Facility Management and its potential new role in active infection control

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Abstract

Indoors, pathogen-carrying aerosol particles are recognized as important infection carriers like those in the current Corona pandemic. This infection route is often underestimated yet represents the infection route that has been least systematically addressed by counter measures to date. Current indoor safety measures (e.g.: distancing, masks, filters) provide only limited protection. Inhalation of hypochlorous acid (HOCl) containing aerosols was recently shown in several studies to be safe and effective in prevention and even in reduction of symptoms of already infected individuals (E. Rasmussen, Robins, and Williams 2021; Boecker et al. 2021b; 2021a; Wang L et al. 2007). We investigated a novel air-disinfection concept utilizing the potential of vaporized HOCl for populated facilities. Aerosolized bacterial microbes were used as surrogates for a viral contamination, particularly the enveloped coronavirus. For the facility air purification tests, we aerosolized bacterial suspensions into a controlled office space. The HOCl concentration was held at constant concentration with a software-controlled injection system (product: aerosolis® device; manufacturer: oji Europe GmbH, Nauen, Germany) and a special HOCl gas sensor unit (manufacturer: Draeger AG, Lübeck, Germany). We confirmed the disinfecting power of the used HOCl in suspensions and demonstrated the high efficacy of vaporized HOCl to deactivate airborne pathogens at safe and non-irritant levels (Test Laboratory: Microbiology Lab of Henkel, Düsseldorf, Ger-many). Incorporating this air-disinfection technology into building ventilation systems could be a valuable contribution for future infection prevention and control. It may take facility management to a new level of providing environmental safety.

Keywords: Hypochlorus acid, Indoor air cleaning, Infection control, Protective atmosphere

Introduction

Hypochlorous acid (HOCl) is a potent broad spectrum fast-acting antimicrobial agent with a favorable safety profile. It also is key actor of the body's innate immune response system offering the highest redox potential of all physiological intracellular occurring defense mechanisms. It was entered into the 'List N' of United States Environmental Protection Agency (EPA) for use in disinfection against the pandemic coronavirus (EPA n.d.; Ryan 2010).

All practical pathways of administering HOCl have been investigated and demonstrated a safe and effective way to enhance or complement the body's innate immune response. The methods span nasal and pharyngeal inhalation, topical applications (e.g.: wound care), and gastro-intestinal and even systemic intra-venous (i.v.) delivery. Increasing evidence is emerging of the beneficial effects of inhaling micro aerosolized hypochlorous acid (HOCl) as a routine intervention in the prevention and treatment of respiratory virus infections, including SARS CoV-2 (E. Rasmussen, Robins, and Williams 2021; Boecker et al. 2021b; 2021a; Wang L et al. 2007). The treatments reduce nasal and pharyngeal viral load and can minimize the progression and spread of the disease.

Nasal-spray treatments with aqueous HOCl solutions for fighting respiratory tract viruses have been explored in several pre-clinical trials (Yu et al. 2017; Burd 2020; 2019; Gutiérrez-García et al. 2022; Delgado-Enciso et al. 2021; E. Rasmussen, Robins, and Williams 2021; Giarratana et al. 2021). These HOCl nasal-spray formulations have shown bactericidal, fungicidal, and virucidal effects (Kim et al. 2008; Wu, Lin, and Jiang 2018; Giarratana et al. 2021; Yu et al. 2017; Sang Yu et al. n.d.; Cho et al. 2016; Bale et al. 2020; Yu MS, Park HW, Kwon HJ 2011; Gutiérrez-García et al. 2022; Stathis et al. 2021). Several of these antiseptics have demonstrated in vitro the ability to cut the viral load of SARS-CoV 2 in 15–30 seconds by 3–4 log10 levels. Several such products are already commercially available for prevention or early treatment of COVID 19 and have shown promising results (Burd 2020; product information: "Esteriflu® Nasal Antiseptic" n.d.). In this way HOCl has proven to serve as a potential solution for upper respiratory tract hygiene to assist intra-cellular defense mechanisms by its extra-cellular attack on pathogens (during the incubation phase of the infection when the virus is adsorbed at the mucosa and not yet inserted its RNA into intracellular space (Burd 2020).

