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HOCl Rapidly Kills Corona, Flu, and Herpes to Prevent Aerosol Spread

H. Guan[1], M. Nuth[1], S.R. Weiss[2], A. Fausto[2], Y. Liu[3], H. Koo[3], M.S. Wolff[4], and R.P. Ricciardi[1,5]

Abstract

The COVID-19 pandemic has escalated the risk of SARS-CoV-2 transmission in the dental practice, especially as droplet-aerosol particles are generated by high-speed instruments. This has heightened awareness of other orally transmitted viruses, including influenza and herpes simplex virus 1 (HSV1), which are capable of threatening life and impairing health. While current disinfection procedures commonly use surface wipe-downs to reduce viral transmission, they are not fully effective. Consequently, this provides the opportunity for a spectrum of emitted viruses to reside airborne for hours and upon surfaces for days. The objective of this study was to develop an experimental platform to identify a safe and effective virucide with the ability to rapidly destroy oral viruses transported within droplets and aerosols. Our test method employed mixing viruses and virucides in a fine-mist bottle atomizer to mimic the generation of oral droplet-aerosols. The results revealed that human betacoronavirus OC43 (related to SARS-CoV-2), human influenza virus (H1N1), and HSV1 from atomizer-produced droplet-aerosols were each fully destroyed by only 100 ppm of hypochlorous acid (HOCl) within 30 s, which was the shortest time point of exposure to the virucide. Importantly, 100 ppm HOCl introduced into the oral cavity is known to be safe for humans. In conclusion, this frontline approach establishes the potential of using 100 ppm HOCl in waterlines to continuously irrigate the oral cavity during dental procedures to expeditiously destroy harmful viruses transmitted within aerosols and droplets to protect practitioners, staff, and other patients.

Keywords: virucide, saliva, infection, high-speed instruments, waterlines, prevention

Introduction

Dentistry more than any other clinical profession is exposed daily to large volumes of airborne infectious agents. Protection against the broad range of known and evolving viruses and bacteria that are emitted from saliva as aerosols generated from high-speed dental devices presents an ongoing challenge to the safety of practitioners, staff, and other patients. It is compelling to reflect that saliva has been known as a source of airborne infection ever since Koch first reported the transmission of tuberculosis in aerosols nearly 140 y ago (Nield 2020). It was not until the arrival of ultrasonic scalers and high-speed devices in the late 1950s, followed by HIV/AIDS in the 1980s, that physical barrier precautions, including gloves, eyewear, face shields, and masks, as well as protocols to disinfect surfaces became routine (Nield 2020). Despite these measures, the challenge to prevent airborne infection in dentistry has never become more important since the emergence of SARS-CoV-2, the highly contagious respiratory virus responsible for the worldwide COVID-19 pandemic. In the United States alone, COVID-19 has achieved the status of becoming the greatest pandemic in history. While the recent and innovative messenger RNA (mRNA) vaccine has reduced the spread of COVID-19, new pandemic strains will continue to arise, as exemplified by the Omicron and Delta variants. Indeed, COVID-19 has emerged as the unmatched all-time challenge to dentistry that has affected patient care and dental office protocols.

Inhalation of SARS-CoV-2 leads to infection that initiates in the respiratory upper airways and progresses to the lower airways, where the virus enters the lung alveoli, causing destruction of these air sacks and resulting in loss of oxygen uptake (Ashraf et al. 2021). In a recent landmark study, the oral cavity was proven to be the major anatomical location where infectious SARS-CoV-2 is produced (Huang et al. 2021). This study revealed that the predominant hot spots of SARS-CoV-2 replication are the minor salivary glands, of which there are

[1]Department of Basic and Translational Sciences, Penn Dental Medicine, University of Pennsylvania, Philadelphia, PA, USA
[2]Department of Microbiology, Perlman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA
[3]Department of Orthodontics, Divisions of Pediatric Dentistry and Community Oral Health, School of Dental Medicine, University of Pennsylvania, Philadelphia, PA, USA
[4]Department of Preventive and Restorative Sciences, School of Dental Medicine, University of Pennsylvania, Philadelphia, PA, USA
[5]Abramson Cancer Center, School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

A supplemental appendix to this article is available online.

Corresponding Author:
R.P. Ricciardi, Department of Basic and Translational Sciences, Penn Dental Medicine, University of Pennsylvania, 240 South 40th Street, Rm 222, Levy Bldg., Philadelphia, PA 19104, United States.
Email: ricciard@upenn.edu

about 1,000 distributed throughout the mucosa (Huang et al. 2021). The major salivary glands were also shown to be factory sites for producing SARS-CoV-2. Thus, SARS-CoV-2 in saliva, which is transmissible by speaking and coughing, is mainly generated by the salivary glands, with only a minor fraction of the viral load contributed by the nasal cavity (Huang et al. 2021). Significantly, an individual with a viral load of 2.35×10^9 copies per milliliter of saliva may generate as many as 1.23×10^5 copies of airborne viruses in a single cough (Stadnytskyi et al. 2020; Wang et al. 2020). Remarkably, the viral load in saliva can be nearly equivalent between symptomatic and asymptomatic COVID-19 patients (Ra et al. 2021).

In addition to SARS-CoV-2, influenza and herpes simplex virus 1 (HSV1) are 2 major infectious agents that can reside in saliva as a source of transmission. Influenza virus is of yearly concern with a history of seasonal epidemics and several large-scale global outbreaks, as primarily exemplified by the famous pandemic of 1918, which killed 50 million people. Each year, the seasonal incidence of influenza ranges from 5% to 20% of the population (Tokars et al. 2018). Influenza is an acute respiratory disease that correlates with viral replication occurring in the epithelial cells throughout both the upper and lower respiratory tracts (Taubenberger and Morens 2008). Influenza virus is readily detected in saliva of infected individuals (Sueki et al. 2016). Aerosols and droplets generated by coughing, sneezing, talking, and breathing are major modes of influenza transmission (Tellier 2006; Tellier 2009; Leung 2021). HSV1 infections in the oral cavity appear as lesions, often referred to as cold sores or blisters on the buccal mucosa, gingiva, and hard and soft palate (Atyeo 2021). The global prevalence is approximately 63% (James 2020). The lesions are often painful and leak highly contagious fluids into saliva that enable HSV1 to become transmitted upon contact. Moreover, lifelong recurrence of the infectious oral lesions follows the initial infection, which is due to reactivation of latent HSV1 within the trigeminal ganglia (Atyeo 2021).

