Editorial Note

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Efficacy of chlorine dioxide as a disinfectant

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Abstract: Chlorine dioxide plays a significant role in the industrial settings as disinfectants due to its broad antimicrobial property. Despite commonly use as germicide, chlorine dioxide demonstrates a good safety profile, rendering its suitability for use at water treatment and food preparation zones. Protein denaturation including envelope proteins is the major mechanism of chlorine dioxide to inactivate microorganisms even at low concentrations. Adverse reactions are not widely reported due to the typical use at a low concentration. The effectiveness of chlorine dioxide against various microorganisms, in both liquid and gaseous forms, over a wide range of pH and at an extremely low concentration has confirmed chlorine dioxide as a vital and versatile disinfectant.

Keywords: Disinfectants; Chlorine dioxide; SARS-CoV; Anti-microbial

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Introduction

Chlorine dioxide (ClO_2), a strong oxidant, has a long-standing significant role in the industrial settings as disinfectants, especially at water purification and food preparation areas, due to its wide spectrum antimicrobial property [1]. The significance of its antimicrobial role is further enhanced during the outbreak of *Bacillus anthracis* in 2001, when fumigation of vaporous hydrogen peroxide and ClO_2 was used to destroy *B. anthracis* spores, along with a combination of HEPA vacuuming, cleaning and bleach application. In this article, we revisit the efficacy and safety of ClO_2 as a suitable sanitizing agent during the current COVID-19 pandemic crisis.

Recently, it is shown that ClO_2 is a potent disinfectant in preventing infectious disease outbreaks due to its oxidative properties in eliminating microbes [2]. In gaseous form, ClO_2 is able to eliminate culturable bacteria and detoxify bioterrorism agents such as *Bacillus* spores. Moreover, ClO_2, when used as a disinfectant on surfaces, has been reported to exhibit antimicrobial properties against various kinds of microbes efficiently even in wet environments. A concentration of 700-1100 ppm of ClO_2 is also a feasible alternative in replacing glutaraldehyde-based disinfectants [3, 4]. Aside from its possibility as a potent disinfectant, ClO_2 has been reported to be a disinfectant without causing side effects due to its rapid action and safe antimicrobial properties [5]. Furthermore, ClO_2 can be used a keratolytic compound with anti-inflammatory properties but is non-toxic to human tissue [6]. In addition, this chemical compound has a history of being used in water purification and disinfection process during food preparation due to its wide spectrum of antimicrobial effects. ClO_2 is also found to be more effective than hydrogen peroxide as bleaching agent of teeth [7].

A very recent review on dermatologic reactions to various types of disinfectants used to reduce the risk of coronavirus infection indicated that ClO_2 is safe, even with prolonged skin contact [8]. ClO_2 solution is also closely examined for its potential use to inactivate viruses, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [9] and human papillomavirus (HPV) [10]. Interestingly, ClO_2 solution was also used to sterilize recycled KN95s or surgical face masks during critical shortage of such supplies [2].

Mechanisms behind the efficacy of ClO_2 against microbes

A study revealed that due to interactions between ClO_2 and biological thiol groups of amino acids, bacteria are unable to develop resistance against ClO_2 [5].

ClO_2-based disinfectants have been shown to be effective in eliminating *B. anthracis* spores in solutions and less toxic than sodium hypochlorite in an *in vitro* study with human skin keratinocytes [11]. Besides, another study has shown that virus inactivation by ClO_2 is achieved through denaturation of viral envelope proteins, thereby able to prevent aerosol-induced influenza virus infection at low concentrations [12].

The potential role of ClO_2 in completely inactivating porcine reproductive and respiratory syndrome virus (PRRSV) was demonstrated through the action of degrading the genome and proteins of the virus [4]. This study also confirmed that the expression of inflammatory cytokines induced by this virus can be reduced by ClO_2. This is further supported by studies reporting protein-denaturing activities due to covalent oxidative modification of cysteine, tryptophan and tyrosine residues of model proteins (bovine serum albumin and G6PD of *Saccharomyces cerevisiae*) as the mechanism behind the efficacy of ClO_2 against microbes [13,14]. Furthermore, 0.03 ppm of ClO_2 has been indicated to prevent aerosol-induced influenza A virus by denaturing the envelope proteins of the virus [12]. The mechanism of norovirus inactivation by ClO_2 is attained through degradation of viral protein, including viral genomic RNA and disruption of viral strucutre [15]. In addition, an observation on ClO_2-reduced lysozyme activities showed the potential role of ClO_2 in denaturation and degradation of protein using Raman spectroscopy and gel electrophoresis [16].

Revisit the literature

The wide spectrum of antimicrobial properties of ClO_2 is supported by its ability to inactivate various kinds of microbes including Gram-positive and Gram-negative bacteria, enveloped and non-enveloped viruses in low concentrations (as low as 0.05 ppm) and wet states [17]. In a quantitative bactericidal suspension test, it is demonstrated that vegetative forms of bacteria such as *Staphylococcus aureus* and *Escherichia coli* can be killed in the 100 mg/L of ClO_2 solution [18]. Furthermore, ClO_2 concentration at as low as 0.03 ppm is effective against aerosol-induced influenza virus infection in a study with mice models [12]. However, concentrations of ClO_2 equal to or more than 0.6 mg/L are required for a complete inactivation of viruses such as hepatitis A viruses, Norwalk and Norwalk-like viruses [19]. A 3-log reduction in murine norovirus 1 (MNV-1) was found when stainless steel contact surfaces were treated with ClO_2 gas at 2 mg/L for 5 minutes and 2.5 mg/L for 2 minutes while a complete virus inactivation was shown in a 1-minute treatment with 4 mg/L of ClO_2 gas [15]. Although free residues of chlorine over a concentration of 2.19 mg/L of ClO_2 in wastewater do not entirely inactivating *E. coli* and f2 phage, it is able to completely inactivate SARS-CoV [20].

Low-concentration ClO_2 gas (mean 0.05 ppmv, 0.14 mg/ m^3) treatment in an area with a high humidity is useful in decreasing the risk of infection by norovirus without side effects [17]. Furthermore, propidium monoazide (PMAxx)-viability RTqPCR assay revealed that ClO_2 is effective to a certain level in inactivating genogroup I and II Human norovirus (HuNoV) strains on contaminated food [21]. Laboratory investigations also showed that the counts of natural or inoculated microbes including bacteria, yeast and mold can be reduced effectively in the range of 1-5 log by using 3-100 ppm of ClO_2 solution [22]. Elimination of *B. subtilis* spores by ClO_2 was found due to damages to its membrane but no DNA damage [23]. Also, a study on the disinfection of wastewater revealed that ClO_2 is capable of inactivating bacteria such as coliforms although not as effective as chlorine of the same dosage [20].

Concluding Remarks

The broad-range activity against microorganisms, effectiveness over a wide pH range (pH 4.0-10.0), rapid action together with the versatility of using it in either liquid or gaseous state have conferred ClO_2 as an important disinfectant for daily use in the past two decades. In comparison to other disinfectants, ClO_2 offers a higher antimicrobial performance at an extremely low concentration with no microbial resistance developed at present.

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Conflicts of Interest

The authors declare that there is no conflict of interest in this work.

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Authors' Contributions

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