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COVID-19 pandemic lesson learned- critical parameters and research needs for UVC inactivation of viral aerosols

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ABSTRACT

The COVID-19 pandemic highlighted public awareness of airborne disease transmission in indoor settings and emphasized the need for reliable air disinfection technologies. This increased awareness will carry in the post-pandemic era along with the ever-emerging SARS-CoV variants, necessitating effective and well-defined protocols, methods, and devices for air disinfection. Ultraviolet (UV)-based air disinfection demonstrated promising results in inactivating viral bioaerosols. However, the reported data diversity on the required UVC doses has hindered determining the best UVC practices and led to confusion among the public and regulators. This article reviews available information on critical parameters influencing the efficacy of a UVC air disinfection system and, consequently, the required dose including the system's components as well as operational and environmental factors. There is a consensus in the literature that the interrelation of humidity and air temperature has a significant impact on the UVC susceptibility, which translate to changing the UVC efficacy of commercialized devices in indoor settings under varying conditions. Sampling and aerosolization techniques reported to have major influence on the result interpretation and it is recommended to use several sampling methods simultaneously to generate comparable and conclusive data.

We also considered the safety concerns and the potential safe alternative of UVC, far-UVC. Finally, the gaps in each critical parameter and the future research needs of the field are represented. This paper is the first step to consolidating literature towards developing a standard validation protocol for UVC air disinfection devices which is determined as the one of the research needs.

1. Introduction

Regional and global pandemics have imposed death tolls on society throughout the ages. The 2002 Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) pandemic was followed in 2015 by the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) outbreak. The emergence of the novel coronaviruses (SARS-CoV-2) caused the 2019 (COVID-19) pandemic. As of September 2022, over 6.49 million people have died from SARS-CoV-2 and its variants (World Health Organization WHO, 2022) and there have been significant socio-economic impacts (World Health Organization WHO, 2022). The global growth rate declined by 6.3% in 2020, a considerable drop (Statista Research Department, 2020). The original forecasted change in global GDP for 2020 was 2.9%, and due to the pandemic, the GDP declined by 3.4%, which translates to 84.54 trillion US dollars (Statista Research Department, 2020). Like MERS-CoV and Influenza, SARS-CoV-2 has significant airborne transmission through coughing, sneezing and even breathing (Nardell and Nathavitharana, 2020) of virus droplets (1- 5 μm) travelling beyond 1 meter (Zhang et al., 2020). Various methods are used today for inactivating viral airborne particles. These include techniques such as germicidal ultraviolet (UVC) (Heßling et al., 2020), filtration, nanomaterials (Li et al., 2021), ventilation (Vlaskin, 2022), plasma inactivation (Filipić et al., 2020), photochemical oxidation (Habibi-Yangjeh et al., 2020) and essential oils. A recent review reports on the advantages and limitations of these techniques. While ventilation is the most practiced method to manage indoor air quality, it is not sustainable and effective. The existing ventilation systems are dated and not designed and optimized to reduce the bioaerosol load, including

Abbreviations: CDC, centre for disease control and prevention (USA); CMD, count median diameter; DNA, deoxyribonucleic acid; DSB, double strand break; dsDNA, double-stranded deoxyribonucleic acid; Far-UVC, ultraviolet irradiation in the 'far' range of 200–230 nm; GTC, growth tube collectors; LED, light emitting diode; LPUV, low-pressure ultraviolet lamp; NIOSH, national institute for occupational safety and health; PBS, phosphate buffered saline; PRRS, porcine reproductive and respiratory syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; SSB, single strand break; ssRNA, single-stranded ribonucleic acid; REL, recommended exposure limit; RH, relative humidity; RNA, ribonucleic acid; ROS, reactive oxygen species; UV, ultraviolet irradiation; UVC, ultraviolet irradiation in the 'C', or germicidal, spectrum from 200 to 290 nm; UVGI, ultraviolet germicidal irradiation; UV-LED, light emitting diode in the ultraviolet range.

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viruses. Additionally, by increasing the ventilation rate, the energy consumption per building and the carbon footprint increases. Air filters, including the high-efficiency particulate air (HEPA) filtration technique, are applied to trap and reduce infectious bioaerosols (World Health Organization WHO, 2022). According to EPA, CDC, ASHRAE and Health Canada, applying technologies such as filtration and ventilation is insufficient to reduce the risk of airborne disease, including COVID. Therefore, other techniques must be adopted. The most adopted method for inactivating airborne pathogens is UVC which damages the microbial nucleotides effectively and suppresses the reproduction. Since the emergence of COVID-19 in late 2019, commercial UVC products flooded the market, often before proper validation, leading to public confusion. The COVID-19 pandemic highlighted the potentials of UVC for disinfecting air in common areas like public transport, office spaces, and hospitals. Our growing understanding of the highly germicidal UVC and far-UVC wavelengths gives further promises. However, significant variations in required UVC doses reported in the literature at seemingly similar conditions lead to poor dissemination from research to the public, policymakers, and the UVC industry. The ongoing COVID-19 pandemic and its variants will not be the last airborne pathogens that societies encounter. Therefore, it is timely to assess air disinfection technologies using ultraviolet germicidal irradiation (UVGI), to reduce the airborne spread of diseases, with a particular focus on UVC wavelengths. Validation of disinfection products benefits regulators, policymakers, and the public to access safe and reliable technologies. Therefore, it is necessary to understand the design and operational criteria affecting the efficacy of UVC air disinfection first in the lab-scale setups, followed by the larger-scale, industrial devices.

This article reviews the operational and environmental factors influencing the efficacy of UVC air disinfection in lab-scale setups in an attempt to unify testing procedure aimed at reducing the variations in required UVC doses. While this review focusses on UVC for viral airborne disinfection, specifically SARS-CoV-2, our learning is enhanced by times broadening the scope, such as to include selecting viral surrogate, viral airborne pathogens aerosolization (i.e., nebulization), sampling techniques, industrial applications, and safety concerns. Finally, a gap analysis informs a discussion on future research needs. This review represents a step toward consolidating literature for a standardized validation protocol for UVC air disinfection devices.

2. History and background of UVC air disinfection

In 1877 Downes and Blunt reported that the germicidal properties of light depended on intensity and duration (i.e., dose) and that shorter wavelengths were more effective (Downes and Blunt, 1877; Downes and Blunt, 1879). In 1890, the germicidal effect of sunlight was demonstrated for *tubercula bacillus*, foretelling its importance in tuberculosis infections over the next century (Koch, 1890), while the first UVC water plant opened in 1909 (Bahnfleth, 2020). Exemplifying an early understanding of the importance of UVC disinfection, Niels Ryberg Finsen received the 1903 Nobel Prize in Medicine for his use of UVC radiation in reducing the transmission of lupus vulgaris.

Research on light-based disinfection technologies and mechanisms increases following disease outbreaks. In the early 1900s, clinical studies observed UVC-based air disinfection even before a mechanistic understanding was available (Reed, 2010). A 1942 multi-year study in Philadelphia schools reported measles infection rates fell from > 50% to below 16% in classrooms with upper-air UVC irradiation (Wells et al., 1942). During the 1957 Influenza, the infection rates in hospital wards dropped from 19% to < 2% when upper-room UVC irradiation was used (Jordan, 1961).

In the late 1900s, clinical experiments pursued an understanding of the UVC disinfection mechanisms. Jensen reported 99.9% inactivation of influenza and vaccinia virus and 96.8% of adenovirus in a UVC cell at a high air flow rate of 100 ft^3/min (Jensen, 1964). In the 1970s, Richard Riley became well-known after testing upper-room UVC systems for tuberculosis control (Riley and Permutt, 1971; Riley, 1988). Riley also created luminaires with directional louvres to limit lower-room exposure (Fig. 1A), which were employed during tuberculosis outbreaks in the 1980s (Nardell and Riley, 2020; First et al., 2007). Over the coming years, the performance of upper-room UVC systems were better understood (Fig. 1B).

In 1985, tuberculosis cases for the first time in the twentieth century increased in the United States. Outbreaks have since been reported at prisons, refugee camps, hospitals in sub-Saharan Africa, Asia and the former Soviet Union (Brickner et al., 2003). To coordinate a global approach, the WHO recommended UVC for controlling tuberculosis infections in 1999, and the US Centre for Disease Control recommended its use in 1994 (Burwen et al., 1994). Following, Kowalski and colleagues released a comprehensive model of UVGI airborne disinfection, including a survival curve incorporating a two-stage inactivation and a shoulder (Kowalski et al., 2000). Their model generalized decades of disinfection experiments, which they confirmed through re-evaluating prior studies.

Fig. 2 provides an overview of some key events in the history of UVC air disinfection. Despite early success of UVC, its usage soon diminished due to a variety of reasons (e.g., lack of reproducibility, lack of studies of UVC exposure on health effects, etc). However, the discovery of the UVC inactivation of *mycobacterium tuberculosis* and later *cryptosporidium, giardia* paved the way to a remarkable future of UVC irradiation for commercial applications.

