Review Article

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COVID 19: The safety profile of common disinfectants used for sanitization

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Abstract: With the recent outbreak of COVID-19, sanitization is a must for the community as daily safety prevention. The common ingredients found in disinfectant including glycol, sodium hypochlorite, silver ion, iodophor iodine and polyvinylpyrrolidone iodine. An ideal disinfectant should have a wide anti-microbial spectrum, low dermatologically toxicity profile, and stable storage properties. Glycol is widely used as a personal care product due to its low toxicity profile. Although it has a wide anti-microbial spectrum, it must be co-formulated with other agent due to its lower microbial killing strength. It has been demonstrated that sodium hypochlorite is not only capable of destroying bacteria and viruses but also about inactivating viral antigens by breaking down the high concentration protein resulting in the isolation of necrotic tissue particles. Yet, due to its strong alkaline pH and oxidizing capacity, it can cause corrosive reaction when mucous membranes and skin are in touch with it. Besides, silver ion also plays an effective role in curbing SARS coronavirus. It is used widely in disinfecting medical equipment, wound therapy, and utilized in water purification systems by its bacteriostatic and active ingredient properties. Researches have proven that iodophor iodine is effective in against non-enveloped virus in which 1% of povidone-iodine is effective against coronaviruses. However, it can cause a chemical burn, blistering, and skin sloughing if it used as skin disinfection. This report will discuss the safety of these disinfectants in sanitization.

Keywords: Coronavirus; sanitization; disinfectants; safety; skin

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Introduction

Disinfectant is an agent with antiseptic properties that is effective against microbials. With the recent outbreak of COVID-19, studies have shown the importance of preventive measures especially the role of disinfectants in reducing the risk of transmission of this pandemic disease. There are many evidences that indicate this virus is transmitted through respiratory droplets or contact[1]. Direct transmission of this virus occurs when contaminated hands touch the mucosa of mouth, nose or eyes, whereas indirect contact transmission is facilitated by transferring of the virus from one surface to another by contaminated hands[2]. Inevitably, the onus is on us to practice hand hygiene that not only prevents the spread of COVID-19 virus but also other viruses and bacteria as well.

Among all types of disinfectants used for sanitization purpose, the most common traditional active ingredients include chlorine, alcohol and phenol[3]. Table 1 shows active ingredients commonly used in disinfectants, namely glycol, sodium hypochlorite, silver ion and iodophor iodine or polyvinylpyrrolidone iodine which are found to be effective against coronavirus. These chemicals although are effective against viruses and bacteria, but they also have risks associated with them ranging from skin irritation to long term effects, including occupational asthma.

The primary purpose of disinfectants is to eliminate microbials and pathogens. In other words, they are noxious to cells and none of them are completely harmless. However, there are some active ingredients used in the production of disinfectants that are safer for human health and the environmental than others. Hence, this report aims to discuss on the role of these common disinfectants in sanitization of COVID-19 and the safety of its usage.

Disinfectant	Advantages	Disadvantages	Shelf life[4]	Anti-viral	Recommended dosage (concentration)
Sodium hypochlorite	Low toxicity profile (medical disinfection), wide range anti-microbial properties, cheap[5,6]	Skin irritation, swelling, rash, pain, corrosive[7,8]	2 years[9, 10]	+++	0.5%[9,11,12]
Silver ion	Low toxicity profile, Potent antimicrobial agent[13–17]	Argyria, silver dermatitis, interrupt drug absorption[18–21]	At least 7 months[22]	++	0.01%[23]
Iodophor	Wide range of anti-microbial, Stable storage, Low toxicity profile[24]	Chemical burn, Blistering, Skin sloughing[25]	2 years[4,26]	++++	1% at 6 to 75 ppm[27–30]
Glycol	Wide range of anti-microbial, Low toxicity profile[31,32]	lower microbial killing strength, Sensory skin irritation[33,34,35]	2 years[36]	+	<0.5% (insufficient data)[33]

Table 1. Summaries of characteristics of common disinfectants.

Sodium hypochlorite

Sodium hypochlorite was discovered in 1785 and has been commonly used on a large scale as a bleaching agent or disinfectant since then. It is generally used dissolved in water at various concentrations and appears as colourless or slightly greenish-yellow colour solution with corrosive properties. This chemical compound is also capable in dissolving proteins in high concentrations, inactivating viral antigens as well as having bactericidal and viricidal properties. A recent study reveals that surface disinfection with 0.1 % sodium hypochlorite significantly reduces coronavirus infectivity on surfaces within 1 min exposure time[37]. Aside from the effective disinfection of coronavirus by 0.1% sodium hypochlorite, the use of bleach agents containing 5.25%–8.25% sodium hypochlorite is also recommended by CDC[12].

