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Short review

Potential of pulsed light technology for control of SARS-CoV-2 in hospital environments

Julie Jean [a], María Isabel Rodríguez-López [b], Eric Jubinville [a], Estrella Núñez-Delicado [b], Vicente M. Gómez-López [c,*]

[a] Département des Sciences des Aliments, Faculté des Sciences de l'Agriculture et de l'Alimentation, Université Laval, Quebec City, QC, Canada
[b] Departamento de Tecnología de la Alimentación y Nutrición, Universidad Católica San Antonio de Murcia, Campus de los Jerónimos, E-30107 Murcia, Spain
[c] Catedra Alimentos para la Salud, Universidad Católica San Antonio de Murcia, Campus de los Jerónimos, E-30107 Murcia, Spain

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ABSTRACT

The emergence of the SARS-CoV-2 infection and its potential transmission through touching surfaces in clinical environments have impelled the use of conventional and novel methods of disinfection to prevent its spreading. Among the latter, pulsed light may be an effective, non-chemical decontamination alternative. Pulsed light technology inactivates microorganisms and viruses by using high intensity polychromatic light pulses, which degrades nucleic acids and proteins. This review describes this technology, compiles and critically analyzes the evidence about the virucidal efficacy of pulsed light technology with view on its potential use against SARS-CoV-2 in touching surfaces in health-care facilities. The efficacy of pulsed light proved against many different kind of viruses allows to conclude that is a suitable candidate to inactivate SARS-CoV-2 as long as the required fluence is applied and the appropriated exposure to contaminated surfaces is guaranteed.

1. Introduction

The virus currently known as SARS-CoV-2, which produces COVID-19 illness, emerged in the city of Wuhan in China in December 2019. Specifically, the WHO office in China was notified on December 31, 2019 that there were several patients with respiratory infections of unknown origin in Wuhan, in Hubei province. And it was not until January 12, 2020 when this new virus was identified as 2019-nCoV by the WHO (WHO). A report on the situation of the WHO from January 30 determines the existence of a total of 7818 confirmed cases worldwide, most of them in China and 82 in 18 other countries. The WHO assesses the risk in China as very high and the global risk as high. But about a month later, and due to the alarming levels of virus spread, its severity, along with the alarming levels of inaction by different countries, the WHO is conducting a new assessment. The WHO determines in its evaluation of March 11 that COVID-19 can be considered a pandemic, since the volume of cases outside China multiplied by 13, and the number of countries involved reached 114, with a total of 118,000 cases and more than 4000 deaths (WHO) [1] By the end of September, there were 33,119,791 cases diagnosed in 188 countries, 997,966 deaths and 22,930,309 people recovered worldwide, these statistics increase daily [2]. The transmission of SARS-CoV-2 through air and fomites makes necessary to look for effective methods for its inactivation, especially in hospital environments, where COVID-19 patients can spread this virus.

Pulsed light (PL) is a technology for microbial inactivation based on the application of high-intensity flashes of incoherent, wide-spectrum light [3]. The spectrum of light ranges from infrared to ultraviolet light. The microbicidal action of pulsed light is due to wavelengths in the range 200–300 nm, so mainly UV-C and a small portion of UV-B and its main target are the nucleic acids [4]. The efficacy of PL against a wide variety of viruses has been proved in hospitals environments and may also be efficient for the inactivation of SARS-CoV-2. In consequence, this review aims to compile in a systematic way and analyze the evidence generated so far about the virucidal efficacy of pulsed light technology with view on its potential use against SARS-CoV-2 in touching surfaces in health-care facilities.

2. Description of SARS-CoV-2

Coronaviruses are known to infect a wide variety of vertebrate species [5] including birds, bats, mice, livestock and other animals in addition to humans [6,7]. They are spherical and bear numerous

* Corresponding author.
E-mail address: vmgomez@ucam.edu (V.M. Gómez-López).

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glycoprotein spikes that confer to them a unique crown-like appearance. The nucleocapsid is symmetrical with a diameter ranging from 60 nm to 140 nm [5–9].