Spurred by the 2002 SARS and 2015 MERS outbreaks, recent efforts advanced our understanding of UVGI disinfection (McDevitt et al., 2012). Recently, the SARS-CoV-2 pandemic again increased interest in UVGI for public spaces. Ultraviolet offers an attractive disinfection system: easy-to-install (including retrofitting to existing facilities), low maintenance, non-invasive, and low hazard (when correctly installed). With a growing understanding of UVGI including the focus on UVC and further far-UVC, the application of UVGI systems is primed to increase.

3. UVC inactivation of viral aerosols

3.1. Ultraviolet pathogen inactivation

The ultraviolet light spectrum ranges from 10 to 480 nm, including three regions of importance, UVA (320–400 nm), UVB (290–320 nm), and UVC (200–290 nm) (Hadi et al., 2020). The maximum absorbance of DNA is around 265 nm, so UVC radiation exhibits the highest antimicrobial properties. When DNA/RNA absorbs UV radiation, dimeric lesions occur in the genome, preventing DNA/RNA transcription and translation and thereby inactivating the microorganism. Following the adsorption of UVC by DNA/RNA, the most critical photoproducts are cis-syn cyclobutene dimers between adjacent pyrimidines, like thymine-thymine dimers (Kowalski, 2009; Beck et al., 2016), and the formation of covalent linkage between the 6- and 4- position of two pyrimidine bases, called the ‘6-4-photoproduct’ (Douki and Cadet, 1994). Less significant to overall damage are single-strand breaks (SSB) resulting from DNA-protein cross-links (Kiefer, 2007), hydrolytic deamination which converts one base to another (i.e., cytosine <-> uracil), and hydrolytic depurination/ depyrimidination which removes a base entirely (Rastogi et al., 2010). Meanwhile, the formation of reactive oxidant species (ROS) by UVC radiation can cause damage beyond the DNA and RNA, affecting lipids, proteins and other cellular structures (Valko et al., 2007). UVC-induced damage does not directly kill pathogens but can lead to replication arrest, rendering cells unviable (Brickner et al., 2003; Dunkern and Kaina, 2002). When DNA/RNA polymerase encounters a base lesion, a Y-shaped DNA structure is created. Endonucleases recognize this incorrect DNA/RNA architecture and nick the template strand, creating a double-strand break (DSB) (Batista et al., 2009). Interestingly, single-stranded nucleic acid (ssRNA and ssDNA) viruses are more susceptible to inactivation by UVC than double-stranded nucleic acids (dsRNA and dsDNA) viruses (Thurston-Enriquez et al., 2003; Tseng and

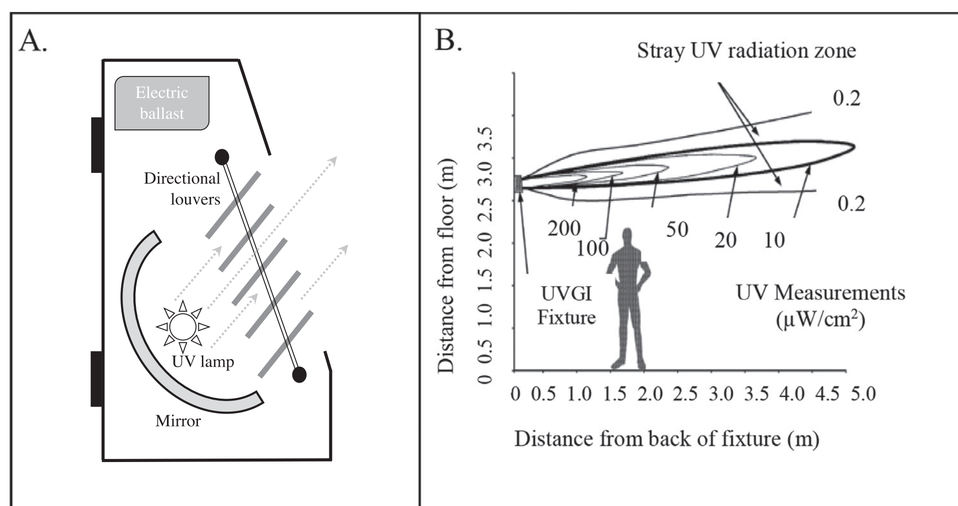

Fig. 1. (A) Design of an ultraviolet lamp with directional louvres, like that used by Riley in the 1970s. (B) Profile of UVGI dose across a room with a UVGI lamp, as could be used in a hospital or school setting. Adapted from [ASHRAE 2019, "Ultraviolet Air and Surface Treatment"] (ASHRAE, 2019).

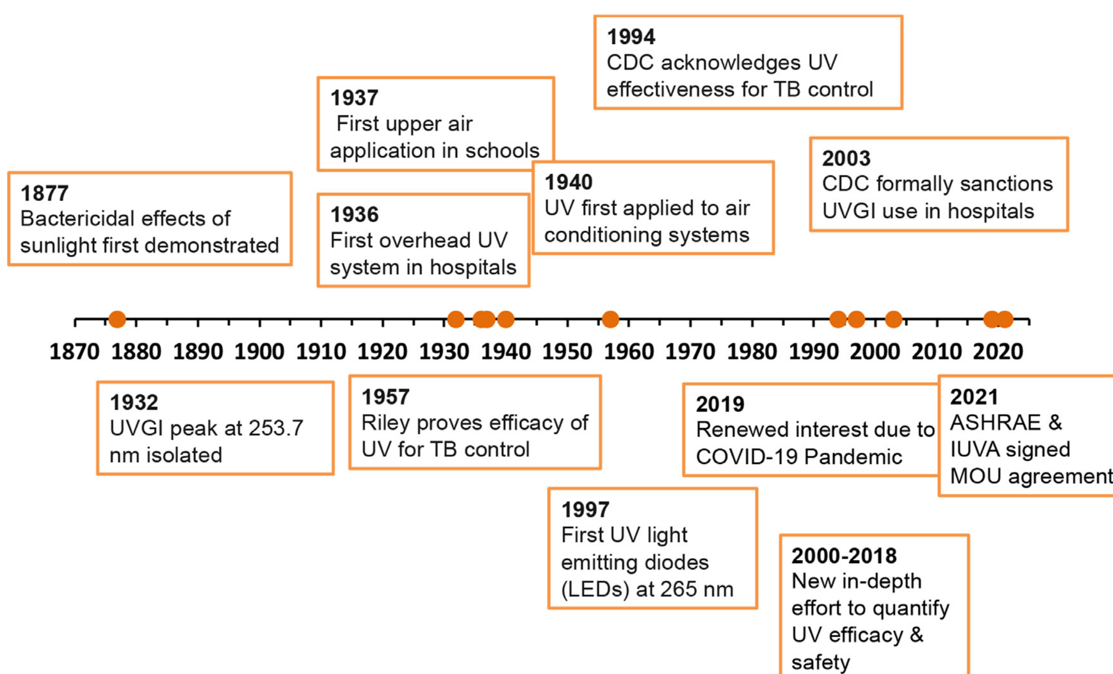

Fig. 2. Overview of selected key events in the history of UVC air disinfection (Kowalski, 2009)

Li, 2005a). Tseng and colleagues reported that the UVC dose required for 99% inactivation of dsRNA and dsDNA viruses was twice that of ssRNA and ssDNA viruses (Tseng and Li, 2005a). In case of viruses and phages, it has been shown that UVC damages inhibits the genome injection to the host cells through capsid protein damage (Wigginton et al., 2012).

Different UVC wavelengths may affect the dominant pathogen inactivation mechanism. Eischeid and Linden (2011) reported that polychromatic medium-pressure mercury lamps were more effective at damaging adenoviral proteins than low-pressure mercury lamps, suggesting the additional UVC-spectrum activated more damage mechanisms (Eischeid and Linden, 2011) while Gerchman and colleagues reported that shorter wavelengths (267 nm) were more effective at inactivation of HCoV-OC43 (Fig. 3). For longer wavelengths (i.e., UVA and UVB), this means that a higher UV dose is required to achieve the same log inactivation. In fact, increasing UV wavelength to 300 nm requires a 10-fold greater dose to achieve similar inactivation when compared to 280–290 nm for MS2, Qβ, feline calicivirus, H1N1 viruses and human Coronavirus (HCoV-OC43) (Gerchman et al., 2020). Beck et al., studied the action spectra for MS2, T1UV, Qβ, T7, and T7m Coliphages, and observed that the UVC susceptibility decreases by increasing radiation wavelength from 210 to 240 nm with the highest at peak at 210 nm, then increases from 240 to 260/270 nm, and then there is another sharp decline by increasing from 270 to 300 nm (Fig. 4) (Beck et al., 2015).