As early as 1918, clinicians are keen to know the adverse effect of skin exposure to hypochlorite and its resulting chlorine. The action of the hypochlorite solution and chlorine on tissue results in the separation of particles of epithelial scales, hair, coagulated serum, necrotic tissue, and a period of at least 17 hours was needed for a gradual digestion of these substances [6]. It is found that hypochlorite's strong alkaline pH and oxidizing capacity is corrosive to mucous membranes and skin. A review on sodium hypochlorite isolated incidences of hypochlorite-induced delayed type hypersensitivity (allergic contact dermatitis), as well as immediate-type reactions from inhalation or topical challenge of sensitized individuals. A possibility of irritation and damage to the skin as a result of excessive and prolonged exposure to hypochlorite was also concluded in a review elsewhere[7]. Several cases reported also highlighted cases of dermatitis induced by exposure to sodium hypochlorite[38–40]. Almost 20% electrical workers that have prolonged exposure to chlorine mixture solution were diagnosed with skin diseases such as dermatitis, chloracne and folliculitis[8]. Vesicular eruption occurred to a female adult shortly after an irritant dermatitis caused by sodium hypochlorite found in the household bleach detergent. Direct immunofluorescence revealed linear deposits of IgA and C3 in the epidermal basement membrane and the serum of the patient contained IgA that immunoblotted a 180-kD polypeptide in extracts of human keratinocytes[41]. To fully understand this, the interaction between sodium hypochlorite and human stratum corneum were determined using human clinical trial study. Goffin *et al.* recruited fifteen volunteers to receive patch tests of a sodium hypochlorite for 15, 30, 45, 60, and 90 min. Results showed that the stratum subclinical corneum alteration occurred, in the form of reduced skin conductance without significant TEWL change. Squamometry finding also confirmed sodium hypochlorite caused desquamating effect through loosening of its physical integrity[42].

The use of 0.5% sodium hypochlorite or 1/100 of the household bleach concentration for effective disinfectant properties is recommended by CDC[11]. Sodium hypochlorite is highly reactive and volatile. Due to its unstable chemical properties, sodium hypochlorite should be kept away from heat, sunlight, certain metals as well as poisonous and corrosive gasses, such as chlorine gas. The stability of sodium hypochlorite solution when used as disinfectants can be maintained for 2 years at 4°C. Apart from that, sodium hypochlorite prepared at a pH of 6-8 can degrade substantially within 2–3 weeks. An increase in the pH of sodium hypochlorite would increase its stability and thus prolonging its shelf life[43].

Silver ion

Metal ion, particularly silver ion is a potent disinfectant with a wide spectrum of antimicrobial properties against protozoa, bacteria and viruses[13,14,15,44,45]. Due to its broad coverage of antimicrobial activities, silver ions are used to disinfect medical equipment and in wound therapy[16,46,47]. It is also commonly utilized in water purification systems in hospital, community water systems, pools and spa[48]. A study using conventional plate count method and flow cytometric (FC) analysis found that silver ion, instead of bactericidal, it is bacteriostatic against S. aureus and E. coli bacteria[16]. Apart from that, silver ion as an active ingredient and carrier, such as in silver zirconium phosphate (AgZrP), is effective in SARS coronavirus inactivation at a concentration of 23.4 µg/mL or above[49]. Another study also revealed that through a direct contact with 100 mg/L of AgZrP for 8 hours, complete elimination of E. coli and 99.9% of S. aureus is possible[50]. Another compound, silver zeolite at concentrations above 375 mg/L was reported to be effective in complete inactivation of both SARS-CoV-P8 and SARS-CoV-P11 strains of coronavirus within 2 hours[17]. Besides that, a study demonstrates that silver nanocluster/ silica composite coating deposited on facial masks is viricidal against coronavirus[51]. Scientific evidences further showed that silver ion reacts with thiol group of l-cysteine resulting in inhibition of essential enzymatic functions of microbes[16,52–55]. Increased production of reactive oxygen species (ROS) due to the action of silver-ion-mediated perturbation of the bacterial respiratory chain have been concluded in detail elsewhere[16,56]. The interaction of silver ions with nucleic acids[54,57,58] and bacterial cell envelope[59] could also play a role in its antimicrobial activity.

