2008](#)). Ethanol exposure can be associated with acute liver damage, myoglobinuria, hypokalemia, hypomagnesemia, hypocalcemia, hypophosphatemia ([Wilson et al., 2015](#)) and water diuresis ([Bouthoorn et al., 2011](#)).

Concluding the debate, frequent and prolonged use of ethanol based hand sanitizer may lead towards the health hazards. Dermal absorption can lead to the toxic level if someone use ethanol based hand rub for months and several times a day, as currently happening as a result of COVID-19 prevention measure. Negligence or mishandling by ingestion of such product can cause serious health issues as reflected by various reports ([Bouthoorn et al., 2011](#); [Gormley et al., 2012](#); [Salomone et al., 2018](#)).

### 3.2. Isopropyl alcohol toxicity

Isopropyl based sanitizer intoxication is somehow in line of ethanol toxicity but is more intense compared to ethanol due to its higher molecular weight ([Wilson et al., 2015](#)). Toxicity of isopropyl alcohol occurs mainly due to accidental ingestion of the compound and sometime due to rectal or topical applications. 160–240 ml ([Ashkar and miller, 1971](#)) and 250 ml ([McBay, 1973](#)) considered to be the lethal dose of isopropyl alcohol. There are several studies reported that lead topical application of isopropyl alcohol to unconsciousness ([McFadden and Haddow, 1969](#); [Moss, 1970](#); [Wise, 1969](#); [Vermeulen, 1966](#)). According to Material Safety Data Sheet by Halloo Enterprises, acute toxicity in humans occurs at LD50 > 2000 mg/kg (orally), through dermal exposure acute toxicity will occur at LD50 > 2000 mg/kg and via inhalation it will be LC50 > 5 mg/l. Concentrations of 1 g/l of blood or more have been found in fatal poisonings ([Adelson, 1962](#)). The fatal dose is about 250 ml ([McBay, 1973](#)).

Exposure of minimum dose has not proved any serious health issue while consumption of 20–30 ml (50% isopropanol solution) showed minor signs and symptoms ([Fuller and Hunter, 1927](#)). Results of a case series showed that ingestion of 1 ounce (oz) of isopropanol solution results serious clinical effects in children under age of six years ([Stremski and Hennes, 2000](#)). Approximately 0.5–1 ml/kg of 70% isopropyl alcohol-based sanitizer is considered toxic dose but it may differ from person to person depending on individual tolerance level ([Matteucci, 2011](#)). Possible lethal dose of isopropanol for adults is 240 ml approximately ([Gosselin et al., 1984](#)). If orally ingested, isopropyl alcohol absorbs completely within 2 h, where liver metabolize isopropyl alcohol into acetone and kidney excrete this acetone ([Zaman et al., 2002](#)).

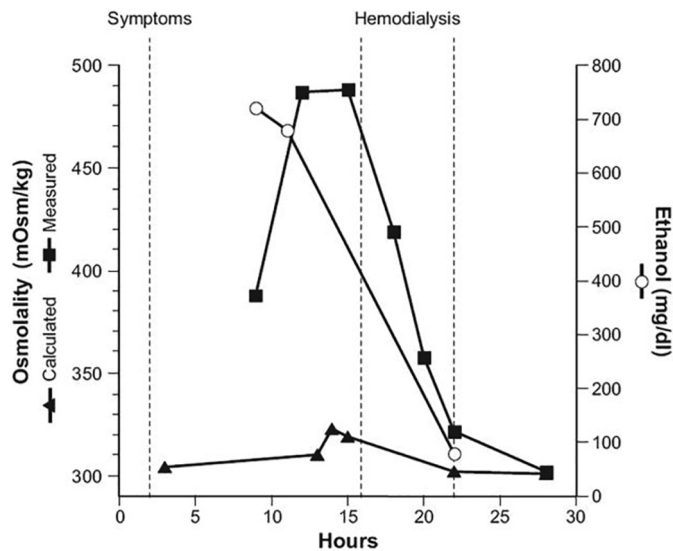
Isopropyl alcohol- a CNS depressant, metabolized into acetone which may result into prolonged CNS depression, decrease respiratory drive and hypotension ([Trummel et al., 1996](#); [Matteucci, 2011](#)). Isopropyl alcohol also irritates mucosal lining in gastrointestinal tract ([Slaughter et al., 2014](#)) and contributes to gastritis ([Matteucci, 2011](#)), associated to cause ketosis ([Trummel et al., 1996](#)), hypoglycemia, respiratory depression, and increase in the serum creatinine ([Zaman et al., 2002](#)). Higher dose may cause myocardial depression while its prolonged use contributes to rhabdomyolysis, myoglobinuria, and acute renal failure. Death has been linked with ingestion of 100–200 ml of 70% isopropyl solution and with  $\geq 400$  mg/dl with plasma concentration level ([Zaman et al., 2002](#)). A case was reported in 2007 that a 43 years old person get hypotensive and delirious due to isopropyl