It is important to differentiate the use of HOCl from an unqualified use of common place disinfectants which unfortunately has become popular as a response to the current pandemic. Basically, all of these common disinfectants are inappropriate and harmful for aerosolized use patterns in populated facilities (E. Rasmussen, Robins, and Williams 2021; Zheng, Filippelli, and Salamova 2020; Dindarloo et al. 2020; Dewey et al. 2021). Toxicological evidence of serious adverse side-effects of repeated exposures, especially by inhalation of aero-sols, are emerging (Dewey et al. 2021).

Extensive research has been done previously with exposure to such disinfectant compounds, that is, quaternary ammonium salts (QAS), sodium hypochlorite, hydrogen peroxide, ozone, glutaraldehyde, and alcohols of various types. All of these were linked with an increased risk of either chronic obstructive pulmonary disease (COPD), asthma, and eye irritation on health workers and individuals when used regularly for internal or respiratory interventions (Rai, Ashok, and Akondi 2020; Casey et al. 2017; Dumas et al. 2019; Weinmann et al. 2019; Bracco et al. 2005). Also, the harmful and toxic effect of strong alkaline solutions of sodium hypochlorite (NaOCl) is often confused with the safe utilization of vaporized hypochlorous acid (HOCl) (Ashok, and Akondi 2020; Casey et al. 2017; Dumas et al. 2019; Weinmann et al. 2019).

Safety of any HOCl application is of course the most important concern. HOCl, when used as the sole component within approved limits, shows no negative side effects on living cells in topical, inhaling and even systemic applications. In animal studies with vaporized HOCl (way beyond necessary limits to be effective as a virucide) no detectable blood parameter change, nor any significant change of lung function was observed (Burd 2020). Also, in hu-man studies no observable changes in the endoscopic scores were detected after 8 weeks of regular exposure with HOCl via nasal irrigation (Yu et al. 2017). Thus, HOCl application could be considered safe to be used from a facility management perspective.

Methods and Materials

1.4. Suspension Tests

The biocidal effect of HOCl was demonstrated by a series of standard suspension deactivation tests, performed according to the methods of DIN EN 1656:2019 and CEN Technical committee 216: EN 1276, 13624, and 14476. This is important to prove efficacy of HOCl.

1.5. Room Air Purification

For room air purification tests, we aerosolized bacterial suspensions (with a protein load of 0.1 or 0.3 %) into lab chambers preloaded with a constant level of vaporized HOCl. The HOCl concentration was measured with special gas sensors (manufacturer: DRÄGER GmbH, Lübeck, Germany) and maintained at constant level with a software-controlled vaporization device (product: aerosolis® (manufacturer: oji Europe GmbH, Nauen, Germany). Tests were carried out in two controlled measuring chambers (1m3 and 34 m3). The comparison and especially the experiments in the large chamber allow to draw conclusions regarding the efficacy of the application in regular rooms.

A newly developed two-step experimental procedure was used to determine the efficacy of vaporized biocide in the gas phase (no standard procedure is available yet):

1. *1. Determination of bacterial self-decay ('BLANCs')*
2. *2. Measurement of HOCl biocidal effectiveness*

Aerosolizing a bacterial suspension into a test chamber with an HOCl laden atmosphere results in a concentration/time profile determined by three factors: (1) number of injected bacteria, (2) self-decay rate of aerosolized bacteria, and (3) HOCl biocidal effect. Taking separate BLANC measurements (baseline) and HOCl laden measurements (cumulated bacterial self-decay and HOCl effect), allows to net out the biocidal HOCl effect.