Several studies have reported a number of toxic effects of silver ion, including a decrease in the activities of glutathione peroxidase and lactate dehydrogenase as well as the peroxidation of membrane lipids[18–21]. An in-vitro study using human skin fibroblasts further demonstrates that silver ion toxicity is due to its induction of cellular oxidative stress and alteration of the intracellular zinc homeostasis of the cells[60]. Studies have shown that percutaneous absorption of silver ion in intact skin is lower compared to denuded skin[61,62]. The binding of silver ion with proteins and amino acid residues have been documented as the basis of silver-protein complexes found in the skin[47,61] which most likely possible in slowing down the systemic absorption of silver, but may cause local effects as a reservoir may be formed for the prolonged release of silver ions in the skin[63]. Sizes of aggregates between 150 nm-2 μm is found in both epidermis and dermis[63,64]. Transmission electron microscope (TEM), atomic force microscopy and scanning electron microscopy with energy dispersive X-ray analysis (SEM-EDX) can be used in determining human skin penetration by silver ions[62–64]. A recent study highlighted that silver ions were released more by silver nanoparticles coated with oleic acid in the presence of phospholipids[65]. Although argyria is the most widely publicized clinical condition due to excessive silver ingestion, an incidence of argyria secondary to topical use of silver-based product have been reported[66]. Apart from argyria, cases of silver dermatitis have also been reported [67–76] and a recent review deduced that other ingredients in silver-based products may be the cause for the allergic reaction[77].

Despite the lack of scientific information to determine an appropriate range of doses for silver ion, 0.01% silver ion can be found in hand sanitizers[23]. Apart from this, it was also reported that the shelf life of nano silver colloids produced is at least 7 months[22,78].

Iodophor Iodine, polyvinylpyrrolidone iodine

Iodophor is a variform complex compound that is formed by the polymer of iodine, surfactant, and reinforcer[79]. Povidone-iodine (Betadine) is the most popular iodophor, which effective against a wide range of microbial, as well as having stable storage and low toxicity profile[24]. A variety of crucial pathogens correlated with health care, namely vancomycin-resistant enterococci, methicillin-resistant Staphylococcus aureus, norovirus, Acinetobacter, and Clostridium difficile have been found susceptible to this disinfectant[80]. Furthermore, a research on disinfection of virus-contaminated non-porous inanimate surfaces using iodophor was conducted with adenovirus, coronavirus, coxsackievirus, and parainfluenza virus type 3. The results of this study shows that this disinfectant might have enhanced activity against non-enveloped viruses and can improve both iodine and acid action if there is an appropriate non-ionic surfactant[27].

Previous studies on disinfection options demonstrate that 1% povidone iodine[27] and 50 ppm iodine in iodophor[28] is effective against coronavirus. In a study of 107 patients show that preoperatively, iodophor impregnated plastic adhesive drape (‘Ioban’) at the preliminary 24-hour incision site demonstrated a capability of lowering the infection risk from 15% to 1·6% [29]. The use of iodophor was statistically significant for wound infections with incidence of 6.8% to 2.7% in a series of 666 operations in a similar series of patients[30]. Besides, another research shows that a 10 minutes contact time of 4 048 mg/L povidone iodine can inactivate poliovirus with an average inactivation logarithmic value (4.00), thus effective in the inactivation of poliovirus[80]. Also, an animal study was used to conduct experimental investigations on the subacute toxicity of povidone iodine spray.

On the other hand, iodophor was tested to have a possibility in causing chemical burn, blistering and skin sloughing when used for skin disinfection purpose. Necrosis of the skin commonly results when there is an overdose of solution that comes in contact with the skin for an extended period of time[25]. As far as the concentrated product itself, National Chemicals suggests a two-year shelf life for storage[26].

Glycol

1,2-hexanediol belongs to the glycol class of disinfectant. It is also widely known for its use as an emollient, humectant and enhancers in cosmetics and personal care products[34,81,82]. It is liquid form with light yellow colour with boiling point of 223°C and 0.951 g/mL of density at 25 °C. Although 1,2-hexanediol has wide anti-microbial spectrum, previous studies have shown that it must be co-formulated with other agent due to its lower microbial killing strength[34,83–89].

1,2-hexanediol was tested and known to have a low toxicity profile[31,32]. In addition, scientific evidences have revealed that 1,2-alkanediols demonstrate enhanced risk for anti-microbial and sensory distress as their length of alkane chain grows[33,34]. Sensory skin irritation potential test were used to determine the skin reaction caused by 1,2-hexanediol.

Conversely, another study demonstrates 1,2-Hexanediol having high cytotoxicity properties against Raw 264.7 cells and HK-2 cells. The results show that 0.5% concentration of 1,2-Hexanediol has considerable toxicity properties[35]. Another study was conducted using filter paper discs covered with twenty microlitres of 1,2-hexanediol in IQ test chambers, which are applied to each side of the nasolabial fold and cheek of the selected stingers. The results of stinging and burning reactions were recorded at 0.5 hour and 24 hours. A visual scoring was performed using a numerical erythema scale from 0 (none) to 3 (severe) and recorded which confirmed that 1,2-hexanediol has low skin irritation potential: 0.34 ± 0.10 for 1% 1,2-hexanediol and 0.63 ± 0.46 for 20% 1,2-hexanediol[33]. However, researches on the toxicity profile of 1,2-hexanediol reported by scientific journals are not enough to conclude. As far as the concentrated product itself, National Chemicals suggests a two-year shelf life for storage[36].