**Table 1**

Acute and chronic toxicity by active ingredients of hand sanitizers.

Active ingredients	Acute toxicity	Chronic toxicity	Source
Ethanol	Central nervous system and respiratory depression, Lactic acidosis, Ketoacidosis, Nausea	Cardiac arrhythmia, Acute liver injury, Myoglobinuria, Hypokalemia, Hypomagnesemia, Hypocalcemia, Hypophosphatemia, Cardiac arrest and death	<a href="#">Wilson et al., 2015</a> <a href="#">Vonghia et al., 2008</a>
Isopropanol	Similar to ethanol including central nervous system and respiratory depression, skin and mucous membrane irritation	Death, Ketosis, Osmolal gap ketonemia, Rhabdomyolysis, Myoglobinuria, Acute renal failure	<a href="#">Zaman et al., 2002</a> <a href="#">New Jersey Department of Health (NJH), 2016a</a>
3% H <sub>2</sub> O <sub>2</sub>	Mild gastrointestinal and mucosal irritation, vomiting, skin irritation.	Air embolism Death in rare cases	<a href="#">Moon et al., 2006</a> . ATSDR, 2014 <a href="#">New Jersey Department of Health (NJH), 2016c</a> <a href="#">Sung et al., 2018</a>





**Fig. 1.** Osmolality status of a person who ingested 61% ethanol based hand sanitizer. Reprinted from The rising incidence of intentional ingestion of ethanol-containing hand sanitizers by Gormley et al., 2012. Retrieved from DOI: <https://doi.org/10.1097/CCM.0b013e31822f09c0>. Copyright © 2012 by the Society of Critical Care Medicine and Lippincott Williams & Wilkins.

alcohol consumption (Emadi and Coberly, 2007). Dermal absorption of isopropanol can cause irritation of skin and ice, prolonged and frequent exposure results in skin rash, itching, redness and dryness (New Jersey Department of Health (NJH), 2016a).

### 3.3. Hydrogen peroxide toxicity

Toxicity of hydrogen peroxide is dependent on its concentration with ingestion as common route of exposure (Food and drug administration (FDA), 2003). It has been recognized that ingestion of low concentration of hydrogen peroxide (3% solution) is not acute hazardous for human health, and is responsible for minor health problems (Moon et al., 2006). In few cases it causes portal vein embolism, gastrointestinal issues, mild mucosal irritation and vomiting (ATSDR, 2014; Sung et al., 2018.) Bowel dilation has also been reported to be associated with exposure to 3% hydrogen peroxide (Watt et al., 2004; Moon et al., 2006).

Hydrogen peroxide causes toxicity by gas formation and local tissue injury, where it interacts with tissue catalase and decomposes into oxygen and water. Amount of released oxygen is associated with concentration of hydrogen peroxide. 1 ml of 3% hydrogen peroxide is responsible to produce 10 ml of oxygen at standard temperature and pressure which is responsible for gastric distension and gas emboli. When higher amount of oxygen produced within the small lumen for instance

stomach, bubbles can be forced through epithelial interstices. Due to presence of abundant tissue catalase and  $H_2O_2$  access to vascular system, gas emboli may occur easily in multiple organs (Moon et al., 2006).