3.2. Viral surrogate selection

Inactivation rate constants (k_{uv}) describe the susceptibility of a microorganism population to UVC radiation. Brickner et al. (2003) summarized the k_{uv} of dozens of viruses, bacteria and fungal spores from 0.0034 to 0.96 m^2/J, confirming a species-dependent response to UVC-radiation (Jensen, 1964; Hollaender, 1943). Generally, susceptibility to UVC radiation can be ranked as: viruses> vegetative bacteria> mycobacteria> bacterial spores> fungal spores (Fig. 5A) (ASHRAE, 2019). Selecting a representative viral surrogate is crucial, as working with viral pathogens such as SARS-CoV-2 requires stringent safety lab protocols (Biosafety

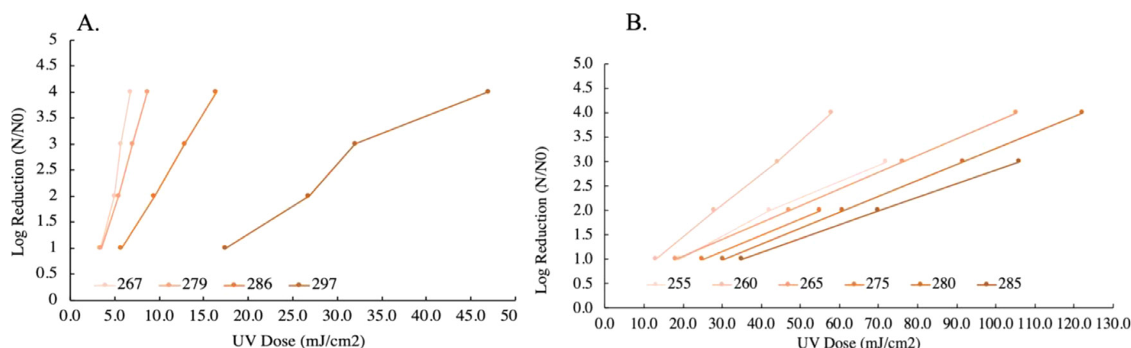

Fig. 3. Higher UV wavelengths require higher doses to achieve the same log reduction for the same pathogen. (a) Human Coronavirus (HCoV-OC43), (b) viral surrogate, MS2. Note that the reported UV fluences were determined in the liquid. Produced with data from (Gerchman et al., 2020).

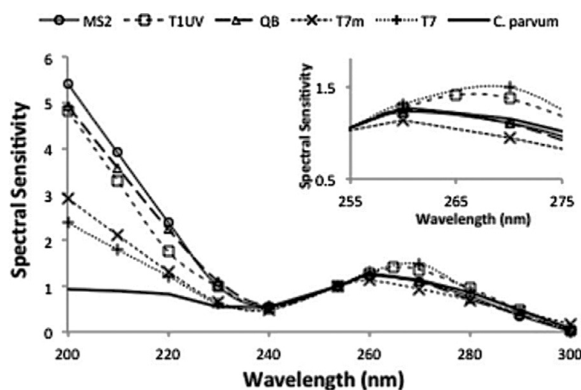

Fig. 4. Spectral sensitivity (i.e., UVC susceptibility along the UVC action spectral) of different viruses (Beck et al., 2015)

level 3 (BSL-3)). Also, different species have vastly different log inactivation efficiency when exposed to UVC (Fig. 5B). In UVC air disinfection studies, one of the main criteria for surrogate selection is similarity in UVC susceptibility. Various pathogens show different inactivation dose responses due to the following reasons (1) the presence of a cell wall and its thickness, (2) larger genomes present a larger target for UV damage, (3) single-stranded genomes lack a repair template (compared to double-stranded), and (4) the specific protein composition of the capsid, like UV-absorbing chromophores (Tseng and Li, 2005a; Meng and Gerba, 1996).

A virus repair mechanism impacts their UV susceptibility: dsDNA viruses go through reactivation once in the cell host. The possibility of a pathogen's ability for genomic repair should be considered when selecting a viral surrogate and the applied analysis method (i.e., nebulization) (HARM, 1961; DayIII, 1974). Table S1 provides detailed information about the different types of common viruses and virus surrogates composition (e.g., TT, TC, CT, and CC, etc.), genome size and type, and repair mechanism. This dataset can help researchers to make informed decisions about selecting the virus surrogate (Rockey et al., 2021).

Common surrogates for SARS-CoV-2 in air and surface disinfection include murine hepatitis virus (MHV), human coronavirus 229 E, transmissible gastroenteritis virus (TGEV), feline infectious peritonitis virus (FIPV) (Kumar et al., 2020), human coronavirus OC43 (Buonanno et al., 2020), and influenza H1N1 (Welch et al., 2018).

Another approach to choose a surrogate that has a similar inactivation rate is through using the mathematical models specifically facing new and emerging pathogens. However, the few genomic mathematical models developed thus far are based on the UVC data obtained in water disinfection studies. While the UVC rate constant in water can be used implicitly for viral airborne inactivation, there is still a need to develop a protocol for airborne UVC disinfection, consolidate data, and establish the genomic modelling for airborne pathogens separately. UVC inactivation rate constant in water includes the UV scattering and absorption, which differ from those in the air. The genomic predictive modelling can help select the proper viral surrogate (i.e., similar to that of viral pathogen) based on the inactivation rate and susceptibility similarity and predicts the required irradiation dose.

3.3. UVC susceptibility

Airborne microbes are more sensitive to UVC when compared to microbes in films or suspensions. This effect varies between organism, with bacteria generally ~5-fold more resistant in water than in air at low humidity. Similarly, viruses were 3-fold more resistant to UVGI inactivation when suspended in water compared to dry air (Kowalski, 2009). This was attributed to (i.) absorbance of UVC radiation by water, (ii.)

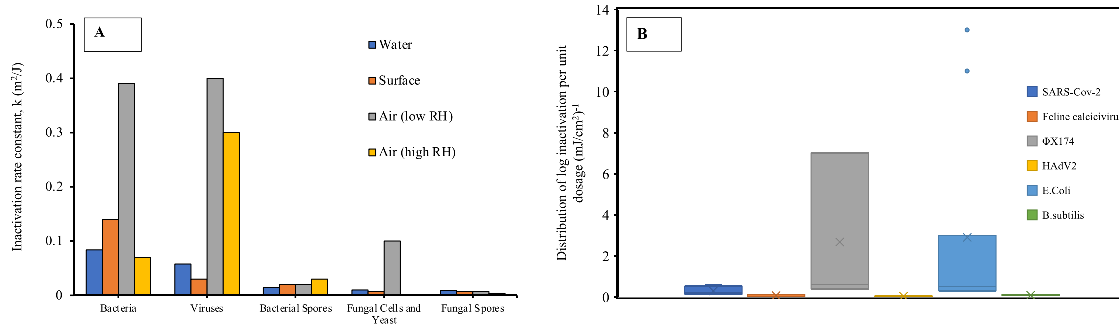

Fig. 5. (A) Average UV rate constants for bacteria, viruses and fungi in air, water and on surfaces. Figure created with data from. (B) Log inactivation per dosage for different pathogens including SARS-CoV2 demonstrates that different pathogen can have noticeably different inactivation rate, thus selecting a proper surrogate with similar inactivation response is of importance.

Table 1
UVC dose inactivation for aerosolized virus and viral surrogate.

		Log Reduction UVC Dose mJ/cm^2					
Virus/Viral Surrogate	UVC Source	1	2	3	4	5	[Ref] Year
Bovine CoV	LPUV- 254 nm		5.00*				(Snelling et al., 2022) 2022
MS2	LPUV- 254 nm				8.27**		(Snelling et al., 2022) 2022
Human Coronavirus HCoV-OC43	Far-UV- 222 nm	0.39					(Buonanno et al., 2020) 2020
Human Coronavirus HCoV-229E	Far-UV- 222 nm	0.56					(Buonanno et al., 2020) 2020
Phi X174	UV-LED- 278 nm				4.6		(Kim and Kang, 2018) 2018
QB	UV-LED- 278 nm					46	(Kim and Kang, 2018) 2018
MS2	UV-LED- 278 nm				46		(Kim and Kang, 2018) 2018
Influenza A	KrCl Lamps- 222 nm	2****					2018
PRRSV	LPUV- 254 nm			1.21			(Cutler et al., 2012) 2012
Influenza A	LPUV- 254 nm	1.48***					(McDevitt et al., 2012) 2012
Influenza A	KrCl Lamps- 222 nm	2****					2018
MS2	LPUV- 254 nm	2.6					(Walker and Ko, 2007) 2007
MHV Coronavirus	LPUV- 254 nm	0.66					(Walker and Ko, 2007) 2007
Murine Coronavirus	LPUV- 254 nm	0.66					(Walker and Ko, 2007) 2007
MS2	LPUV- 254 nm	0.34–0.42	0.8–0.91				(Tseng and Li, 2005a) 2005

PRRSV= Porcine Reproductive and Respiratory Syndrome Virus- * 2.4 log reduction, ** 4.16 log reduction, ***1.4 log reduction, **** 1.3 log reduction.

turbulence in air improving the mixing of airborne organisms, (iii.) physical damage during aerosolization, and (iv.) oxygenation and dehydration at low humidity increasing pathogen vulnerability to UV inactivation.

Table 1 shows the reported log reduction of viruses in air using UVC sources. Table S2 provides the inactivation doses for viral pathogens and viral surrogates in the liquid. The number of studies is limited, and a direct comparison is not possible considering experimental variability (Section 4), operating conditions (Section 5), and measurement techniques (e.g., radiometers). Nonetheless, one can conclude that an average dose of 2 mJ/cm^2 could provide one log reduction (90% inactivation) of airborne viruses. Further study is needed using a uniform protocol to standardize the experimental conditions and ensure a reliable comparison.