The dental profession has employed sound measures aimed at preventing contamination and spread of pathogens. However, the COVID-19 pandemic of 2019 has prompted the need for more stringent methods and physical redesign of dental facilities, to eliminate transmission of infectious agents, especially those that can cause severe viral diseases, such as SARS-CoV-2.

A foremost challenge is the aerosol particles produced from ultrasonic scalers and high-speed handpieces. In addition to droplets, these devices can generate 100,000 aerosolized viruses per cubic foot and project 6 feet, where they can remain suspended for up to several hours (Froum and Strange 2020). Less than optimal suction at the mouth will not sufficiently capture droplets and aerosols generated by ultrasonic scalers and high-speed handpieces (Komperda et al. 2021). Accordingly, these aerosol-producing instruments are defined by the Occupational Safety and Health Act as extremely high risk (Froum and Strange 2020).

Although standard protective procedures routinely use wipe-downs and atomizer spray to diminish and confine droplet and aerosol transmission, they are neither completely effective per se nor uniform in their application across all dental practices. Consequently, this provides the opportunity for a spectrum of emitted viruses to linger as aerosols for hours and to reside upon surfaces for days. Another protective measure is mouth rinsing with solutions comprising antimicrobial ingredients, such as chlorhexidine or povidone-iodine that reduce SARS-CoV-2 transmission during dental procedures, but they fall short of being completely and consistently effective due to intermittent and varied rinsing times among patients (Reis et al. 2021). Since the daily production of saliva ranges from 0.5 to 1.5 L/d or 0.3 to 0.4 mL/min (Lorgulescu 2009; Zhang et al. 2016; Fini 2020), the volume produced by an infected patient between intermittent rinsing can amount to several milliliters, creating an opportunity for viral transmission just by speaking and coughing. Thus, elimination of virus achieved immediately following mouth washing is not sustained due to new SARS-CoV-2 that can be introduced into saliva during intervals of rinsing.

Since the salivary glands have now been proven to be the primary source of SARS-CoV-2 production (Huang et al. 2021), a method of rapidly destroying the virus the moment it becomes delivered within saliva would greatly alleviate concerns of droplet-aerosol transmission generated by high-speed instruments. Ideally, a continuously present nontoxic virucide that kills not only SARS-CoV-2 but other oral cavity viruses, including influenza virus, HSV1, Epstein–Barr virus (EBV), and rhinoviruses, would promote universal infection control against a broad range of infectious diseases.

The goal of this study was to identify a safe and effective virucidal solution to immediately destroy viruses transmitted from the oral cavity as aerosols and droplets during dental procedures. In this study, we examined the virucidal effect of 2 disinfectants, hydrogen peroxide (H_2O_2) and hypochlorous acid (HOCl), in aerosols and droplets. We demonstrate that HOCl is a more effective virucide than H_2O_2. At 100 ppm, HOCl can completely kill the human SARS-CoV-2–related coronavirus OC43, human influenza virus (H1N1), and HSV1 that are released as droplet-aerosols from a spray-atomizer after only 30 s of contact, which is the shortest measurable time of exposure. Of utmost importance, 100 ppm HOCl introduced into the oral cavity is totally safe for humans (Lafaurie 2018). Therefore, we propose that continuous irrigation of HOCl via waterlines in all dental practices could provide a standardized and safe method of controlling transmission of SARS-CoV-2, influenza, HSV1, and other viruses within saliva droplets and aerosols.

Materials and Methods

Please see the Appendix for a description of viruses, reagents, cell lines, and the procedures of treating viruses with H_2O_2 or HOCl and quantitation of viral titers and statistical methods.

Results

An Oral Droplet-Aerosol Simulation Platform to Compare the Virucidal Actions of H_2O_2 and HOCl

Identifying a safe, effective virucide that can instantly kill oral viruses to prevent their droplet-aerosol transmission during dental procedures will provide strong protection to practitioners, staff, and patients. Two powerful oxidizing disinfectants

are H_2O_2 (Linley et al. 2012; Rutala and Weber 2016; Phaniendra et al. 2015) and HOCl (Phaniendra et al. 2015; Block and Rowan 2020), both of which can damage proteins and nucleic acids that are inherent to all viruses as well as lipids, which form a bilayer that serves as an outer envelope common to a large subset of viruses, including SARS-CoV-2, HSV1, and influenza.

We constructed an oral droplet-aerosol simulation platform to compare the antiviral efficacy of H_2O_2 and HOCl (Fig. 1). For this procedure, virus was first mixed with saliva (or control ddH_2O) in a fine-mist bottle atomizer (representing the oral cavity) in which either H_2O_2 or HOCl (representing a virucide in the dental waterline) was then added. After contact times of 30 s, 1 min, or 5 min, viral droplet-aerosols were generated from the atomizer and introduced into separate flasks. The titers of infectious virus in the settled droplet-aerosols that survived virucidal treatment were then quantitated by plaque reduction assays and/or by measurement of the 50% tissue culture infective dose ($TCID_{50}$).