A study reported 670 cases of 3%  $H_2O_2$  exposure, revealed that 77% were ingestion cases and about half of 77% were children under age of 6 years. All these exposures cases did not exhibited gas emboli and revealed only mild symptoms such as nausea and vomiting. Only a child, which ingested 2–4 oz. of 3%  $H_2O_2$  was affected by gastric ulcer and duodenal erosion, whereas mucosal injury was also indicated in that child through endoscopy (Herny et al., 1996). However, very few cases of ingestion of 3%  $H_2O_2$  in sanitizer caused death when exposed with higher dose (Moon et al., 2006). The death of 18 months old child was reported due to ingestion of 8 oz. of 3%  $H_2O_2$  solution caused by fatal air embolism. Dermal contact with 3% hydrogen peroxide leads towards mild irritation of skin and mucous membrane (New Jersey Department of Health (NJH), 2016c).

### 3.4. Risk factor for children

Most of hand sanitizers are available in brightly hued bottles and have appealing smell like candy or any food flavor which is very tempting to young children. If a child licks a small amount of sanitizer to taste, is probably not going to become sick but ingesting any more than a taste could be at risk of alcohol poisoning (American Association of Poison Control Centers (AAPCC), 2020). Young children including infants are more susceptible to get sick from alcohol intoxication than adolescents. Young children have declined liver glycogen stores, which increase their susceptibility to develop hypoglycemia and numerous pharmacokinetic factors which make them more prone to alcohol poisoning. Recent reports have recognized serious concerns, including apnea, acidosis, and coma in young children who ingested alcohol-based (alcohol) hand sanitizer (Santos et al., 2017).

A publication from CDC researchers investigated data that reported to National Poison Data System (NPDS) from 2011 to 14 on exposures to hand sanitizers in children  $\leq 12$  years old (Table 2). Analysis was stratified by the age group (0–5 years and 6–12 years). About 70,669 hand sanitizer exposures were reported in this age group, 92% were exposed with alcohol-based sanitizers and remaining 8% with non-alcoholic sanitizers. Number of expositors with hand sanitizers in children is given in Fig. 2 (Santos et al., 2017).

After the outbreak of COVID-19 in December 2019 usage of hand sanitizer were suggested by WHO as a preventive measure to control this pandemic, which leads to exponentially increased usage of alcohol based hand sanitizers as hand hygiene. In early five months of 2020, American Association of Poison Control Center reported 9504 alcoholic hand sanitizer exposure cases in children under the age of 12 years (Table 3) and recognized that even a small amount of alcohol can cause alcohol poisoning in children that is responsible for confusion, vomiting and drowsiness, and in severe cases, respiratory arrest and death (American Association of Poison Control Centers (AAPCC), 2020).

## 4. Increased risk of other viral diseases

Medical experts have started to warn that excessive use of alcohol based hand sanitizer as a preventive measure against coronavirus indirectly increase the risk of infection through skin disorders. Too much use of sanitizer against new pneumonia causing virus is responsible for skin damage and reduce its ability to work as a barrier against other harmful viruses (Tachikawa, 2020).

