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DISINFECTION OF VIRUS IN ROOM AIR

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ABSTRACT

Pandemics of viral respiratory diseases are primarily, if not solely, spread via virus-containing aerosols expelled from the mouths of infected people. Due to this mechanism, infectious diseases are frequently spread in a crowded room. To prevent the spread of viral respiratory diseases, it is mandatory to disinfect virus-containing aerosols in room air. To evaluate the evidence for the disinfection of viruses in the air of enclosed areas, we searched for literature for studies published between 1957 and 2021 using PubMed and Google Scholar. We focused on literature that described practical and possible methods to disinfect viruses floating in room air. Our literature search showed that disinfection using ozone (O_3) and chlorine dioxide (ClO_2) gases are the only practical methods to disinfect virus-containing aerosols in room air. However, ozone requires relatively high concentrations for this purpose, which might be toxic to humans present in the room. On the other hand, chlorine dioxide gas can be used in rooms where people are present. Chlorine dioxide gas is the only practical and currently available disinfection agent that can disinfect viruses in room air to prevent viral respiratory diseases.

KEYWORDS: Chlorine dioxide, Gas, Aerosol, Respiratory infection, SARS-CoV-2.

INTRODUCTION

In view of the current global outbreak of COVID-19 virus (SARS-CoV-2) (severe acute respiratory syndrome coronavirus 2) infection,[1−5] the development of effective and safe medicines and vaccines is urgently needed.[6−10] The development of safe and effective methods to inactivate virus floating in room air are also required because some respiratory viruses, such as the SARS-CoV-2 virus and influenza virus, are spread via droplets, aerosols, or dried aerosols floating in room air.[11−15] Here, we review the current methods to inactivate viruses floating in room air. While the mechanism of transmission of respiratory virus between humans has not been completely proven, many reports strongly suggest that airborne virus is the cause of human-to-human transmission of respiratory diseases.[16, 17]

The mode of transmission of viral diseases relevant to this review is by particles, mostly aerosols, expelled from the mouth or nose of virus-infected humans, which then float in the air.[18] In the case of influenza virus, aerosolized particles of 1-4 μm diameter mostly contain the infective virus.[18] For aerosols to fall 3 m in height, particles of 20 μm diameter require 4 min, those of 10 μm diameter require 17 min, and those of 5 μm diameter require 67 min.[19] It is important to consider the time until droplets become desiccated and become "droplet nuclei" in ambient air.[19] For instance, for aerosols of a diameter less than 20 μm, it takes less than 1 s to become a droplet nucleus.[20] Aerosols with a diameter of 5 μm or less can easily reach the respiratory tract and travel all the way to the alveoli of the lungs,[19] suggesting the potential infectivity of aerosol particles. We searched PubMed and Google Scholar for literature published between 1957 and 2021. We selected papers using the keywords disinfection, virus, respiratory disease, aerosol, and pandemic. We will focus on the disinfection of virus-contaminated room air. There are currently three methods to disinfect room air including gas, aerosol spray, and ultraviolet (UV) light, which have virus-inactivating activities.

RESULTS

Ozone

Virus-inactivating gases that can be used safely include ozone and chlorine dioxide. Ozone gas can be used at concentrations of 1-1000 parts per million (ppmv, volume/volume ratio) to disinfect viruses and bacteria in room air.[21-40] Ozone can be generated using low-cost devices and air. It is a strong oxidant[28] and has long been used to inactivate pathogenic microbes in water.[41,42] Ozone can be used to inactivate pathological microbes on the surfaces of objects and aerosols.[43−45] Using corona pseudoviruses, Zucker et al. demonstrated that 30, 100, and 1000 ppmv of ozone inactivated pseudoviruses after 30 min, and that this inactivation activity was similar to the effect of ozone on coronavirus 229E.[28] An important finding of their experiments was that the inactivation was observed on many surfaces of objects and even on the interior surface of a partially opened chamber.[28] Hudson et al. also found ozone inactivated viruses, including mouse coronavirus, on glass and stainless steel.[46] They reported that 20-25 ppmv ozone with 90% relative humidity was effective at inactivating 12 viruses on hard or porous surfaces to a level of 10^{-3}.[46]