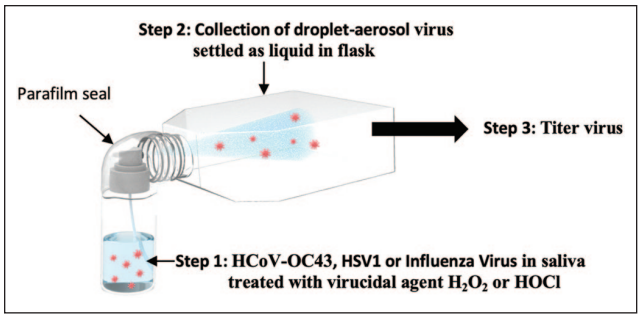

Figure 1. Platform for simulating virus-laden saliva aerosols treated with virucidal agents hydrogen peroxide (H_2O_2) or hypochlorous acid (HOCl) for blocking infection of cultured cells. **Step 1.** To simulate the formation of viral aerosols and droplets generated by dental procedures, 1 volume of human coronavirus OC43 (~10^6 plaque-forming units [PFU]) or herpes simplex virus 1 (HSV1) (~10^7 PFU) or human influenza virus (H1N1) (10^7 PFU) was first mixed with 3 volumes of human saliva or control ddH_2O in a spray-bottle atomizer (representing the oral cavity), followed by addition of H_2O_2 or HOCl (representing application via the dental waterline); the final volume of the mixture was 3 mL. After 30 s, 1 min, and 5 min, respectively, virus was aerosolized by triggering the actuator nozzle of the vertically held spray-bottle atomizer 3 times into a horizontally positioned flask. To avoid releasing viral particles outside the flasks, the orifices were sealed with Parafilm. **Step 2.** After 1 min, the portion of aerosolized virus that had settled as liquid was collected from each flask and neutralized by serial dilutions. **Step 3.** Virus titers were determined by plaque reduction assays and/or by measurement of the 50% tissue culture infective dose (TCID50).

Virucidal action of H_2O_2 against HSV1 is not effective in a short contact time. We first tested inhibition of HSV1 infection following treatment with 1%, 2%, and 3% H_2O_2 for 30 s, 1 min, and 5 min, respectively. As shown in Figure 2A, in the absence of saliva, HSV1 was inactivated by H_2O_2 in both a dose-dependent and a contact time–dependent manner. As shown in Figure 2B, in the presence of saliva, the trends were the same but less efficient, likely due to the possible breakdown of H_2O_2 by salivary catalase and peroxidase enzymes as well as the presence of competing cellular protein substrates, including amylase, lipase, immunoglobulins (IgA), and mucins. While increasing times and concentrations of H_2O_2 caused a striking decrease in HSV1 infection, complete inhibition was never absolutely achieved in either the absence or the presence of saliva (Fig. 2A, B, respectively).

A detailed examination of the data in Figure 2 reveals that in the absence of saliva, 8.3% and 1.2% HSV1 survived treatment with 3% H_2O_2 for 30 s and 1 min, respectively (Fig. 2A, rightmost panel), which represents 91.7% to 98.8% efficacy of virus killing. By contrast, in the presence of saliva, as much as 22.2% and 12.4% HSV1 survived treatment with 3% H_2O_2 for 30 s and 1 min, respectively (Fig. 2B, rightmost panel). However, when the contact time was extended to 5 min, 3% H_2O_2 was able to destroy 99.4% HSV1 even in the presence of saliva, nearly equivalent to the 99.7% virucidal efficacy without saliva (rightmost panels of Fig. 2A, B). Compared with 3% H_2O_2, lower concentrations of H_2O_2 at 1% and 2% exhibited dramatically less potency in HSV1 inactivation, especially in the presence of saliva (Fig. 2A, B, left and center panels). It is noted that saliva per se exhibited little or no effect on Vero cells used for the viral plaque reduction assays but did have a minor inhibitory effect on plaque formation by the virus.

Virucidal action of HOCl against HSV1 is very effective. We next tested the virucidal efficacy of HOCl against HSV1 in the plaque reduction assay. The results shown in Figure 3A reveal that in the absence of saliva, 100% HSV1 was destroyed by HOCl at all concentrations and times, except at the lowest dose (10 ppm) and shortest time (30 s) in which 1.2% of virus survived (Fig. 3A). By contrast, as shown in Figure 3B (left and center panels), in the presence of saliva, HOCl was less efficient at eliminating HSV1 infection at the lower doses of 10 ppm and 20 ppm with the single exception of 20 ppm for 5 min, in which HSV1 infection was completely nullified. Dramatically, however, as shown in Figure 3B (right panel), in the presence of saliva, 100% of HSV1 was eliminated by contact with 30 ppm HOCl within just 30 s, as well as contact times of 1 min and 5 min.

Virucidal action of HOCl against coronavirus OC43 is greatly effective. The above experiments using HSV1 clearly demonstrated that HOCl is exceedingly more potent than H_2O_2 in inactivating HSV. Hence, we assessed HOCl for its virucidal efficacy against OC43, which, like SARS-CoV-2, is subclassified as a *Betacoronavirus*, 1 of the 4 genera of coronaviruses (Singh et al. 2021). We used OC43 as a surrogate for SARS-CoV-2, since OC43 has milder pathogenicity (Garcia-Beltran et al. 2021) and can be easily handled in a biosafety level 2 (BSL-2) cabinet. We found that compared with HSV1, OC43 was more resistant to HOCl. Following exposure to 30 ppm and even 50 ppm HOCl, a residual fraction of OC43 persisted at each virucidal contact time (30 s, 1 min, 5 min) in both the presence and the absence of saliva (Fig. 4A, B, left and center panels). In striking contrast, OC43 was completely destroyed