1.6. Materials

Used test organisms for suspension tests: Enterococcus hirae DSM 3320 (corresponding to ATCC 10541), Pseudomonas aeruginosa DSM 939 (ATCC 15442), Staphylococcus aureus DSM 799 (ATCC 6538), Escherichia coli K12 DSM 11250 (NCTC 10538) and Candida albicans DSM 1386 (ATCC 10231). Vaccinia virus (strain Elstree) ATCC VR-1549 was used as test virus in combination withVero-B4-A 33 (DSM) indicator cells.

Test organisms used for room air purification: Staphylococcus aureus and Staphylococcus warnerii, Pseudomonas aeruginosa, and Escherichia coli K12 (strains all as above).

Table 1: Investigated microbes in aerosolization experiments

Bacterium	Type	Envelope
Pseudomonas aeruginosa	gram -	liquid membrane
Staphylococcus aureus	gram +	murein capsid
Staphylococcus warnerii	gram +	murein capsid
Escherichia coli	gram -	liquid membrane

A commercial preparation of Hypochlorous acid was used as biocidal agent: Biodyozon Clean Air (manufacturer. Biodyozon GmbH, Dreieich, Germany) with a 1,000 ppm HOCl stock solution, diluted with distilled water to 500 ppm.

Results

1.1. Suspension Tests

In standard suspension experiments we tested all relevant organisms with varying concentrations of our HOCl solution at low soil conditions (0.03% protein). Vaccinia virus as a model for enveloped viruses appeared to be even more sensitive. An overview of the obtained RF values is given in the following table:

Table 2: Biocidal effect of HOCl on various microbes [suspension tests]

	Pseudom. aeruginosa	**Staph. aureus**	**E. hirae**	**E. coli**	**C. albicans**	**Staph. warnerii**	**Vaccinia virus**
C [ppm]	**Standard: EN 1276**				**EN 13624**	**Additional organism**	**EN 144476**
800	**>5,33**	**>5,22**	**>5,16**	**>5,11**		nt	**4,75**
400	**>5,33**	**>5,22**	**>5,16**	**>5,11**	**>4,11**	nt	nt
300	**>5,46**	**>5,32**	**>5,54**	**>5,05**		nt	**4,75**
200	**>5,46**	**>5,32**	**>5,54**	**>5,05**	**>4,11**	**>5,50**	**4,50**
50	2,74	<0,95	1,52	4,53	<0,74	1,66	**4,00**
10	<1,09	<0,95	<1,17	<0,68		<0,68	0,50

Under the selected conditions (room temperature, low organic load and incubation time 30 sec), sufficient efficacy was found for all organisms (4 bacteria according to EN 1276, C. albicans according to EN 13624 as well as vaccinia virus according to EN 14476) at concentrations from 200 ppm HOCl. At a concentration of 50 ppm, however, efficacy against bacteria and yeasts was no longer sufficient. Against vaccinia virus, 50 ppm was still just sufficient, but 10 ppm no longer.

1.2. Room Air Purification Tests

The following graph shows the result of a typical HOCl induced biocidal measurement together with the corresponding BLANC test run. The dotted lines represent the exponential fits of the two curves for the period post the bacterial injection phase (t > 300 s).