An important point when using ozone at high concentrations for the disinfection of room air or object surfaces is its potential toxicity to humans and animals.[47] For instance, ozone exposure causes irritation, airway hypersensitivity, airway inflammation, and emphysema in humans and mice.[47] Sokolowska et al. reported a mouse experiment where a single exposure to 1 ppmv ozone for 60 min caused damage to the bronchiolar epithelium within 2 hours, disrupted epithelial tight junctions, and promoted cell death, which was followed by reactive oxygen species production.[47] This result indicates the difficulty of using ozone as a disinfectant against viruses in the presence of humans in rooms. Chronic exposure of humans to ozone causes the progressive and irreversible loss of alveolar epithelial cells and eventually emphysema occurs.[48] Therefore, although the effectiveness of ozone has been proven, its use, especially in terms of concentrations and exposure periods, should be carefully controlled to avoid accidental side effects. Furthermore, it has not been demonstrated explicitly in the literature whether ozone can be used to disinfect room air without evacuating people from the room.

Chlorine dioxide

Chlorine dioxide inactivates many viruses. For instance, Morino et al. reported that feline calicivirus was inactivated to levels of 10^{-2} to 10^{-3} by treatment for 5 h using a chlorine dioxide gas-generating canister that generated gas at a rate of 1.7 mg/h.[49] However, the actual concentration of gas in the test air was not reported in their study.[49] The inactivation activity of chlorine dioxide against feline calicivirus and influenza A virus was 0.05 ppmv for 5 h, and the reduction of virus was to a level of 10^{-5}.[50] Tulane virus, which sticks to blueberries, was inactivated to a level of less than $10^{-2.2}$ after 15 min exposure to 0.6 mg/L chlorine dioxide.[51,52] Hepatitis A virus on blueberries was inactivated by 1 mg/L (1 ppm) of chlorine dioxide.[53] Inactivation of feline calicivirus by gas depends upon the presence of water. According to the experiments of Morino et al., a reduction of viable virus to a level lower than 10^{-3} was obtained with 0.08 ppmv chlorine dioxide for 6 h when the relative humidity was 45-55%, and it took 10 h with 75-85% relative humidity to attain the same level of inactivation.[54] Their result indicates that humidity plays an important role in the inactivation of virus. Using a minute mouse virus, Lutgan reported the successful fumigation of a building with chlorine dioxide.[55] Inactivation of viruses by chlorine dioxide aqueous solution was also demonstrated. Sanekata et al. found that human influenza virus, measles virus, canine distemper virus, human herpes virus, human and canine adenoviruses, and canine parvovirus were inactivated by chlorine dioxide aqueous solution.[56] Hepatitis A virus was completely inactivated after 10 min in a 7.5 mg/L aqueous solution of chlorine dioxide.[57] The cause of inactivation of the virus was related to the complete loss of antigenicity of the virus and the loss of the 5’ non-translated region of its genome.[57,58] MS2 virus, human immunodeficiency virus type 1, and other viruses were also inactivated by an aqueous solution of chlorine dioxide.[59−61]

Chlorine dioxide is a relatively stable free radical[62,63] that denatures proteins by oxidizing their tyrosine and tryptophan residues.[64−66] It is very likely that it oxidizes the proteins of a virus, which inactivates its infectious capacity.[49,50,54,67−69] Wigginton et al. demonstrated that chlorine dioxide caused extensive damage to the coat protein of the bacteriophage MS2 and had a prominent effect on the integrity of assembly proteins, and these effects of chlorine dioxide caused the loss of the binding ability of MS2 to host cells.[70] Simonet and Gantzser found that the poliovirus genome was denatured and degraded by chlorine dioxide.[71] This effect on the genome was supported by the fact that chlorine dioxide denatures nucleotides.[72,73] Therefore, chlorine dioxide can be used effectively and safely at relatively low concentrations against viruses and bacteria.[56,74−86]