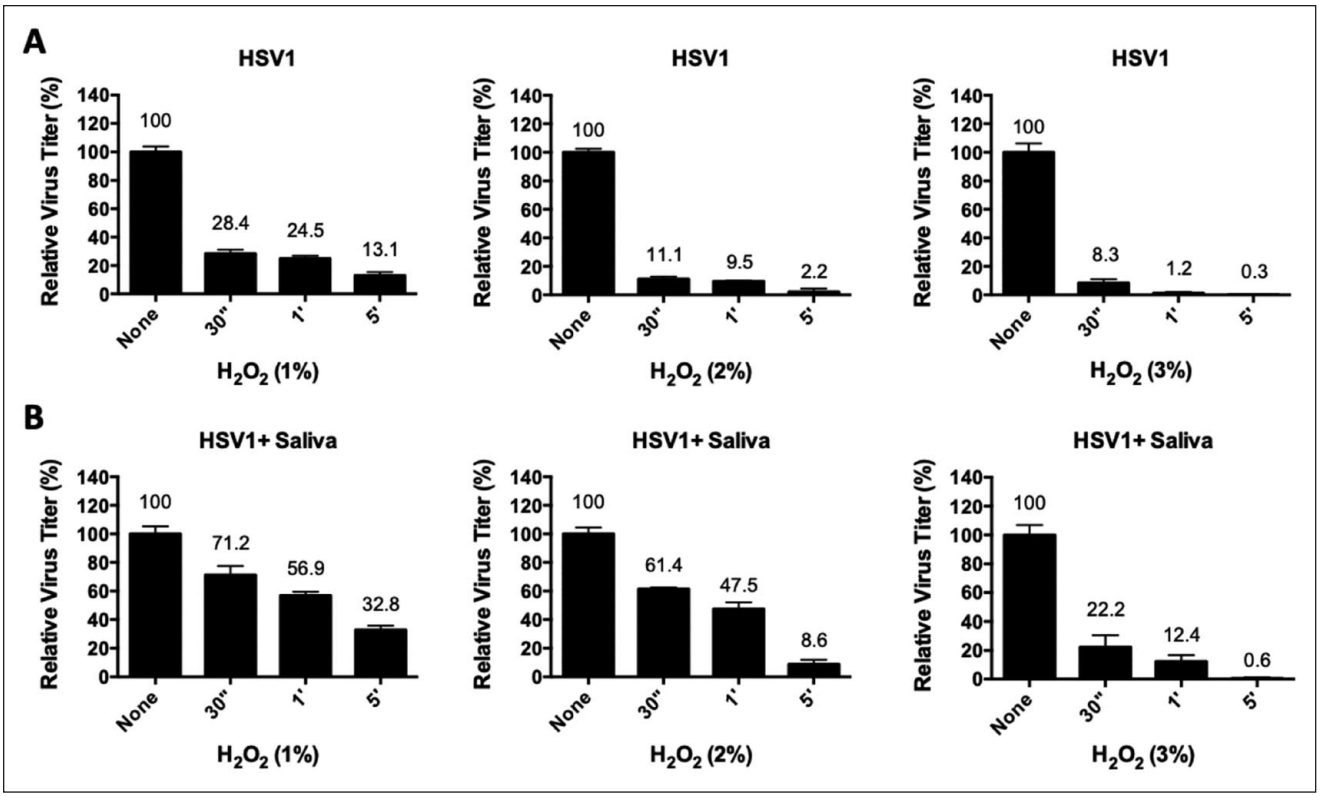

Figure 2. Virucidal efficacy of hydrogen peroxide (H_2O_2) against herpes simplex virus 1 (HSV1). HSV1 (~10^7 plaque-forming units [PFU]) was treated with 1%, 2%, or 3% H_2O_2 in a spray atomizer in the absence (**A**) or in the presence (**B**) of saliva for 30 s, 1 min, and 5 min, respectively. Each viral treatment was aerosolized by spraying into a collection flask. Droplet-aerosols that had settled after 1 min were serially diluted, and virus titers were determined by plaque reduction assays performed in triplicate. The data represent mean ± SD from at least 2 independent experiments. The relative mean virus titers are shown. "None" refers to treatment with water as a negative control. $P \leq 0.0003$ for all treatments versus control.

within 30 s in 100 ppm HOCl, in both the absence and the presence of saliva (Fig. 4A, B, rightmost panels).

These plaque reduction assay results were confirmed by quantitating the $\log_{10}$ reduction of OC43 by HOCl, using the median tissue culture infectious dose ($TCID_{50}$) assay (Reed and Muench 1938). These $TCID_{50}$ assay quantitative results are in complete agreement with the respective OC43 survival rates of 3.7% (50 ppm) and 0% (100 ppm) obtained from the plaque reduction assay (Fig. 4B, center and right panels).

Virucidal action of HOCl against influenza virus is greatly effective. We next examined HOCl for its virucidal efficacy against human influenza subtype H1N1 virus using the oral simulation platform. As determined by the plaque reduction assay shown in Figure 5A, B, 100% influenza H1N1 was destroyed completely by 100 ppm HOCl within 30 s in both the absence and the presence of saliva. At the lower 30 ppm and 50 ppm concentrations of HOCl, there was a small amount of remaining virus after 30 s in the presence or absence of saliva, as indicated in Figure 5A, B.

Discussion

Dentistry has made extraordinary progress over the past decades in protecting personnel and patients from practice-acquired infections. SARS-CoV-2, responsible for the COVID-19 pandemic, however, has presented the profession its latest and greatest challenge, requiring the modification of office heating, ventilation, and air conditioning (HVAC) and the utilization of well-fitting NIOSH (National Institute for Occupational Safety and Health)–approved respirators for personnel protection in the work environment. The urgency to find an efficacious means of diminishing this risk is intensified by the realization that despite being vaccinated, dental patients may carry variants of SARS-CoV-2 that escape immunization (Garcia-Beltran et al. 2021) and continue to be shed from epithelial cells that line the salivary glands, which are the major sites for viral production (Huang et al. 2021). The problem is further heightened by the fact that even asymptomatic patients have the potential to shed SARS-CoV-2 (Ra et al. 2021).