3.4. Outlook

The literature lacks a description of the impact of the viral envelop and nucleocapsids on UVC susceptibility. Future research should seek to understand their implications for UVC efficacy. As the dose-response of each microorganism depends on the UVC wavelength, care should be taken on selecting a surrogate pathogen. However, a lack of data on UVC dose-response and protein damage, means that there is currently no solid mechanistic understanding on viral aerosol inactivation. Therefore, further research is needed to understand this inactivation mechanism across diverse species, and to develop a genomic predictive model to enable researchers to select a surrogate.

Also, few existing genomic mathematical models representing the mechanistic UVC inactivation are based on data obtained in water disinfection studies. While the UVC rate constant in water can be implicitly used for airborne inactivation, there remains a need to develop a protocol for airborne UVC disinfection, consolidate data, and establish a separate genomic model for airborne pathogens. Such a genomic predictive model can help select the proper viral surrogate based on inactivation rate and susceptibility, and predicts the required irradiation dose, and the airborne medium.

4. Effect of experimental setups

4.1. Nebulizers (pathogens aerosolization)

Pathogens can become airborne; when nebulized (i.e., aerosolized) they are referred to as bioaerosols. The probability of its survival depends on its ability to resist the stress of aerosolization (Verreault et al., 2008). Pathogens may be aerosolized by various mechanisms (Verreault et al., 2008; Aller et al., 2005)

- *Primary aerosolization* involves the spread of microorganisms directly into the surrounding air, i.e., sneezing.
- *Secondary aerosolization* involves the spread of microorganisms through fluids or surfaces, which later become sources of airborne transmission. For example, liquid splashes can aerosolize pathogens on liquids and surfaces.

Generation of aerosols in an experimental setting tries to mimic the primary or secondary aerosolization via different techniques and devices. Aerosols generation in a controlled environment provides the ability to study the viability, transformability, infectivity and inactivation using different disinfestation techniques more accurately. However, there are different steps prior to aerosolization that may impact the data interpretation including preparation and storage of the viral surrogates or pathogens followed by the aerosolization technique and finally the collection method (Alsved et al., 2020)

Most aerosol particles (greater than 10 μm) will not pass the upper airways of the human respiratory system and pose little concern for disease transmission. However, smaller particles travel more efficiently and may infect the tracheobronchial and alveolar regions of the human respiratory systems (Lauck, 2000). Therefore, future studies examining the efficacy of UVC for the disinfection of aerosolized microorganisms should focus on this smaller particle size.

Airborne pathogens aggregate rapidly (Lauck, 2000). Several factors, including the size distribution of the airborne particles, thermo-/hydro-dynamic conditions, relative humidity and the aerosol concentration, govern the rate of pathogen aggregation (Kowalski, 2009; Verreault et al., 2008). Bioaerosols generated in the natural environment often shrinks rapidly due to the differences in the relative humidity between the respiratory tract and the outside environment (Fig. 6). Further, airborne particles in clean environments are more likely to remain smaller than particles in a dirty atmosphere, with more potential to grow by adhering to other airborne particles (Morawska, 2006). Artificially generated aerosols are often tested in controlled environments where the nebulized particles cannot bind (Verreault et al., 2008). However, laboratory-specific factors like relative humidity (RH) and temperature may impact the droplet's solute concentration, resulting in variable disinfection efficacy (Verreault et al., 2008). Thus, even controlled studies from different research facilities are difficult to compare.

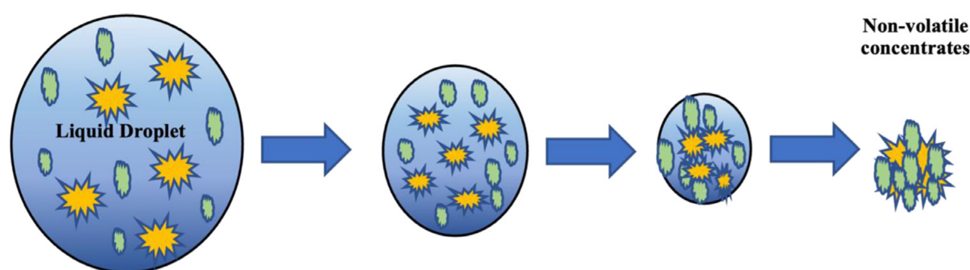

Fig. 6. Evaporation of a liquid droplet. As the process progresses, the non-evaporative content concentrates until a droplet nucleus is remaining. Schematic redesigned using information from (Verreault et al., 2008)

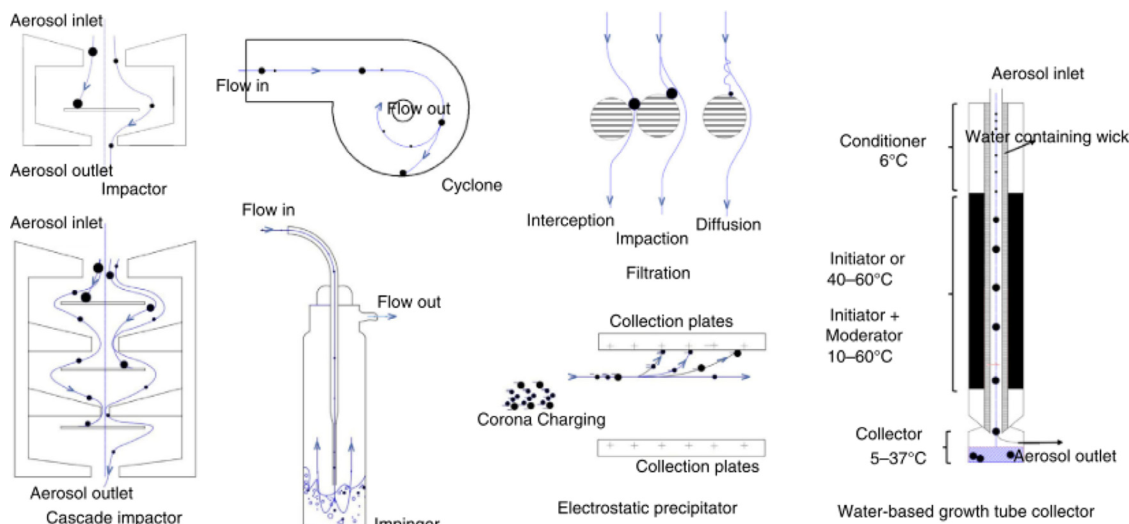

Fig. 7. Different sampling methods for bioaerosols. Reproduced from (Pan et al., 2019).

4.2. Sampling techniques

Aerosolized particles attach to a surface via van der Waals and electrostatic forces (Lauck, 2000). Thus, most air sampling techniques depend on factors governing the adhesion properties of airborne particles, like the aerodynamic radius, thermal gradients, Brownian motion, and particle inertia. Airborne particles of <100 nm are more susceptible to Brownian motion than larger particles, primarily due to the collision frequency of encounters with gas molecules (Verreault et al., 2008). Smaller particles with higher diffusivity exhibit a greater probability of adhering to a surface that they contact. This is the basis for the efficient removal of small particles by filtration. By contrast, larger airborne particles (μm scale) are dominated by gravitational attraction, causing them to settle on surfaces. The larger particles are also more easily diverted from a gas streamline, leading to impaction on surfaces at high velocity and consequent adhesion.

The sampling of airborne pathogens is challenged by physical collection efficiency, viability losses of the airborne pathogen due to dehydration during the collection, damages because of the impaction and re-aerosolization (particularly in impingers), and losses from bioaerosol retention to the sampler (Pan et al., 2019). Sampling techniques to collect airborne pathogens, particularly for viruses and viral surrogates (Fig. 7) are described below in Table 2.

The Andersen sampler has a very low inlet efficiency and high wall losses. Impinger and Cyclone should be fully characterized for the wall loses and inlet efficiency (Henningson and Ahlberg, 1994). It has been noted that that no single sampling method is suitable for all types of bioaerosol and in choosing the appropriate sampling technique factors such as type of airborne pathogen, sampling time and volume, and suspending medium should be taken into consideration. Each sampling method provide different physical and biological efficiency as well as detection limit (Borges et al., 2021a). It is recommended that researchers should use several sampling techniques simultaneously so that limitation of one sampling technique will be compensated with others. The knowledge of the researcher about the pros and cons and limitation of sampling techniques help interpret results more accurately (Borges et al., 2021a).

Reliable data collection for the development and assessment of UVGI systems necessitates accurate and standardized sampling methods, including bioaerosols sampling. Based on the Center for Disease Control and Prevention (CDC) recommendation, bioaerosols collection (e.g., fungi, bacteria and viruses) need new sampling methods with reduced handling risk and enhanced detection accuracy (Borges et al., 2021b). UVC systems for airborne pathogen inactivation is possible with commercial air samplers described above. Table 3 shows sampling techniques and nebulizers used in the UVC inactivation studies in the last 20 years.