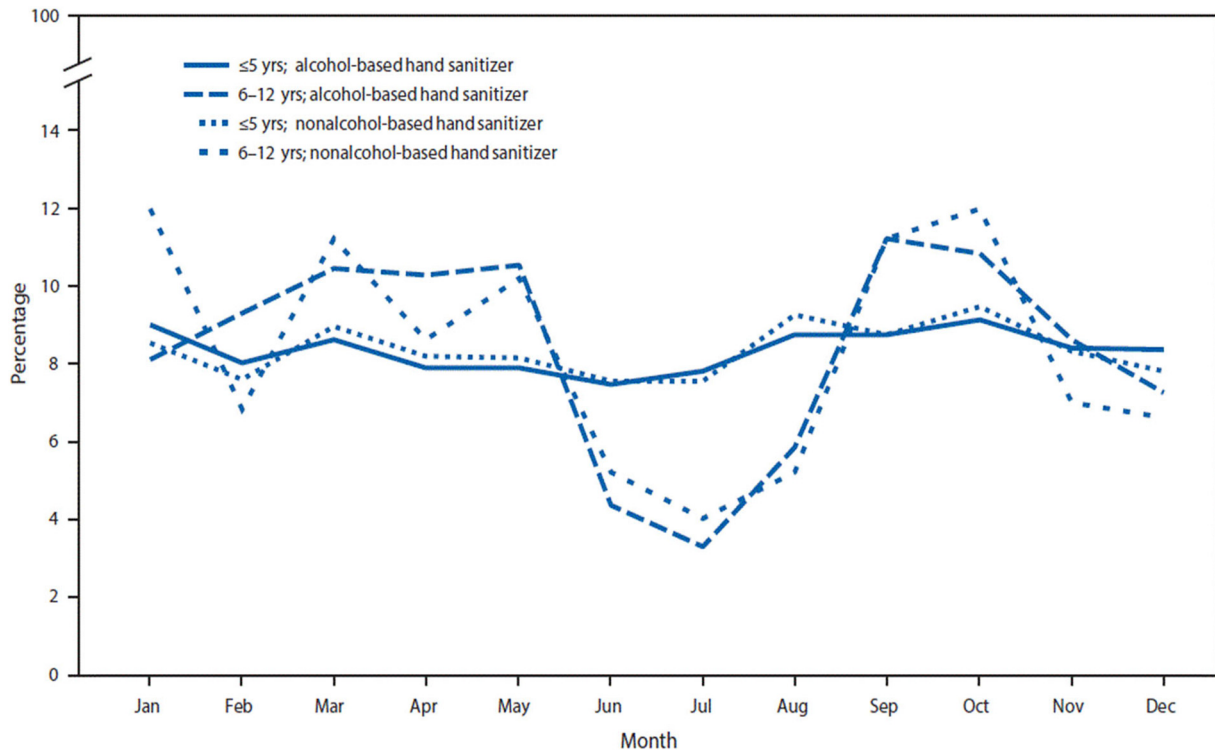
Sanitizers have been frequently used all over the world as a disinfectant for better hand hygiene. Excessive use of alcohol based sanitizer increased permeability of skin and deprives oil and water from skin and leads to skin roughness and irritation. Dry and damaged skin is hotbed for many diseases causing bacteria with increased risk of virus entry into skin (Tachikawa, 2020). Research reports have been indicated that overuse of sanitizers in some cases may increase risk of viral

**Table 2**

Number of cases reported to NPDS about exposure to alcohol and non-alcohol hand sanitizer in children  $\leq 12$  years old in 2011–14.

No. (%) of exposures			
Year	Alcohol	Non-alcohol	Total
Total	65,293 (92.4)	5376 (7.6)	70,669
2011	15,971 (92.5)	1286 (7.5)	17,257
2012	16,571 (92.4)	1355 (7.6)	17,926
2013	16,423 (92.5)	1338 (7.5)	17,761
2014	16,328 (92.1)	1397 (7.9)	17,725

Note: Reprinted from Reported Adverse Health Effects in Children from Ingestion of Alcohol-Based Hand Sanitizers — United States, 2011–2014 by Santos et al., 2017. Retrieved from: <https://www.cdc.gov/mmwr/volumes/66/wr/pdfs/mm6608a5.pdf>.



**Fig. 2.** Percentage of exposure with hand sanitizer in children. Reprinted from Reported Adverse Health Effects in Children from Ingestion of Alcohol-Based Hand Sanitizers – United States, 2011–2014 by Santos et al., 2017. Retrieved from: <https://www.cdc.gov/mmwr/volumes/66/wr/pdfs/mm6608a5.pdf>.

outbreaks (Vogel, 2011). Previously published report revealed that the extensive use of alcohol based hand sanitizer results the increased risk of noro-virus outbreak. Survey of 160 care facilities was conducted to identify the association between preferential use of alcohol based sanitizer and noro-virus outbreak. Out of total surveyed facilities, 91 responded positively in survey with outcomes of 73 outbreaks in which 29 were confirmed for norovirus. Staff in facilities that experienced norovirus was likely to use hand sanitizers six times more than soap and water (Blaney et al., 2011).