Akamatsu et al. demonstrated the safety of a low concentration of chlorine dioxide in an animal experiment. Rats exposed to whole-body inhalation of 0.1 ppmv chlorine dioxide for six months with a two-week recovery period showed no differences in body weight gain, food intake, water intake, relative organ weight, blood biochemistry data, and haematology examination data compared with control rats not exposed to chlorine dioxide.[86] In their experiment, rats were exposed to chlorine dioxide for 24 hours/day and 7 days/week. Furthermore, the concentration of gas was precisely controlled within ± 25% of the target concentration.[86] Their result strongly suggests that chlorine dioxide at or below 0.1 ppmv can be used safely to disinfect room air in the presence of humans for a long period. A concentration of 0.1 ppmv chlorine dioxide was effective at inactivating virus in room air.[67,68] The US Department of Labor of the Occupational Safety and Health Administration (OSHA) stated that the permissible exposure concentration of chlorine dioxide for humans for an 8-hour time-weighted average was 0.1 ppmv.[87] Dalhamn reported a no-observed-adverse-effect-level (NOAEL) of 0.1 ppmv in rats exposed to chlorine dioxide for 5 hours/day for 10 weeks.[88]

Other disinfection methods

Ultraviolet (UV) light and photochemical reactions have been used to inactivate viruses.[89−107] Regarding UV light irradiation, 254 nm light is usually used.[108−109] While this method is quite useful for inactivating viruses floating in room air or stuck on objects in a room, its disadvantages include that it cannot inactivate virus in the blind spots of a room where UV light does not penetrate. Furthermore, humans cannot be present because UV irradiation causes cataracts[110] and dermal neoplasms.[111] There are other similar methods that can inactivate viruses. For instance, viruses are inactivated by photochemical reactions using titanium oxide.[112] However, this method is useful predominantly to inactivate viruses stuck on objects. Furthermore, it has not been proven to be effective at inactivating virus floating in room air or away from object surfaces.

Aerosol sprays are also used to disinfect room air containing pathological viruses. For this purpose, hypochlorous acid (HOCl) in water is frequently used as a spray to inactivate avian influenza virus, Newcastle disease virus, and coronavirus.[113,114] Hakim et al. demonstrated that avian influenza virus of $10^{5.78}$ tissue culture infective dose 50 ($TCID_{50}$)/ml treated for 10 min with a spray of 200 ppm (200 mg/L) hypochlorous acid in water had a $TCID_{50}$ less than $10^{2.5}$.[113] An aqueous solution of sodium hypochlorite (NaClO) was also used as a spray to disinfect viruses.[115,116] However, both hypochlorous acid and sodium hypochlorite solution sprays are primarily used to disinfect viruses on the surfaces of objects. While useful, they are rarely used to disinfect room air, and their effectiveness at inactivating viruses floating in room air has not been demonstrated quantitatively.

Ventilation

The mechanical or natural ventilation of room air is a simple, effective, and inexpensive way to minimize the airborne transmission of respiratory viruses.[117] The Center for Disease Control and Prevention recommends a ventilation of 6-15 room air changes per hour to minimize the transmission of microbes.[117] However, the efficient ventilation of room air is accompanied by unwanted warming or cooling of room air unless an ambient temperature is appropriate. This requires extra energy expenditure aside from that required for mechanical ventilation, and such procedures go against the earth-warming policies of many countries. Thus, the safe and effective inactivation of viruses in room air by methods other than ventilation should consider energy saving. In summary, after a survey of the current literature, low-concentration chlorine dioxide is the most suitable agent for the safe and efficient disinfection of room air contaminated with viruses without evacuating people from the room. A chlorine dioxide-based disinfection system might suppress the potential transmission of aerosol-related viral infections.

DISCUSSION

As discussed above, ozone gas is very effective at inactivating viruses floating in the air. However, its toxicity becomes a serious problem when it is used as a disinfectant in places where humans are continuously present in a room; humans should be evacuated temporarily when the ozone gas is in use to disinfect the air of a room.[46–48] On the other hand, chlorine dioxide gas can be used in a room at concentrations that are effective in inactivating viruses and which are safe to humans.[86]

CONCLUSION

We conclude that chlorine dioxide gas can be used at very low concentrations with humans present in a room during disinfection. This is the only useful and safe method that can be used for viral disinfection without evacuating people from a room.

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