4.3. UVC chamber

Experimental setups for testing UVC inactivation of pathogens typically comprise a flow chamber, a specimen rack, and a UVC radiation source (Fig. 8) (Kowalski, 2009). Narrow-band spectral ultraviolet sources are used with mirrors to direct radiation. The radiation pattern and flow velocity must guarantee uniform dose delivery: entrance baffles create a well-mixed and consistent flow stream. The test chamber temperature and humidity are controlled. The distance from ultraviolet source to the flow stream determines a uniform light distribution and dose delivery to bioaerosols.

Table 2
Summary of sampling techniques for bioaerosols. Graphic depictions are provided in Fig. 7.

Sampling Technique	Procedure Description
Solid impactors	Sampling is conducted in three stages: *Stage 1:* The particles accelerate through narrow holes or slits in the device. *Stage 2:* The airstream moves towards a solid surface and abruptly changes direction. *Stage 3:* The particles' inertia causes them to deviate from the airflow and impact the surface, typically holding a petri dish with a culture medium. Examples include: Andersen samplers, slit samplers, and cyclone samplers, are used for capturing large particles (Tseng and Li, 2005b, Ijaz et al., 1987).
Cyclone samplers	Use centrifugal forces to sample aerosolized pathogens (Errington and Powell, 1969). A scrubbing liquid is injected as the cyclones accelerate the air using a centrifugal vortex. Thus, cyclones rely on inertia to push airborne particles towards a solid surface, resulting in adhesion and consequent detection.
Liquid impactors	Accelerate airborne particles through a narrow orifice by creating a pressure drop (Verreault et al., 2008; May and Harper, 1957; Henningson and Ahlberg, 1994). The air enters horizontally through a glass tube that curves vertically. This forces the air to change direction and flow downward. The glass tube diameter abruptly narrows in the impactor, creating a critical flow orifice and accelerating the air to a sonic velocity. All-glass impingers (AGIs) and BioSamplers are the most often used samplers to capture airborne viruses. While liquid impactors are popular because the liquid collecting medium maintains the virus viability and eliminates the extraction process (in the case of filter application), the re-aerosolization of the collected viruses is the leading cause of collection efficiency loss.
Filters	Particles with an aerodynamic size of <500 nm are captured (Verreault et al., 2008; Lauck, 2000). Filter efficacy is governed by: *Interception:* When a particle following in a streamline is intercepted by an obstacle due to its size. *Inertial impaction:* when a particle's inertia forces it to divert from the streamline and to impact a surface. *Diffusion:* The adhesion of very small particles affected by Brownian motion. *Gravitational settling:* Particles of larger aerodynamic diameter are pushed downwards due to gravity. *Electrostatic attraction:* Electrostatic forces influence the trajectory of particles, governed by the size and charge of the particle and the charge difference with the filter. The microorganism extraction procedure from filters plays a significant role in detection and quantification, through substantial inactivation of collected microorganisms (Alonso et al., 2017). PTFE, cellulose, polycarbonate, and gelatin filters are commonly used. The gelatin filters have a higher recovery rate as it dissolves into liquid and can be used for culture-based and molecular enumeration. The recovery rate of Influenza viruses using Teflon and gelatin filters was 22% and 10%, respectively, compared to a BioSampler (impinger) (Fabian et al., 2009). In another study, the nanofiber filter had less than 10% extraction efficiency and glass fiber varied between 32% and 162%. It is critical to consider that higher air sample volumes may cause dehydration and impact infectivity (Lednicky et al., 2020).
Gravitational settling	Settle plates employ Petri dishes placed in specific room locations for the desired period on which airborne microbes settle. The use of settle plates for airborne pathogen assays is a standard procedure. However, it provides only comparative data (for example, to compare a room with and without UVC). Settle plate samplers should be placed on the floor or at a breathing height (0.9–1.5 m). The volumetric concentration of microorganisms and air samplers are needed to obtain quantitative estimates.
Electrostatic precipitator	Using electrostatic attraction to collect airborne particles and is used explicitly for smaller particles. However, due to ozone production, it is not a prevalent option for collecting bioaerosols and viral samples (Wells et al., 1991).
Water-based growth tube collectors (GTC)	A new sampling collection device, GTC was compared to BioSampler for MS2 and showed ten times higher collection efficiency (Pan et al., 2016). The early results proved the potential of the GTC for airborne virus sampling as it simulates the breathing and particle collection in the human lungs on a cold day (Pan et al., 2019).

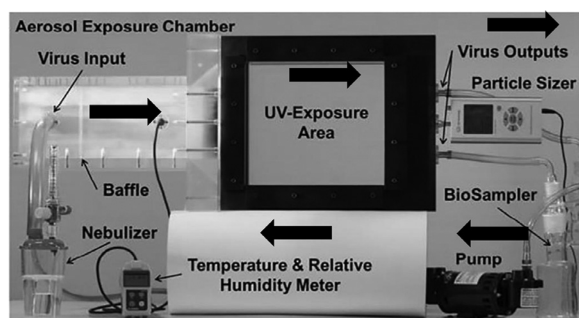

Fig. 8. A lab-scale apparatus for testing the efficiency of UVC airborne disinfection. Reproduced from.

Rotatory drums or dynamic aerosol toroids are ideal for testing aerosols under controlled atmospheric conditions for prolonged durations, particularly for preventing the loss of airborne particles to gravitational settling (Verreault et al., 2008; Henningson and Ahlberg, 1994). Most setups for bioaerosol testing are tailor-made and comparing even controlled studies is often challenging. Some studies use additional components such as neutralizers, humidifiers, and driers to control the aerosol size distribution and humidity. The neutralizer primarily inhibits the particles with opposite charges from attaching and forming larger particles. A desiccator acts as the dryer, and while not common in combination with a humidifier, it assists in adjusting the humidity effectively. Setup variations in different studies is one of the factors contributing to the diverse dose data for even similar aerosolized surrogates. Therefore, applying a standardize test setup can lead to more conclusive data and benefit further the final dose determination for the airborne pathogens.

4.4. Outlook

While several sampling collection techniques exist, the primary challenge is to standardize the viral sampling and detection techniques. Future efforts should also determine the detection limit for each sampling procedure, so that researchers may select an appropriate protocol based on their research needs.

An optimal nebulizing and collecting medium for the targeted bioaerosols is missing: a systematic assessment should determine the optimal nebulizing and collecting medium and assess viral aerosols' collection and storage temperatures. Few studies have reported the impact of relative humidity on the collection efficiency and viability of the viral aerosols. Thus, a thorough investigation of RH and carrier media such as mucus and salt on the viability of viral aerosols could inform future UVGI applications.

5. Impact of operational conditions

The ultraviolet inactivation of bioaerosols in air has not been investigated as comprehensively as in water. The efficacy of the airborne UVGI system requires an understanding of air environmental and operational factors like operating temperature, humidity, and particle size distribution of viral aerosols, discussed below. While this review focuses on UVC for airborne disinfection of SARS-CoV-2, our understanding of this topic

Table 3
Air sampling and nebulizing techniques used for UV inactivation of bioaerosols.

Air Sampling Technique	UV Source	Nebulizer	Microorganism	Airflow	Particle Size	Year
Impinger-SKCBioSampler	LPUV -253.7 nm	HEART[#]	Influenza virus (A/PR/8/34 H1N1),	12.5 L/min	NR*	2012 (McDevitt et al., 2012)
Impinger-SKCBioSampler	Far-UV 222 nm	HEART[#]	H1N1 influenza virus	12.5 L/min	87%: between 0.3 and 0.5 μm, 11%: between 0.5 and 0.7 μm, 2% > 0.7 μm	2018
Impinger	LPUV-253.7 nm	Six-jet collison nebulizer	MS2, Adenovirus, MHV Coronavirus	12.5 L/min	NR*	2007 (Walker and Ko, 2007)
Impinger-AGI-30	UV-LED	Air jet piston compressor	Viruses: MS2, Qβ, ϕX174 Bacteria: E. coli O157:H7, S. Typhimurium, L. monocytogenes, S. aureus Fungi: As. flavu, Al. japonica	35–40 L/min	NR*	2018 (Kim and Kang, 2018)
Impinger- AGI-30	LPUV-253.7 nm	24-jet collison nebulizer	Porcine reproductive and respiratory syndrome (PRRS)	12.5 L/min	1.9 μm diameter	2012 (Cutler et al., 2012)
Impinger- AGI-30, impactor, and nucleopore filtration	LPUV-253.7 nm	Three-jet collison nebulizer	*Legionella pneumophila* (CCRC 16084)	AGI: 12.5 L/min- 5 min Filter: 2 L/min- 5 min	average geometric mean aerodynamic diameter: 0.72 μm	2003 (Li et al., 2003)
Anderson sampler	UVA-365 nm UVV-185 nm LPUV-254 nm	Aerosol generator ATM 226	*E. coli* (CMCC1.3373)	28.3 L/min- 5 min	1–5 μm	2019 (Wang, Lu and Zhang, 2019)
Andersen Sampler- one stage viable impactor	LPUV-253.7 nm	Three-jet collison nebulizer	T7 phi 6 phi X174, MS2	28.3 L/min	T7: 1.24 μ m phi 6: 1.25 μ m phiX174:1.25 μm MS2: 1.23 μm	2005 (Tseng and Li, 2005a)
Andersen sampler- One/ six-stage	LPUV- 253.7 nm	Six-jet collison nebulize-20 psi	*S. marcescens* (ATCC 8195)	28.3 L/ min	Average of 1.3 μm for three different media	2004 (Lai et al., 2004)
Andersen Sampler- One stage sampler	LPUV-253.7 nm	Six-jet collison nebulizer	*Escherichia coli, Bacillus subtilis, Candida famata, Penicillium citrinum*	NP	NR*	2002 (Lin and Li, 2002)
37-mm gelatin filter – 3 μm pore size	LPUV-253.7 nm	Six-jet collison nebulizer	Vaccina Virus	Airflow: 28.3 L/min	NR*	2007 (McDevitt et al., 2007)

[#] High-output extended aerosol respiratory therapy -* NR: Not Reported

is enhanced by broadening our focus to disinfection of bioaerosols by UVC wavelengths.