A new method of immediately halting viral transmission is needed. Most of the current protective methods are aimed at destroying SARS-CoV-2 after being emitted as droplets and aerosols by high-speed instruments. These methods, which include surface decontamination and negative air filtration, are not guaranteed to be completely reliable due to variation among practices. In vitro and clinical studies using mouthwashes comprising povidone-iodine or other virucides indicated that preprocedural mouth rinsing could effectively destroy SARS-CoV-2 in saliva (reviewed in Chen and Chang 2022; Garcia-Sanchez

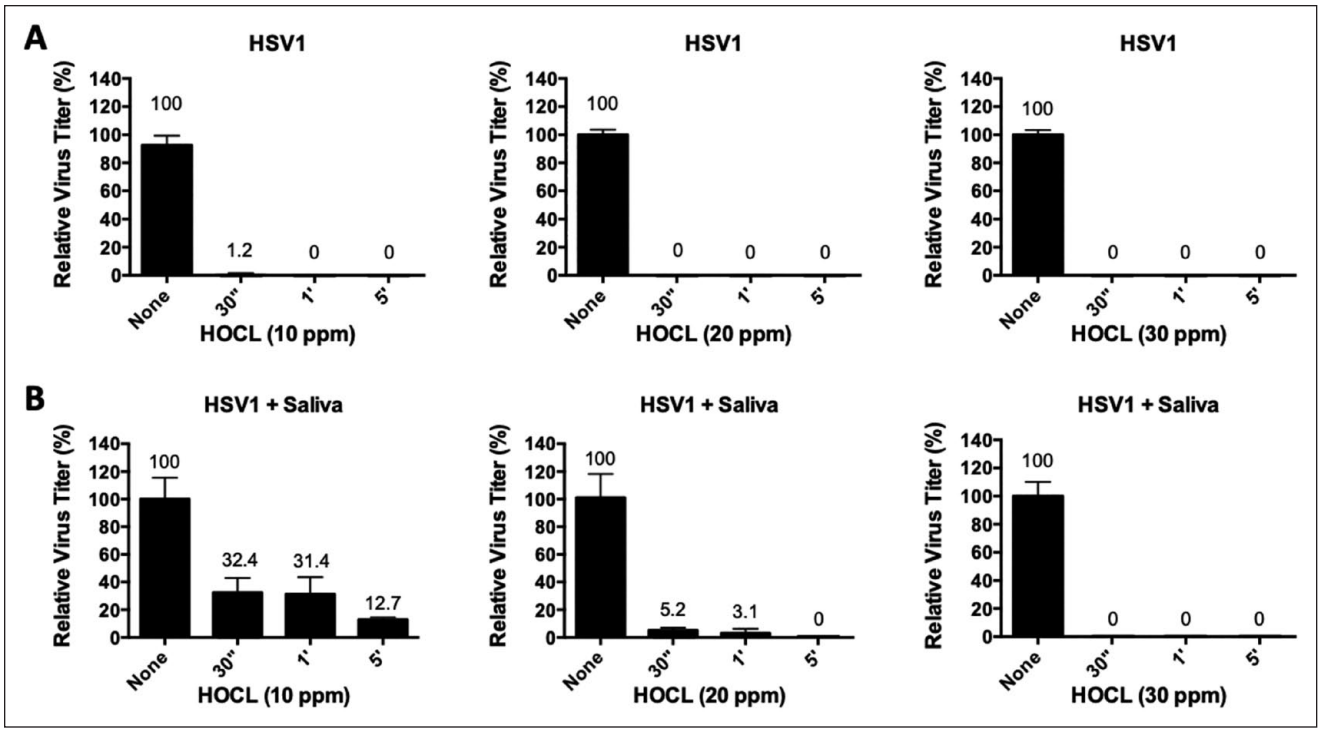

Figure 3. Virucidal efficacy of hypochlorous acid (HOCl) against herpes simplex virus 1 (HSV1). HSV1 (~10^7 plaque-forming units [PFU]) was mixed with 10 ppm, 20 ppm, or 30 ppm HOCl in a spray atomizer (refer to Fig. 1) in the absence (**A**) or in the presence (**B**) of saliva for 30 s, 1 min, and 5 min, respectively. Each viral treatment was aerosolized by spraying into a collection flask. Droplet-aerosols that had settled after 1 min were serially diluted, and virus titers were determined by plaque reduction assays performed in triplicate. The data represent mean ± SD from at least 2 independent experiments. The relative mean virus titers are shown. "None" refers to treatment with water as a negative control. $P \leq 0.0003$ for all treatments versus control.

et al. 2022). However, even these mouthwashes, which are intended to destroy viruses prior to expulsion by high-speed instruments as lethal cargo within droplet-aerosols, are not totally reliable. This drawback of mouthwashes is due to inconsistent timing and length of rinsing among patients, providing an opportunity for continuously shed SARS-CoV-2 to be incorporated into emitted droplet-aerosols.

An ideal method for preventing droplet-aerosol spread of viruses is to introduce via the dental waterline a reagent that remains continuously present at a concentration that is safe and yet capable of rapidly killing not only SARS-CoV-2 but also different viruses such as influenza and HSV1 that are examples of yearly and recurrent infectious agents. As a first step toward this goal, we devised an experimental platform that simulates the oral cavity to identify a nontoxic virucide, HOCl, that can rapidly destroy viruses that are released with droplet-aerosols. Our findings revealed that the human betacoronavirus OC43 (similar to SARS-CoV-2), H1N1, and HSV1 were each completely destroyed within 30 s upon exposure to 100 ppm HOCl. Interestingly, compared with OC43 and H1N1, HSV1 is more sensitive to HOCl destruction (refer to Figs. 3–5). Unlike many other viruses, HSV1 requires the coordination of multiple envelope glycoproteins including gB, gD, gH, and gL for cell entry and infection (Madavaraju et al. 2021). We speculate that damage of any of these glycoproteins by HOCl is able to destroy HSV1 infectivity, thus making it more susceptible to HOCl. Viral destruction is likely instantaneous given that 30 s was the shortest possible time for terminating exposure to HOCl. Significantly, 100 ppm HOCl is well within the safety range, considering that certain mouthwashes contain 500 ppm HOCl (Lafaurie et al. 2018). In contrast to virucidal chemicals used in many mouthwashes (e.g., povidone-iodine), HOCl is an endogenous product in all mammals and has a good safety profile (Block and Rowan 2020). Notably, HOCl has proven to be a bacterial disinfectant of dental waterlines per se (Shajahan et al. 2016).