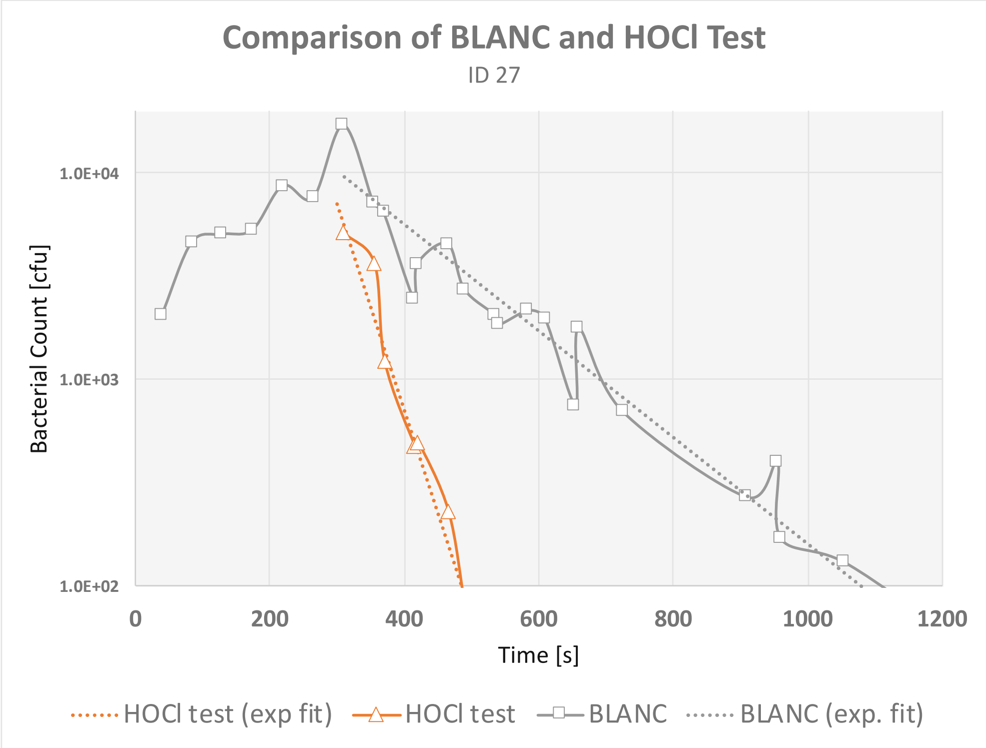

Fig. 1: BLANC and corresponding HOCl measurement

The determination of the net bacterial inactivation by HOCl (D_{B2}) is obtained under the premise that the bacterial self-deactivation (d_2), as determined through the BLANC tests (grey curve), and the HOCl caused effect are independent processes and behave multiplicatively to yield D_{comb}, which is measured in the HOCl tests (orange curve).

This provides for D_{B2}:

$$\boxed{D_{B2} = 100 - \frac{100 - D_{Comb}}{100 - d_2}}$$

The following graph shows the results for the disinfection rates D_{B2} for studied bacteria at different HOCl in-air concentrations.

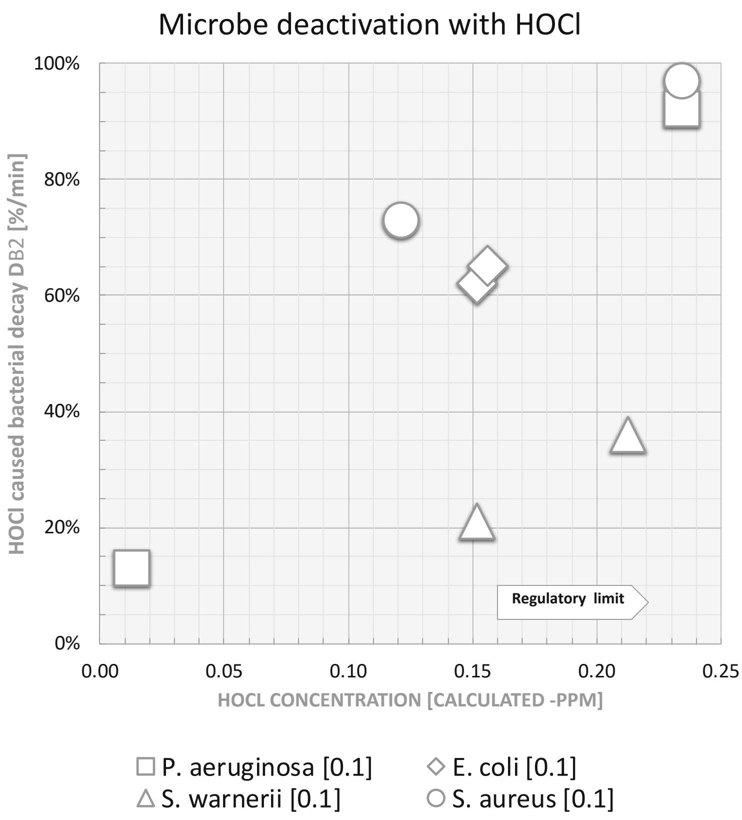

Fig. 2: Disinfection rates DB2 for various microbes at different HOCl inconcentrations