5.1. Temperature

Temperature impacts the survivability, infectivity, and the UVC susceptibility of airborne microorganisms (Ijaz et al., 1985; Lowen and Steel, 2014). Operating temperature should be considered when designing a set-up and comparing the results in the literature as an effective variable on the required UVC dose.

The survivability of bioaerosols, including viruses, vegetative bacteria, spores, and fungi, have been studied over a temperature range from sub-zero to 50°C (Haddrell and Thomas, 2017, Ehrlich and Miller, 1973, Tang, 2009, Wathes et al., 1986). Extreme temperatures disrupt cellular protein, decreasing survival (Tang, 2009). However, B. subtilis spores decay rate showed no significant difference from -40 to 49°C (Ehrlich et al., 1970). Airborne Influenza survived longer at low (7–8°C) compared to moderate (20.5–24°C) and high (> 30°C) temperatures (Harper, 1961). More information on survivability changes based on the temperature are tabulated in Table S3.

At lower temperatures, the UVC susceptibility of the porcine reproductive and respiratory syndrome (PRRS) virus increased (Cutler et al., 2012). However, Zhang et al. (2020) reported a maximum UVC disinfection efficacy at 20–21°C when considering a range between 15 and 26°C on aerosolized bacteria Staphylococcus epidermidis, Pseudomonas alcaligenes, and Escherichia coli (Zhang et al., 2020). However, the mechanism of temperature's effect on bioaerosols survivability has yet to be described. Table S4 provides the UVC susceptibility changes as a response to temperature and RH humidity.

Raising temperature changes the output of ultraviolet lamp and 254 nm conversion efficiency. There is an optimal vapor pressure at which mercury emits the highest 254 nm and with increasing temperature the optimum pressure deviates and the 254 nm conversion efficiency decreases (He, 2012). Therefore, understanding and optimizing the temperature effects on airborne microorganism survivability and UV lamp output are crucial considerations toward commercial applications.

5.2. Relative humidity

Despite a report by Walker and Ko (2007) that increasing relative humidity (RH, reported in percentage) did not decrease the inactivation rate of aerosolized MS2 (Walker and Ko, 2007), it has been documented that most viruses (e.g. Influenza A, Vaccinia virus, PRRSV) and viral surrogates (e.g., MS2, phiX174, phi6, T7) exhibit a decrease in UV susceptibility at higher RH (Thornton et al., 2022). Riley and Kaufman (1972) reported a decrease in UVC inactivation for Serratia marcescens at RH above 60% (Riley and Kaufman, 1972). Koller (1939) and Whiser (1940) claimed that airborne bacteria are ten times more resistant to ultraviolet light in high- than low-RH conditions (Rentschler et al., 1941). Peccia et al. (2001) reported a decrease in the inactivation rate of three bacteria species at RH above 50% (Jordan et al., 2001). Cutler et al. (2012) assessed the temperature and RH effects on UVC inactivation of airborne PRRS virus. The statistical analysis showed the significant impact of UVC dose, temperature, RH, and the interactions between UV dose and temperature and the product of UV dose and RH. The highest PRRS virus inactivation rate happened at RH between 25% and 79% (Cutler et al., 2012). More information on UVC susceptibility due to (Ma et al., 2020)the RH and temperature are tabulated in Table S4.

The reduction in the inactivation rate at higher RH may result from the protective layer of water coating around bioaerosols. Also, larger particle sizes may better protect against the destructive impact of UV radiation (Tang, 2009). Non-enveloped viruses like respiratory adenoviruses and rhinoviruses tend to survive longer at higher humidity levels (70–90%). Whereas lipid-enveloped viruses survive longer at low RH (20–30%), including Influenza, coronaviruses (SARS-CoVs), respiratory syncytial virus, parainfluenza viruses, measles virus, rubella, and varicella-zoster virus (Tang, 2009). The survival rate disparities in various RHs are associated with cross-linking between the virus surface protein moieties (Cox, 1989). The nature of reactions determined the extent of the damage to the viruses, which occurred through different mechanisms like hydration/ dehydration, UV radiation, ozonation and other stressors (Cox, 1989). it has been reported that lower temperature and humidity are linked to higher transmissibility of SARS-CoV-2 which translate to higher survivability (Ma et al., 2020). Therefore, it is critical for researchers to consider RH and temperature in their studies on SARS-CoV-2 inactivation

5.3. Particle size distribution and suspending media

Particles may change size due to (i) changing RH, (ii) suspending medium composition, and (iii) cell aggregation. Although studies report the survivability of bacteria and viruses in different suspending media in air, few studies consider the interaction between these factors and ultraviolet radiation.

Increasing RH in turn increases particle sizes and bioaerosol survivability (Jordan et al., 2001; Ko et al., 2000; Riley and Kaufman, 1972). An increase in count median diameter (CMD) of *Serratia marcescens* was reported from 6% to 16% following an increase in RH, regardless of the suspending medium (Lai et al., 2004). Ko et al. (2000) reported an increase in CMD from 1.9 μm to 2.6 μm when increasing the RH from ~30% to ~90% for Serratia marcescens. Meanwhile, the UV resistance of both Serratia marcescens and BCG increased at higher RH (Ko et al., 2000).

The suspending medium composition influences the bioaerosol droplet size and its UVC susceptibility (Schaffer et al., 1976, Benbough, 1969, Benbough, 1971, Dubovi and Akers, 1970, Karim et al., 1985). Lai et al. (2004) studied the impact of suspending media on bioaerosol droplet size and formation, concluding that more organic matter in the medium results in lower UV susceptibility. Interestingly, the protective impact of the suspending medium and humidity shows a compounding effect (Lai et al., 2004; VanOsdell and Foarde, 2002). A suspending medium's proteinaceous composition can create a protective layer around the cells (Di Noto and Mecozzi, 1997). The inactivation of ssRNA viruses, hepatitis A virus, and norovirus surrogates by pulsed light required a higher dose when suspended in a medium containing both phosphate-buffered saline (PBS) and fetal bovine serum (5% v/v; 0.2% v/v protein) than in PBS alone (Jean et al., 2011).

In general, aggregates have greater survival than single microorganisms, where aggregation increases resistance to UV radiation (Haddrell and Thomas, 2017). As the droplets dry out, non-volatile components of the suspending medium may adhere to cells, increasing cell aggregation (Lai et al., 2004; Haddrell and Thomas, 2017). Some surrogate Gram-negative bacteria (Pantoea agglomerans, Serratia marcescens, Escherichia coli and Xanthomonas arboricola) had higher survivability when in clusters (~3.5 μm) compared to a single cell (~1 μm). Among them, E. coli showed the greatest increase in stability (D_{90}= 287 min) when in cluster form compared to in a single-cell state (one-log reduction, i.e., D_{90}= 14 min) (Dybwad and Skogan, 2017). Schaffer et al. (1976) showed that the protein content of the suspending medium impacts airborne stability of the Influenza virus below 0.1 mg/ml at high (80%) and low (50%) RH (Schaffer et al., 1976). Fig. 9 shows a typical bacterium in a cluster and single cell format, representing the size changes in two forms.

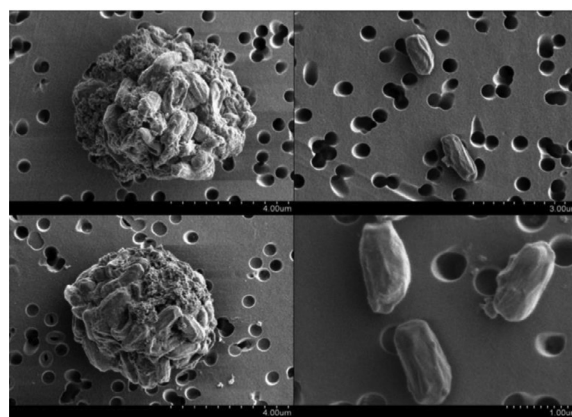

Fig. 9. SEM image of Bacillus atrophaeus in the cluster and single-cell particle collected on a polycarbonate filter with 0.4 μm pore size.