**5. Antimicrobial resistance caused by over application of hand sanitizer**

Since coronavirus pandemic number of scientists, doctors and government advice community people for the best hygiene practices and protect them from COVID-19 by using hand sanitizers (Morgan, 2020). Alcohol based sanitizer have been used since last few decades to control many microbial-born diseases worldwide (Pidot et al., 2018). It has been observed that overuse of alcohol based hand sanitizer results

antimicrobial resistance, which can put more burdens on already struggling healthcare professionals. Repeated exposure of disinfectant, antibiotics or other genotoxic chemicals to microbes tends them to get mutations through natural process that make them resistant to survive from repeated use of hand sanitizer (Morgan, 2020).

Pidot et al., 2018 published report on antimicrobial resistant in *Enterococcus faecium* against alcohol based hand rubs. Alcohol resistance in *E. faecium* was tested in 139 hospital isolates during 1997 to 2015 and results showed that *E. faecium* isolates after 2010 were 10 times more resistant to alcohol than older isolates. In early 2000, Australian hospitals started to mount more hand sanitizers that caused rise in enterococcal infections with more rapidly. Similar outcomes were observed from other parts of the world due to over use of alcohol based hand sanitizer (Schreiber, 2018). It has been reported that *E. coli* and *Pseudomonas aeruginosa* were 48% and 64%, respectively, resistant against all available sanitizers in market. *Pnemoumia aeruginosa* and *Micrococcus leutusbutit* has been found resistant against sunshine hand sanitizers. Almost all the Gram negative bacteria are resistant against Cool n cool, Safeguard, Purell, Fresh up, Insta foam sanitizers (Hayat and Munnawar, 2016).

**Table 3**  
No of exposure in children (12 years or younger) with hand sanitizer in 2020.

Month	No. of exposure cases
January	1609
February	1668
March	2443
April	1873
May	1903

Note: Adapted from Hand Sanitizer by American Association of Poison Control Centers (AAPCC), 2020. Retrieved from <https://aapcc.org/track/hand-sanitizer>.

**Table 4**  
Ethanol effects on wildlife (USEPA ECOTOX Report, 2011).

Douglas Fir	Applied ethanol concentrations of Seedlings 10% and greater lethal within a week, effects also observed with 5% and 1% solutions
Japanese Quail	Ethanol at 2% in drinking water had significant effects on blood, brain weight and growth after 7-day exposure
Honeybees	Bees fed solutions of ethanol (5% and greater) showed behavioral effects, and mortality with solutions of 50% ethanol.
Little Brown Bat	LD50 of 3.9–4.4 g/kg

## 6. Toxic impacts on environment

### 6.1. Ethanol

Ethanol has its widespread use in industries and homes and its impacts on humans and environment are still debatable (Pendlington et al., 2001). Aquatic organisms could be directly impacted by ethanol spills in water body. Numerous studies have been performed to evaluate the effects of ethanol on different species reflecting different effects. New England Interstate Water Pollution Control Commission (NEIWPCC) (2001) evaluated the data available then and established water quality benchmarks for ethanol usage. They evaluated that for aquatic invertebrates such as *Daphnia* species, rainbow trout and fat-head minnow benchmark level for acute and chronic exposure is 564 mg/l and 63 mg/l, respectively. Later on EPA, ECOTOX database was established to determine additional information produced since New England Interstate Water Pollution Control Commission (NEIWPCC), 2001 (where minimal information was found) related to above mentioned species.

HSDB (2012) found the octanol/water partition coefficient ( $K_{ow}$ ) for ethanol to be 0.49 which indicates that it is improbable for ethanol to bioaccumulate or bioconcentrate in fatty tissues due to high anticipated metabolic rate. New England Interstate Water Pollution Control Commission (NEIWPCC) (2001) evaluated the oxygen depletion impacts after ethanol spills in small stream, average River and large size river 55 mg/l, 32 mg/l and 13 mg/l, respectively.