Fig. 2 shows the results for the disinfection rates D_{B2} for studied bacteria at different HOCl in-air concentrations. Within species the deactivation rate increases with the HOCl concentration. The absolute values are highest for the Gram-negative bacteria. The vertical dashed line marks the EU legal limit (0.21 ppm) for in-air free chlorine for long-term exposure in populated rooms. We demonstrated the dependency of the biocidal efficacy as function of the HOCl concentration (Fig. 3 - experiment with E. coli).

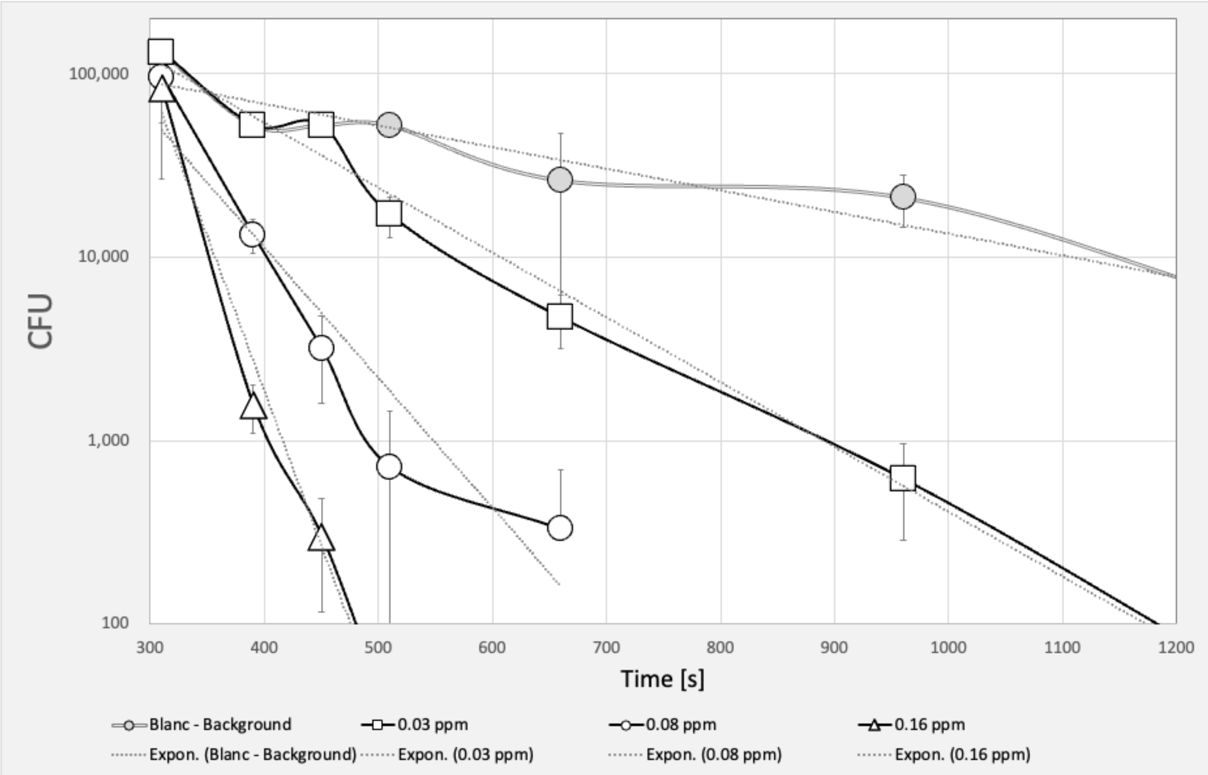

Fig. 3: Deactivation of aerosolized E. coli at different HOCl gas concentrations [95% confidence interval]

Plotting the measured disinfection rates against the respective HOCl concentration shows an almost linear relationship (Fig. 4).