It has been hypothesized that organic matter creates a protective layer around the cell(s) and causes less susceptibility to desiccation and other stressors. No reported mechanism exists to explain the interaction between bioaerosols like viruses (enveloped and non-enveloped), bacteria, fungi and various suspending media. There exists a knowledge gap on the mechanisms of the protective effect of humidity and organic/ non-organic compounds of bioaerosols; this is quite important for understanding disinfection of human-borne pathogens.Finally, it should be noted that the surrounding medium may absorb UVC radiation, affecting the pathogen's decay rate. This varies greatly with the composition of the surrounding medium, such that generalizations are not useful. Suffice to explain that UVC at 254 nm may penetrate 40 cm into distilled water before its intensity is reduced by 30%, while only 10 cm in sea water and 5 cm in a sucrose (10%) solution for the same intensity reductions (Snowball and Hornsey, 1988). The impacts are difficult to quantify due to the changing size of bioaerosol droplets also changing the concentration of salts, proteins and others, which is affected by the environmental RH. Further, it has been well-reported that clumps pathogens offer protection to the innermost individuals, reducing the apparent disinfection potential (Vitzilaiou et al., 2021). Hence, researchers and practitioners should consider these impacts, with a possible a safety-factor on disinfection dosage calculations to account for these effects. Future work could better understand the reduction in UV dosage with changing bioaerosol particle size.

5.4. Outlook

Literature describes the roles of operational and environmental factors on bioaerosol survivability. However, many studies report data for different operating conditions, viruses and applications. The field suffers from a lack of mechanistic studies to describe the impact of operational and environmental factors in combination with the UVC radiation intensity on bioaerosol survivability. As a result, it is challenging to compare these studies and even more challenging to use the diverse literature to create a model for predicting the disinfection potential of different ultraviolet applications.

The range of findings presented suggests the need for a standardized laboratory model with a repeatable and reliable methodology to explain the fundamental differences based on the characteristics of a target viral aerosol and larger scale bioaerosols. For example, a standard procedure to test and compare aerosolized viruses (enveloped vs. non-enveloped), bacteria, and fungi would be of value for developing recommendations on operating conditions for UV devices.

Thankfully, the plethora of studies shows a keen interest in the field by both academia and industry. With improved coordination, it seems likely that UVC air disinfection can be understood for a range of operating conditions and target microorganisms and will prove a valuable

tool to control airborne disease transmission. The effort needs interdisciplinary skills of aerobiology to understand the survivability, engineering for appropriate setup design and photonics to unify the UVC measurement techniques under different conditions. Since this matter is of such great importance to all, it would be desirable if such coordination was spearheaded by an international authority.

6. Industrial application of UV disinfection

The most common UVC germicidal lamps are low-pressure (LP) mercury lamps which emit about 85% of their energy at 254nm and the remaining energy at 185 nm (ASHRAE, 2016). Medium-pressure (MP) mercury lamps are polychromatic, emitting wavelengths of 200- 300 nm which can damage both adenoviral genomes and proteins (Eischeid and Linden, 2011).

6.1. UV-LEDs

Recently, UVC-LED lamps gained popularity for their small size, irradiance control, low operating voltage (Gerchman et al., 2020), fast warmup, long lifetime despite repeated on/off cycles (Song et al., 2016), and containing no hazardous mercury. The wavelength is selected by changing the semiconductor composition (Chen et al., 2017); aluminum nitride-LEDs emit at 210 nm, while aluminum gallium nitride-LEDs emit between 222 and 351 nm (Hirayama et al., 2015). This tunability presents opportunities to tailor for specific industry objectives. In a study using five pathogens (including *Legionella pneumophila* and Bacteriophage Qβ), UVC-LEDs showed the highest inactivation at 265 nm, but the most energy efficient disinfection was achieved at 280 nm. However, the study reported that LP mercury UV lamps had a higher energy efficiency (Rattanakul and Oguma, 2018). Despite low energy consumption during operation. However, the price per watt for UVC-LEDs can be 1000 times higher than LP mercury lamps, and LEDs struggle to convert electrical energy to germicidal output when compared with conventional UVC lamps (Hadi et al., 2020; Sabino et al., 2020). Notwithstanding the many advances in UVC-LED technologies, further developments in efficiency and cost are needed.

6.2. Industrial installation

Early UVC air-disinfection comprised a UV lamp in an upwards-facing aluminum pan hanging below the ceiling (Fig. 1A) (Wells et al., 1942). Today, there are two installation strategies: 1) upper-room systems to radiate the upper airspace of a room and 2) systems installed in a building's air-handling unit to disinfect passing air (ASHRAE, 2019). The typical in-duct UVC provides ~0.02 W/cfm, requiring an irradiance around 1000 to 10,000 μW/cm^2 (ASHRAE, 2019) for large buildings, to target an ~85% single-pass inactivation (Bahnfleth, 2020). Upper-room UVC comprises many smaller lamps of 30–50 μW/cm^2 fluence, for a dose around 1.87 W/m^2 floor area or 6 W/m^3 upper zone volume (NIOSH, 2009), and typically resulting in a higher total power requirement than comparable in-duct UVC designs (Bahnfleth, 2020).

In many cases, UVC is combined with conventional particulate filtration and proper dilution ventilation to optimize cost and energy (ASHRAE, 2019; Ko et al., 1998). Each well-mixed air exchange inactivates about 63% of pathogens, producing a logarithmic decay of airborne pathogens (Brickner et al., 2003). HEPA air filters can provide 99.97% removal of airborne particles 0.3 μm in diameter (Miller-Leiden et al., 1996).

In buildings with sufficient air exchange and appropriately sized HVAC systems, in-duct UVC may provide the energy and cost-efficient disinfection option. However, in older buildings with insufficient air exchange or low vertical air velocities, upper-room UVC may offer a superior design.

7. Safety concerns and far-UVC

7.1. Safety concerns

UVC radiation can cause erythema of the skin and inflammation of the cornea (eye) (Parrish, 1979). Chromophores mainly absorb UV radiation at 254 nm in the outermost layer of dead skin, and only 5% of 254 nm ultraviolet radiation penetrates to the top layer of viable cells. Unlike the protective outer skin layer, the human cornea (eye) is unprotected and more susceptible to injury from ultraviolet radiation (Nardell et al., 2008). Inflammation of the cornea (photokeratitis) usually precedes more harmful inflammation of the conjunctiva (the ocular lining, a condition known as photo keratoconjunctivitis) (ASHRAE, 2016; Talbot et al., 2002).

Despite these rare injuries, UVC disinfection would seem a safe process. Proper UVC system installations can reduce human exposure. In the case of accidental exposure, UVC radiation poses only a small risk to the skin, and while cornea injuries can be painful, the effects were reported to be temporary (ASHRAE, 2016).

In 1972, the US Centre for Disease Control and Prevention (CDC) and the National Institute for Occupational Safety and Health (NIOSH) released a recommended exposure limit (REL) for limiting worker exposure to UV radiation which varies based on the exposure duration (Table S5 (National Institute for Occupational Safety and Health, 1972; Chapter 11-Ultraviolet Radiation, 2019).

Another consideration with UVC is organic materials degradation, such as electrical insulation, sealants, filter media, gaskets and pipe insulation and furnishing and finishes (Kauffman and Wolf, 2012). As a result, UV-resistant materials should be used, especially in the upper-room portion of UVC-irradiated facilities, although this may challenge older buildings' retrofits. While adequately installed UVC systems are unlikely to create unintended exposure, they can further protect occupants by enclosing the radiation source and targeting the bioaerosols.

7.2. Far-UVC as a safe alternative

The shorter wavelengths in UVC range are the so-called 'Far-UVC' spectrum (200–230 nm). Far-UVC is equally or more damaging to pathogens as compared to 254 nm (Riley and Kaufman, 1972), but with far less hazard to humans (Buonanno et al., 2017; Garciá De Abajo et al., 2020). Far-UVC has a much shorter penetration depth than longer wavelength UVC radiation (Buonanno et al., 2013; Goldfarb and Saidel, 1951). It is absorbed by the peptide bond in amino acid residues (Rosenheck and Doty, 1961) and so is blocked by the stratum corneum layer of skin (i.e., outermost skin layer) and, importantly, also blocked by the cornea of the eye (Sabino et al., 2020). Therefore, very little irradiation reaches the superficial layer of the epidermis and even less reaches to the deeper basal layer, where it may alter DNA and cause skin cancer (Cadet, 2020; Barnard et al., 2020). There are not many studies on the impact of far-UVC on the skin and eye tissues due to the low availability of commercialized far-UVC devices. Kaidzu et al. (2021) assessed the photokeratitis threshold in a rat and reported 5000 and 15,000 mJ/cm^2 for UV radiation at 207 and 222 nm. This is well within current safety guidelines.

Far-UVC is commonly generated through barrier discharge excimer lamps which emit quasi-monochromatic radiation (Sosnin et al., 2006). A recent krypton-chloride excimer (Kr-Cl*) lamp emits mostly at ~222 nm (Kang et al., 2019). Far-UVC generation has also been demonstrated using solid-state emitters and conventional UV-LED construction, including thin layers of AlGaN to form the active region, photon-generating (Kneissl, 2016). Current far-UVC LED models suffer from short lifetimes and low power output (~micro-watt range). However, similar challenges are being resolved in UVC-LEDs.