While our oral simulation platform demonstrated that 100 ppm HOCl can kill viruses rapidly in droplets and aerosols, validation of its actual virucidal effect in dental waterlines remains pending until several variables, including flow rate, contact time of oral viruses with HOCl, and patient saliva secretion, are evaluated. A randomized clinical trial study is needed to address these issues and confirm the beneficial application of HOCl in dental procedures.

Conclusion

The COVID-19 pandemic has prompted the urgency to employ an effective means of destroying SARS-CoV-2 contained within droplet-aerosols generated by high-speed dental instruments. This requirement is especially significant since SARS-CoV-2 is produced continuously in the salivary glands of

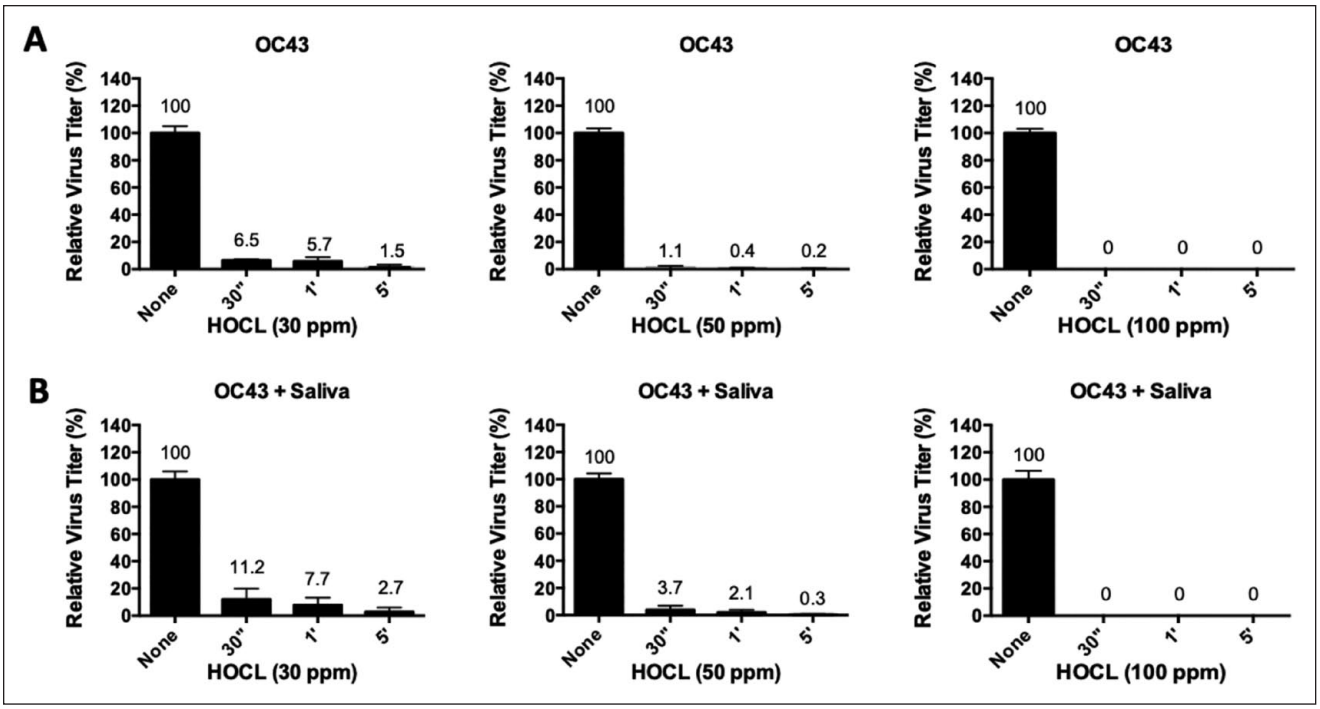

Figure 4. Virucidal efficacy of hypochlorous acid (HOCl) against OC43 coronavirus. OC43 (~10^6 plaque-forming units [PFU]) was treated with 30 ppm, 50 ppm, or 100 ppm HOCl in a spray atomizer in the absence (**A**) or presence (**B**) of saliva for 30 s, 1 min, and 5 min, respectively. Each viral treatment was aerosolized by spraying into a collection flask. Droplet-aerosols that had settled after 1 min were serially diluted, and virus titers were determined by plaque reduction assays performed in triplicate. The data represent mean ± SD from at least 2 independent experiments. The relative mean virus titers are shown. "None" refers to treatment with water as a negative control. $P \leq 0.0001$ for all treatments versus control.