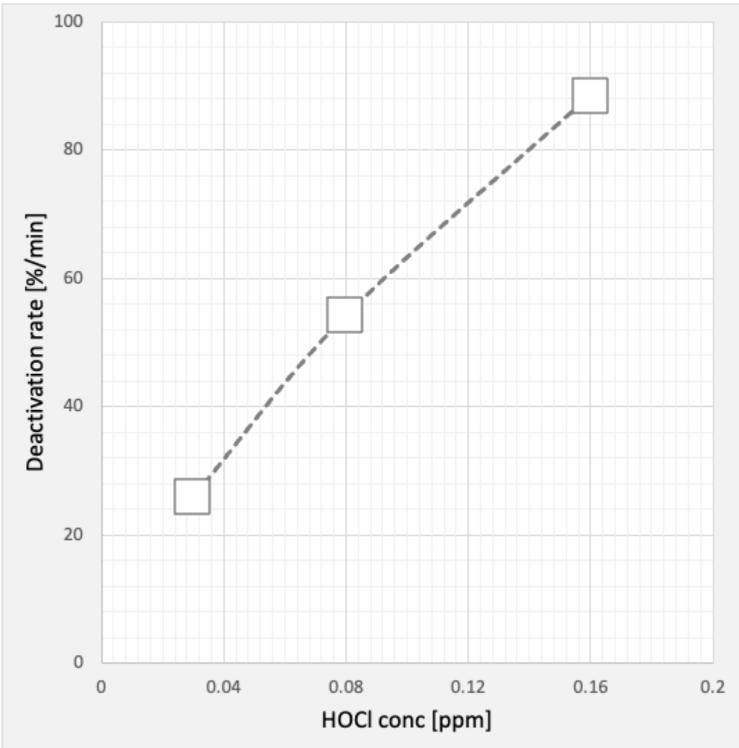

Fig. 4: Deactivation rates of E. coli in the gasphase as f(HOClconc.)

Transferring the results into a time domain of bacterial decay and HOCl exposure time, it becomes apparent how effective HOCl would reduce a bacterial or presumably viral load in a contaminated indoor atmosphere (Fig. 5).

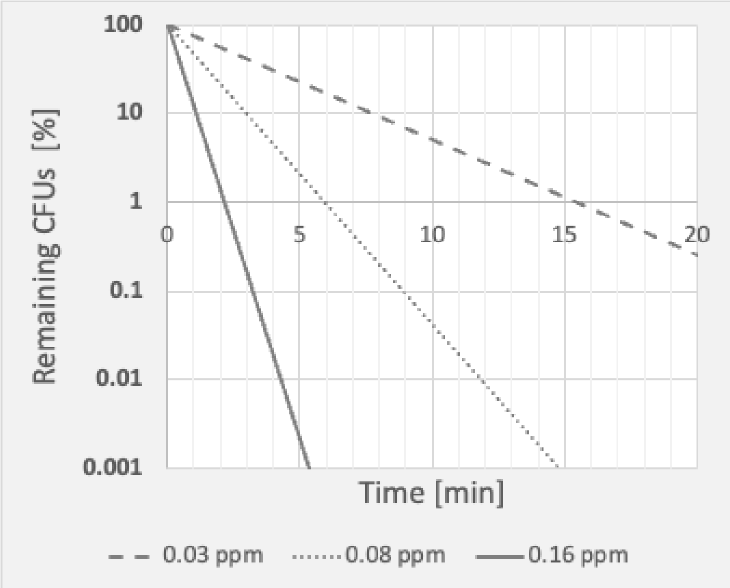

Fig. 5: Log Reduction versus exposure time for different HOCl gas concentrations (E. coli)

For example, the measured gram-negative E. coli bacteria at a concentration of 0.08 ppm (38% of the legal upper limit), the bacterial deactivation rate of 53% would result in a so-called log 4 reduction within 12 minutes. Unfortunately, real life situations are way more complex than a closed and fully controlled lab container. Most importantly, in real-life situations one must expect a more continuous virus contamination through a potential spreader. Therefore, the so-called log reduction – as used in filter classification and surface disinfection protocols for non-populated situations – can only provide a directional information. Thus the next steps need to include real life experiments and studies to confirm the efficacy under these conditions.