Using a fully coupled radiation and fluid dynamic model, the disinfection rate for a typically ventilated room was predicted to increase 50–85% when using the far-UVC radiation compared to just ventilation

(Buchan et al., 2020). Exposure to only 2 mJ/cm^2 of 222 nm UVC inactivated > 95% of aerosolized H1N1 influenza, while only 1.7 and 1.2 mJ/cm^2 were needed for 99.9% inactivation of coronavirus 229E and OC43 in air, respectively (Buonanno et al., 2020). In fact, at the current REL (3 mJ/cm^2/h), far-UVC could inactivate ~90% of viruses in 8 min, 95% in 11 min, and 99.9% in 25 min (Buonanno et al., 2020). This shows great promise for application in high-use public areas such as hospitals, intensive care units and public transit.

While far-UVC presents an opportunity for the safe application of upper- and perhaps even lower-room UVGI systems, the technology is not broadly available on the market, and the cost is expected to be substantially higher than conventional LP-mercury lamps (Sabino et al., 2020). Some far-UVC lamps generate ozone which negatively impacts the respiratory, cardiovascular, and central nervous systems. Based on the WHO guideline, the mean exposure limit to ozone for 8 h is 0.2 mg/m^3 (WHO, 2021). While there is no standard protocol to measure the produced ozone, it is the manufacturer's responsibility to ensure the safety and potential hazard.

8. UVC as a tool against SARS-CoV-2

Research has confirmed that SARS-CoV-2 is airborne (Chia et al., 2020), was detected in air samples from a hospital setting (Santarpia et al., 2020), and that aerosol droplets of a breathable size remained infectious even after 16h (Fears et al., 2020). Prior to the emergence of the SARS-CoV-2 virus, researchers showed that UVC provided a 5-log inactivation of the MERS-CoV and mouse hepatitis viruses (MHV-A59) (Bedell et al., 2016). In studies using SARS-CoV-1, fifteen minutes of exposure to UVC light at 254 nm was sufficient to inactivate the SARS-CoV virus, while UVA light had no effect even at longer durations (Darnell et al., 2004), while elsewhere a lower intensity of UVC light (> 90 μW/cm^2) was able to inactivate the virus after 60 min (Duan et al., 2003). Interestingly, this same study reported successful inactivation of SARS-CoV-1 also using heat treatment above 65°C, alkaline (pH>12) or acidic (pH<3) conditions, or the use of formalin and glutaraldehyde treatment.

Beggs and Avital (2020) provided a simple calculation to determine the average irradiance flux, E_r (in W/m^2) to achieve a given pathogen inactivation level (Beggs and Avital, 2020).

$$E_r = -\frac{1}{Z \times t_{uv}} \times \ln\left(\frac{N}{N_0}\right) \quad (1)$$

where Z is the UV susceptibility constant (m^2/J) for a particular pathogen (i.e., SARS-CoV-2), t_{uv} is average exposure time (i.e., the bioaerosol's residence time in the upper-room or UVC-exposed area), and N/N_0 is the survival fraction (i.e., 4-log such that $N/N_0 = 1/10{,}000$). For predicting the required dosage for the inactivation of SARS-CoV-2, we require a Z value for this specific pathogen. By reviewing 16 studies in the UVC range for the inactivation of SARS-CoV-1, MERS-CoV, and SARS-CoV-2, Beggs et al. reported a Z value for upper-room aerosolized SARS-CoV-2 as 0.377- 0.590 m^2/J, which the authors described as "*highly susceptible to UVC damage when suspended in air*" (Beggs and Avital, 2020).

The UV susceptibility parameter, Z, is similarly expressed as a UV susceptibility rate constant, k_{uv}:

$$k_{uv} = Z \times E \times \frac{h_{uv}}{h_r} \quad (2)$$

where E is the irradiation flux (W/m^2), h_r is the room height and h_{uv} is the height of UV radiance in the room. Elsewhere, upper-room UVGI provided better effective disinfection than a ventilation rate of three air changes per hour (n, in AC/h) (Noakes and Gilkeson, 2015). Combining the UV disinfection rate constant above, k_{uv}, with the mechanical ventilation rate constant, k_v (i.e., $k_v = n/3600$), an expression is obtained for overall decay of viral pathogens in a room space from time zero and after t seconds (C_0 and C_t) (Beggs and Avital, 2020).

$$-C_t = C_0 \times e^{-(k_v + k_{uv} + k_d)t} \quad (3)$$

where k_d is the particulate deposition rate constant (e.g., 0.0014 s^{-1} (Sagripanti and Lytle, 2020)).

Such simple expressions make assumptions such as the room volume being well-mixed. But for practical purposes, this is valid, and so these tools and the newly reported inactivation rate constants for SARS-CoV-2 offer researchers a means to quickly estimate the required UVC dose and the disinfection potential when assessing air disinfection systems.

9. Future research needs

Applying UVC irradiation as a regular and practical means of air disinfection technology faces many technical challenges. Foremost, there is no standard for operational and environmental conditions under which a system must be proven effective. Environmental factors like relative humidity, temperature, suspending medium and type of bioaerosol can impact the efficacy of UVC air disinfection systems. A standard for quantifying laboratory and pilot-scale inactivation efficiency is needed. A second priority is to understand the kinetics of bioaerosol UVC inactivation at baseline environmental conditions and determine the UVC-sensitivity of the intended microorganisms (and their surrogates). This will inform the determination of UVC susceptibility of different bioaerosols, thereby allowing for a generalized model on bioaerosol inactivation by UVC. Another challenge is ensuring the uniformity of bioaerosols and UVC dose distribution in the volume of air. Lacking a standard guideline for measuring UVC dose in a typical air disinfection system is the major source of discrepancies in the reported dose requirements. Accomplishing these priorities will address the gap in defining the baseline of standard environmental conditions, improving the broad industrial relevance of future works, and enabling the facile comparison and interpretation of different laboratory results.

The current research needs to ensure the safe and effective use of UVC air disinfection are summarized as follows:

(1) Research on the inactivation of each pathogen of interest, like SARS-CoV-2, is needed to confirm the efficacy and optimal protocols for disinfection with UVC irradiation and compare the cost-benefit of the commercial UVC systems.
(2) Evaluating the use of UVC irradiation for inactivation of other airborne viruses, particularly pathogenic enveloped and non-enveloped respiratory viruses, in the air.
(3) Evaluating the mechanisms of UVC radiation reacting with viral and bacterial structures (i.e., nucleic acids, proteins, lipid structures, etc.) to enhance our predictions on the ultraviolet inactivation rate and consequently the air disinfection efficacy. This would improve the response time to develop technologies for future emerging airborne pathogens.
(4) The impact of operational and environmental factors on the biological decay rate of bioaerosols have yet to be described. Factors include the aerosolization technique, sampling protocol, humidity, temperature, particle size, aerosol age, and growth phase of the microorganism.
(5) Research is needed on the impact of droplet size and coating with actual or simulated sputum on their inactivation mechanism since this is most relevant for human UVGI applications.
(6) Developing a database for power and time requirements for inactivating a range of common airborne pathogens to guide industry users in selecting UV irradiation power, contact time, RH levels and temperature.

Overall, this article reviewed the literature for viral airborne UVC disinfection in the light of COVID-19 pandemic to represent the current state of knowledge. We studied the gaps and factors associated to the UVC dose discrepancies, subsequently, determined the future research needs hoping to feed into the faster and more informed responses in managing future pandemics and endemics due to the airborne pathogen transmissions using UVC systems.

Reviewing more than 150 articles, it is determined that, while UVC irradiation is an effective tool to inactivate viral aerosols, the operational and environmental factors play a significant role on the efficacy and contributes to the observed discrepancies in required UVC dose. The conditions under which data is being generated in the lab studies is important in translating the knowledge in indoor settings in real case scenarios. For example, the suspending medium applied in the nebulizers impacts the size distribution and UVC adsorption of the aerosolized viral surrogates which should be considered when comparing the results and translating data from a lab study to real-case scenarios. Viral aerosol coughed from humans are covered in sputum which contains proteins that can absorb UVC radiation, hence impacting the required UVC dose for same inactivation level. Also, the viral surrogate selection is proven to be important as the type of surrogate impacts the required UVC dose. The aerosolization (i.e., nebulization) and sample collection techniques can contribute to aerosol's viability and thus it should be taken into consideration when interpreting the inactivation efficacy.

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Supplemental information

Table S1. Genome information on common viruses and viral surrogates

Table S2. Sensitivity of viral pathogens and viral surrogates in the liquid medium to UVC

Table S3. Temperature and RH impact on aerosolized pathogen survivability

Table S4. Temperature and RH impact on UV inactivation of aerosolized pathogen

Table S5. Permissible UV radiation exposures for 254 nm

Declaration of Competing Interest

The authors report no conflict of interest which may have influenced the discussion presented herein.

Data Availability

Data will be made available on request.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.hazadv.2022.100183.

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