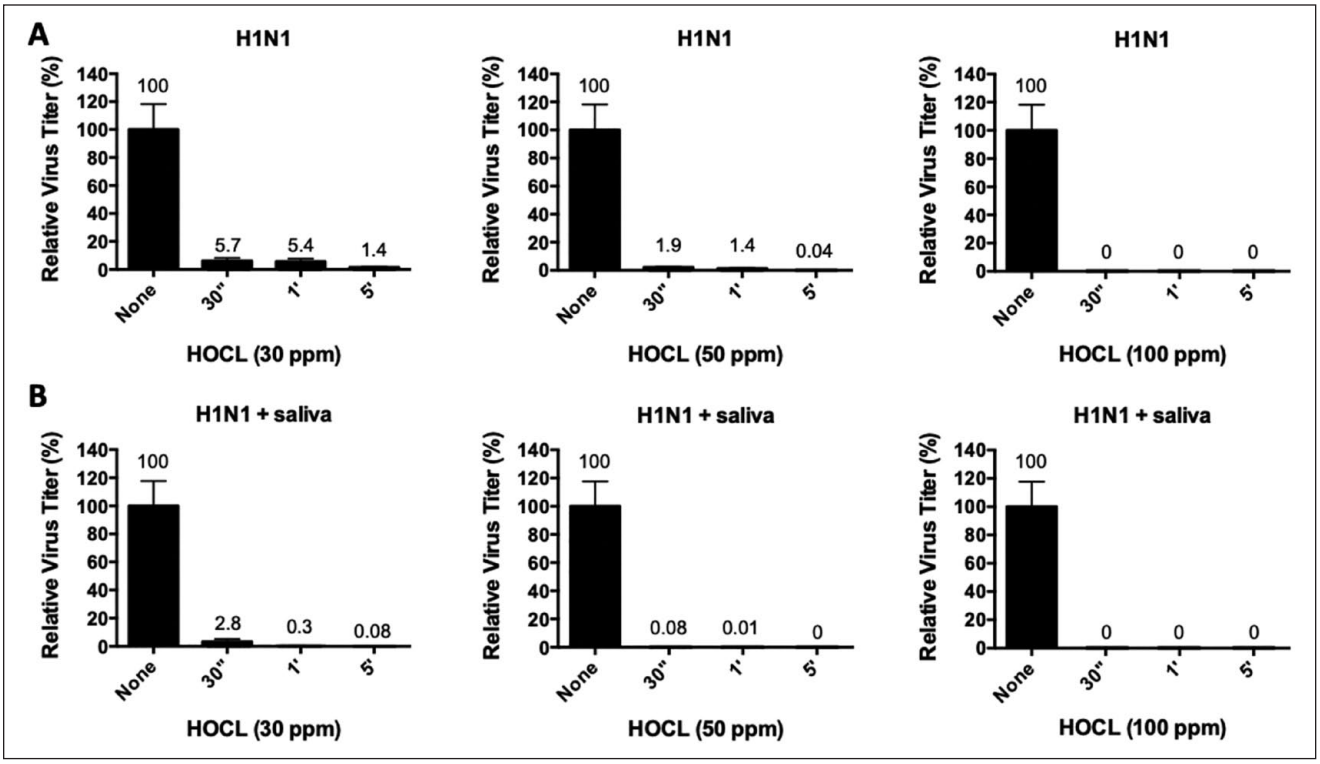

Figure 5. Virucidal efficacy of hypochlorous acid (HOCl) against human influenza virus (H1N1). H1N1 (10^7 plaque-forming units [PFU]) was treated with 30 ppm, 50 ppm, or 100 ppm HOCl in a spray atomizer in the absence (**A**) or presence (**B**) of saliva for 30 s, 1 min, and 5 min, respectively. Each viral treatment was aerosolized by spraying into a collection flask. Droplet-aerosols that had settled after 1 min were serially diluted, and virus titers were determined by plaque reduction assays performed in triplicate. The data represent mean ± SD from at least 2 independent experiments. The relative mean virus titers are shown. "None" refers to treatment with water as a negative control. $P \leq 0.0001$ for all treatments versus control.

infected individuals. Our findings revealed that 100 ppm HOCl can completely kill SARS-CoV-2 within 30 s. A further significant outcome of this study was demonstrating that other important oral viruses—namely, influenza virus and HSV1—can also be equally destroyed by 100 ppm HOCl in 30 s. Importantly, HOCl at 100 ppm is known to be safe. This study provides the potential of using 100 ppm HOCl in dental waterlines as a means for enhancing the protection of providers, staff, and patients from infection by viral transmission.

Author Contributions

H. Guan, contributed to acquisition, analysis, and interpretation of data, critically revised the manuscript; M. Nuth, contributed to data analysis, critically revised the manuscript; S.R. Weiss, contributed to data acquisition of data, critically revised the manuscript; A. Fausto, contributed to data acquisition of data, critically revised the manuscript; Y. Liu, contributed to data acquisition of data, critically revised the manuscript; H. Koo, contributed to conception and design, data analysis and interpretation, drafted and critically revised the manuscript; M.S. Wolff, contributed to conception and design, data analysis and interpretation, drafted and critically revised the manuscript; R.P. Ricciardi, contributed to conception and design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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ORCID iDs

M.S. Wolff https://orcid.org/0000-0003-2314-0519
R.P. Ricciardi https://orcid.org/0000-0002-2206-3657

References

Ashraf UM, Abokor AA, Edwards JM, Waigi EW, Royfman RS, Hasan SA, Smedlund KB, Hardy AMG, Chakravarti R, Koch LG. 2021. SARS-CoV 2, ACE2 expression, and systemic organ invasion. Physiol Genomics. 53(2):51–60.

Atyeo N, Rodriguez MD, Papp B, Toth Z. 2021. Clinical manifestations and epigenetic regulation of oral herpesvirus infections. Viruses. 13(4):681–698.

Block MS, Rowan BG. 2020. Hypochlorous acid: a review. J Oral Maxillofac Surg. 78(9):1461–1466.

Chen MH, Chang PC. 2022. The effectiveness of mouthwash against SARS-CoV-2 infection: a review of scientific and clinical evidence. J Formos Med Assoc. 121(5):879–885.

Fini MB. 2020. Oral saliva and COVID-19. Oral Oncol. 108:104821.