On the other hand terrestrial animals are less likely to be exposed to ethanol spills as it volatilize or penetrate deeper in the soil or into ground water and biodegrade rapidly. But it is expected that local microbes and other invertebrates may get affected by spill (MassDEP, 2011). According to U.S Environmental Protection Agency (USEPA), 2011 ECOTOX Report, wildlife gets affected with different percentage solutions of ethanol.

In Table 4 benchmark concentrations of ethanol impact on aquatic and wildlife suggested that aquatic life is at greater risk as compared to terrestrial life. Hazards associated with ingestion of food containing ethanol are unlikely, as it cause adverse effect due to high volatility of ethanol and no accumulation in fatty tissues. Ethanol wildlife benchmarks are shown in SI Table 3 based on no observed effect levels.

### 6.2. Iso propyl alcohol

If large amounts of isopropanol are spilled on soil, it may get infiltrated and could contaminate the groundwater. Isopropanol has the ability to get oxidized by the photo-chemicals in the air which make it least persistent in the atmosphere. It cannot bio-accumulate due to rapid biodegradability. Large amounts of spill in aquatic bodies may cause environmental impairment because it has high potency to deplete oxygen in water body (BABEC, 2001). This will ultimately impart adverse impacts on aquatic living system. In a reported data, traces quantities of propanol have also been detected in drinking water samples collected from industrial areas and found nontoxic (HSDB, 2012). Rather than accidental spills, normal isopropanol usage does not have any environmental impact. Isopropanol also does not participate to generate ground level ozone and photochemical smog like other volatile organic compounds. Ecological toxicity linked with isopropyl alcohol is presented in SI Table 4.

### 6.3. Hydrogen peroxide

According to ATSDR (2002), hydrogen peroxide does not harm environment due to rapid reaction with other compounds. It degrades in water and soil at fast rate and has no potential to accumulate in food chain. The European (EU) risk assessment for hydrogen peroxide found no abiotic half-life in water or soil because it is a short-lived substance in the environment. The projected half-life in the atmosphere is

24 h. The EU risk assessment for hydrogen peroxide found short-term toxicity data in fish, invertebrates and algae from aquatic environment. The lowermost extended-term aquatic toxicity test result was NOEC of 0.1 mg/l for algae. In addition to algal studies, long-term data are available for zebra mussels as well. A quantifiable risk assessment was achieved for aquatic organisms and microorganisms. The assessment accomplishes that no further information or testing is required for hydrogen peroxide (HERA, 2005).

## 7. Conclusion

Frequent and increased use of hand sanitizer results toxicity that leads to fatal; may be attributed by accidental ingestion, absorption through dermal contact and suicidal ingestion. Ethanol's potential to cause skin cancer through skin absorption and carcinogenicity is in scientific debate and investigation, though it is still unclear due to lack of up to date research. However, ingestion or dermal contact with ethanol based hand sanitizer is associated to minimal systematic toxicity. Similar to ethanol, isopropyl alcohol has some negative impact on human health and environment. Hydrogen peroxide in low concentration (as prescribed by WHO) is reported safe for human health while have minimal impact on environment. Children are at more risk by increased usage of hand sanitizers. American Association of Poison Control Center reported 7593 alcoholic hand sanitizer exposure cases in children under the age of 12 years. In previously reported literature, it has been observed that overuse of alcohol based hand sanitizer results antimicrobial resistance, which can put more burdens on already struggling healthcare professionals. Repeated exposure of disinfectant, antibiotics or other genotoxic chemicals to microbes tends them to get mutations through natural process that make them resistant to survive from repeated use of hand sanitizer.

### CRedit authorship contribution statement

**Adeel Mahmood:** Conceptualization, Writing - original draft, Writing - review & editing, Supervision. **Maryam Eqan:** Investigation, Writing - original draft. **Saher Pervez:** Investigation, Writing - original draft. **Huda Ahmed Alghamdi:** Writing - review & editing. **Amtul Bari Tabinda:** Writing - review & editing. **Abdullah Yasar:** Writing - review & editing. **Kathirvel Brindhadevi:** Writing - review & editing. **Arivalagan Pugazhendhi:** Writing - review & editing.

### Declaration of competing interest

Authors declare there is no conflict of interest in this work.

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### Appendix A. Supplementary data

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