Discussion

The role of disinfectants in our everyday life is crucial especially during this pandemic outbreak of COVID-19. Based on the data collected from recent studies about this disease, it is summarized that transmission from one person to another happens most commonly in close contact cases, via respiratory droplets. Apart from that, there are recent findings about incidences of people who are infected yet do not exhibit any COVID-19 symptoms which plays a role in this pandemic outbreak as well[2]. Current evidence from NIH suggests that SARS-CoV-2 is likely to remain active for hours to days on surfaces that are present in household or hospital settings[90]. Therefore, cleaning and disinfection of visible or non-visible dirty surfaces as well as hand hygiene are the effective preventive measures against COVID-19. Sodium hypochlorite is a widely used disinfectant due to its effectiveness, low cost and ease in preparation. It is also a potent sanitizer as it has strong oxidizing properties[91]. While sodium hypochlorite is very reactive, its useful properties are negatively impacted by factors including high temperature, presence of light and improper pH level[10]. Other disadvantages of sodium hypochlorite also include health concerns related to skin irritation and mucous membrane damage, environmental contamination[38-40,92] and its corrosive properties. Silver ion and its compound have long been discovered and since then used for disinfectant or antiseptic purpose[93]. It is effective because at low concentrations, it is able to show bactericidal and viricidal properties[94]. Meanwhile, though iodophor may be less effective than sodium hypochlorite but it is also an effective sanitizer and disinfectant[95]. This chemical agent performs its role better in situations which have slightly acidic pH level[96]. Although iodine compound can stain surfaces easily, the EPA has confirmed its safety against the environment[31,32,34,83–89,97,98]. Glycol, namely 1,2-hexanediol although was not previously registered and used as a sanitizer or disinfectant, but when combined with other adjunct chemical agents, it is confirmed by EPA of its anti-microbial properties. Even though it has been proven to have the lowest toxicity level designated by the EPA, further investigations are still needed for this chemical agent as there is insufficient scientific evidences to support its effectiveness as a potent disinfectant. With regard to potential application in overcoming COVID-19, all chemical agents except glycol are supported with more scientific evidences of their effectiveness against coronavirus. However, sodium hypochlorite is the only disinfectant among these 4 chemical agents that is being recommended by WHO and CDC against COVID-19 for the time being[8,12]. In terms of tolerability, all 4 disinfectants are associated with risk of side effects. Case reports indicate the possibility of developing skin irritation for all chemical agents with the exception of silver ion that causes argyria. In relation to the preparation and shelf life of these active ingredients, factors such temperature, light and pH value are commonly important and changes in these factors can either prolong or shorten their shelf life[10,14,91,97,99–102]. In light of these considerations, it is probably too early to have a definitive opinion about the best disinfectant which is effective against COVID-19 but iodophor may relatively be the safest chemical agent to be used for sanitization and disinfectant purpose of COVID-19.

Conclusion

The recent outbreak of the pandemic disease, COVID-19 has certainly introduced a new norm in the society: frequent and increased use of disinfectants and hand sanitizer. Consequently, the role, effectiveness, and safety of common disinfectants are important and should be considered. Although researches show that surface disinfection with sodium hypochlorite significantly reduces coronavirus infectivity on the surface, it is potent to cause skin irritation, swelling, rash, pain and has corrosive properties. In spite of the insufficient data about the toxicity profile and viricidal effect of silver ion and glycol against coronavirus, there is a recent study that demonstrates silica composite coating deposited on facial masks is viricidal against coronavirus. In addition, even though glycol plays an effective role as an inactive ingredient in antiseptic, but it cannot be used independently. Meanwhile, iodophor has been considered as the best disinfectant among these 4 chemical agents by having a stable storage and generally low toxicity profile. It is an ideal antiseptic especially in the current pandemic period but repeated exposure tends to cause side effects such as chemical burn, blistering, and skin sloughing especially if it is used in overdose. To avoid these side effects especially on dermatological aspect, the recommended dosage for sodium hypochlorite, silver ion, iodophor and glycol are 0.5%, 0.01%, 1% at 6~75ppm and less than 0.5% respectively. As far as the concentrated product itself, National Chemicals suggests a two-year shelf life of storage for all these chemicals except for silver ion, having a shelf life of at least 7 months when produced as nano silver colloids.

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