Froum S, Strange M. 2020. COVID-19 and the problem with dental aerosols. Perio-Impant Advisory. [accessed 3.37.2-23]. https://www.perioimplantadvisory.com/periodontics/oral-medicine-anesthetics-and-oral-systemic-connection/article/14173521/covid19-and-the-problem-with-dental-aerosols

Garcia-Beltran WF, Lam EC, St Denis K, Nitido AD, Garcia ZH, Hauser BM, Feldman J, Pavlovic MN, Gregory DJ, Poznansky MC, et al. 2021. Multiple SARS-CoV-2 variants escape neutralization by vaccine-induced humoral immunity. Cell. 184(9):2372–2383.

Garcia-Sanchez A, Peña-Cardelles JF, Ordonez-Fernandez E, Montero-Alonso M, Kewalramani N, Salgado-Peralvo AO, Végh D, Gargano A, Parra G, Guerra-Guajardo LI, et al. 2022. Povidone-iodine as a pre-procedural mouthwash to reduce the salivary viral load of SARS-CoV-2: a systematic review of randomized controlled trials. Int J Environ Res Public Health. 19(5):2877.

Huang N, Perez P, Kato T, Mikami Y, Okuda K, Gilmore RC, Conde CD, Gasmi B, Stein S, Beach M, et al. 2021. SARS-CoV-2 infection of the oral cavity and saliva. Nature Med. 27(5):892–903.

James C, Harfouche M, Welton NJ, Turner KM, Abu-Raddad LJ, Gottlieb SL, Looker KJ. 2020. Herpes simplex virus: global infection prevalence and incidence estimates, 2016. Bull World Health Organ. 98(5):315–329.

Komperda J, Peyvan A, Li D, Kashir B, Yarin AL, Megaridis CM, Mirbod P, Paprotny I, Cooper LF, Rowan S, et al. 2021. Computer simulation of the SARS-CoV-2 contamination risk in a large dental clinic. Phys Fluids. 33(3):033328.

Lafaurie GI, Zaror C, Díaz-Báez D, Castillo DM, De Ávila J, Trujillo TG, Calderón-Mendoza J. 2018. Evaluation of substantivity of hypochlorous acid as an antiplaque agent: a randomized controlled trial. Int J Dent Hyg. 16(4):527–534.

Leung NHL. 2021. Transmissibility and transmission of respiratory viruses. Nat Rev Microbiol. 19(8):528–545.

Linley E, Denyer SP, McDonnell G, Simons C, Maillard J-Y. 2012. Use of hydrogen peroxide as a biocide: new consideration of its mechanisms of biocidal action. J Antimicrob Chemother. 67(7):1589–1596.

Lorgulescu GJ 2009. Saliva between normal and pathological important factors in determining systemic and oral health. J Med Life. 2(3):303–307.

Madavaraju K, Koganti R, Volety I, Yadavalli T, Shukla D. 2021. Herpes simplex virus cell entry mechanisms: an update. Front Cell Infect Microbiol. 10:617578.

Nield HA. 2020. A short history of infection control in dentistry. BDJ Team. 7(8):12–15.

Phaniendra A, Jestadi DB, Periyasamy L. 2015. Free radicals: properties, sources, targets, and their implication in various diseases. Ind J Clin Biochem. 30(1):11–26.

Ra SH, Lim JS, Kim G, Kim MJ, Jung J, Sung-Han Kim S-H. 2021. Upper respiratory viral load in asymptomatic individuals and mildly symptomatic patients with SARS-CoV-2 infection. Thorax. 76(1):61–63.

Reed LJ, Muench H. 1938. A simple method of estimating fifty per cent endpoints. Am J Hyg. 27(20):493–497.

Reis INR, Silva do Amaral GCL, Mendoza AAH, Teixeira das Gracas Y, Mendes-Correa MC, Romito GA, Pannuti CM. 2021. Can preprocedural mouthrinses reduce SARS-CoV-2 load in dental aerosols? Med Hypotheses. 146:110436.

Rutala WA, Weber DJ. 2016. Disinfection and sterilization in healthcare facilities: an overview and current issues. Infect Dis Clin North Am. 30(3):609–637.

Shajahan IF, Kandaswamy D, Srikanth P, Narayana LL, Selvarajan R. 2016. Dental unit waterlines disinfection using hypochlorous acid-based disinfectant. J Conserv Dent. 19(4):347–350.

Singh J, Pandit P, McArthur AG, Banerjee A, Mossman K. 2021. Evolutionary trajectory of SARS-CoV-2 and emerging variants. Virol J. 18(1):166.

Stadnytskyi V, Bax CE, Bax A, Philip Anfinrud P. 2020. The airborne lifetime of small speech droplets and their potential importance in SARS-CoV-2 transmission. Proc Natl Acad Sci. 117(22):11875–11877.

Sueki A, Matsuda K, Yamaguchi A, Uehara M, Sugano M, Uehara T, Honda T. 2016. Evaluation of saliva as diagnostic materials for influenza virus infection by PCR-based assays. Clin Chim Acta. 453:71–74.

Taubenberger JK, Morens DM. 2008. The pathology of influenza virus infections. Annu Rev Pathol. 3:499–522.

Tellier R. 2006. Review of aerosol transmission of influenza A virus. Emerg Infect Dis. 12(11):1657–1662.

Tellier R. 2009. Aerosol transmission of influenza A virus: a review of new studies. J R Soc Interface. 6(Suppl 6):S783–S790.

Tokars JI, Olsen SJ, Reed C. 2018. Seasonal incidence of symptomatic influenza in the United States. Clin Infect Dis. 66(10):1511–1518.

Wang Y, Xu G, Huang Y-W. 2020. Modeling the load of SARS-CoV-2 virus in human expelled particles during coughing and speaking. PLoS One. 15(10):e0241539.

Zhang CZ, Cheng XQ, Li JY, Zhang P, Yi P, Xu X, Zhou XD. 2016. Saliva in the diagnosis of diseases. Int J Oral Sci. 8(3):133–137.