Discussion

The results of the suspension test support the biocidal activity of the used HOCl solution in this study. Bacteria and vaccinia virus show high susceptibilities to HOCl (vaccina even more sensitive). These results suggest (according to CEN TC 216) high sensitivity of all enveloped viruses (including SARS-CoV-2) to HOCl.

To measure the virucidal efficacy of an HOCl laden atmosphere is problematic since it would be requesting quantitative recovery of infectious virus particles from the air. Molecular biological detection of viral RNA via PCR methods would include inactivated virus par-ticles as well. As a recourse to this principal issue, representative bacteria were used as surrogate organisms for infectious particles in the tests. Particularly, the vaccinia virus and structurally similar gram-negative bacteria (like E. coli) are considered a surrogate microbe for enveloped viruses (e.g.: SARS-CoV-2). The results indicate that enveloped viruses - given their chemical and structural similarity with Gram-negative bacteria - can be progressively deactivated with increasing HOCl concentration.

Vaporized HOCl can be used as an effective agent to deactivate pathogens mid-air. Aerosolized HOCl solutions (droplet sizes <10µm) vaporize within seconds resulting in an HOCl laden atmosphere (free floating molecules). Such 'active' atmosphere has the potential to interact with virus laden aerosol particles and any other airborne microbes (Spickett et al. 2000). The required concentration for an effective bacterial deactivation rate is well below legal limits, safe, and non-irritant (Nguyen et al. 2021; Rai, Ashok, and Akondi 2020; E. D. Rasmussen 2017).

Aerosolized infectious organisms are attacked by biocidal molecules either by droplet merge (aerosolinf./aerosolHOCl) or from the gas phase (aerosolinf/moleculeHOCl) (Thorn, Robinson, and Reynolds 2013; Masterman 1941; Edward and Lidwell 1943; Hakim et al. 2015), which suggest the transferability of our suspension and in-air test results: If the studied bacteria are deactivated, so will be aerosolized enveloped viruses.

Conclusion

Proactive facility management with novel ventilation concepts can become an important contributor for future infection prevention and control. The importance of our results is two-fold:

1. Infection prevention:

HOCl laden air may offer a safe, low-cost, and efficient way to secure a pathogen free facility atmosphere. In such equipped facilities the threat through infected virus spreading individuals would be contained effectively.

2. Disease progression:

HOCl enriched air has the potential to contain or even invert disease progress by attacking mucosa adsorbed viruses during the incubation phase. In this sense the facility atmosphere could offer a seamless disease containment function.

Today, any microbial insertion (through viral spreaders) will only be partly contained with incumbent safety measures. We confirmed our hypothesis of the high disinfecting power of HOCl-laden atmospheres. The method can be used in populated indoor environments because it is safe at the investigated concentration levels according to many peer-reviewed studies (Rai, Ashok, and Akondi 2020; Lapenna and Cuccurullo 1996; Mohapatra and Wexler 2009).

The potential of HOCl laden atmospheres to convert populated indoor areas into infection safe environments may allow to address other than just COVID related applications. Our here reported results and ongoing field test in large office buildings suggest that use of HOCl based room air decontamination counters the need for high air exchange rates for infection control. In doing so this approach can make a significant contribution to so much sought-after opportunities for energy savings. The HOCl air cleaning method is safe, cost effective, and easy to install and maintain.

Our early results suggest that HOCl based air-cleaning for populated rooms should be considered as a potential alternative or important enhancement to incumbent facility and personal disinfection protocols and should be further evaluated. This also includes further studies regarding the effect of HOCl on biological systems and the human body.

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