Coronaviruses belong to the taxonomic order *Nidovirales*. All viruses in this order are enveloped and contain non-segmented single-stranded positive RNA [10]. SARS-CoV-2 belongs to the family *Coronaviridae*, subfamily *Orthocoronaviridae* [11,12]. Four genera of coronavirus are currently recognized: alpha, beta, gamma and delta (Fehr). Species pathogenic to humans, namely SARS-CoV, MERS-CoV, HCoV-OC43, HcoV-HKU1 and SARS-CoV-2, belong to the β genus [5,10].

A unique feature of coronaviruses is their large genome size, which can vary between 26 and 32 kb, the largest known among the RNA viruses [13]. Coronavirus genomes usually comprise a surface/spike (S) protein, a membrane (M) protein, an envelope I protein and a nucleocapsid (N) protein [9]. Recent studies have shown that the SARS-CoV-2 genome varies from 29.8 to 29.9 kb and has six accessory proteins [14] not found in other coronaviruses. Its sequence similarity to two coronaviruses identified in 2018 in Zhoushan, eastern China and known to cause severe acute respiratory syndrome (SARS) is about 88% [15]. Its similarities to SARS-CoV (2003, isolated in Guangdong, China) and to MERS-CoV (Middle-East respiratory syndrome, 2012, Saudi Arabia) are respectively 79% and 50% [15]. In spite of their differences, SARS-CoV-2 and SARS-CoV use the same surface receptor for cell entry, namely angiotensin-converting enzyme 2 or ACE2 [16], a finding very important for antiviral treatment research.

SARS-CoV is known to have emerged from the Himalayan palm civet and MERS-CoV from the dromedary camel [15,17,18]. The animal origin of SARS-CoV-2 remains unknown. A rumour that it was constructed in a laboratory has been refuted [19]. Knowledge of its origin would provide genetic and functional data that would facilitate outbreak surveillance, resurgence prevention, vaccine development, animal models and inactivation studies.

3. Transmission of SARS-CoV-2

SARS-CoV-2 is transmitted mainly via respiratory droplets (5–10 μm), small speech droplets [20–22] and fomite contacts [23–27], leading to both community and intrafamily transmissions. Although it is thought that SARS-CoV-2 may be transmitted via aerosol, that is, droplets smaller than 5 μm [18], only one study has shown potential aerosolization of SARS-CoV-2 under stringent controlled laboratory conditions [29]. Two studies have shown negative SARS-CoV-2 molecular amplification in the air of symptomatic patient rooms [27,30].

Several other transmission routes have been investigated since SARS-CoV-2 RNA has been detected in different samples, such as fecal specimens, blood, urine [31,32] and wastewater [33–36]. Data supporting fecal-oral transmission remain ambiguous [37]. Wu et al. nevertheless have demonstrated that RNA can be detected in stool 33 days after the last detection of SARS-CoV-2 in respiratory samples [38]. Two studies of small numbers of patients have shown infectious SARS-CoV-2 in stool samples [31,39], and replication of the virus in human intestinal organoids has been shown [40]. Its presence in wastewater further accentuates the need to establish the role of fecal-oral transmission. The human-to-animal route also has been confirmed [41,42], while other intermediate hosts are still being investigated [40,43]. Studying the infectiousness of different samples and surfaces will facilitate pandemic control and the development of SARS-CoV-2 inactivation treatments.

Coronaviruses are known to remain infectious for up to 9 days on glass, plastic and metal at room temperature [44]. SARS-CoV-2 has been shown to be more stable on plastic, stainless steel and glass (72–96 h) than on absorbent surfaces (cardboard, paper, tissue paper) or on copper (< 24 h) [29,45]. Inactivation of coronaviruses including SARS-CoV-2 increases with higher temperature [45,46]. SARS-CoV-2 tolerates a wide range of pH [45]. However, common surface disinfectants, such as 62–71% ethanol, 0.5% hydrogen peroxide and 0.1% sodium hypochlorite solutions are effective in <1 min of contact, while biocidal agents (0.05–0.2% benzalkonium chloride and 0.02% chlorhexidine digluconate) are less effective [44]. Green inactivation technologies already deployed in some facilities could also be of aid in health care systems and guide government decisions.

4. Pulsed Light Technology

PL is a consolidated technology with applications in the food industry, mainly for the decontamination of contact surfaces [3]. It can produce faster results than conventional UV-C, both, on energy and time basis [4]. The use of PL is restricted to surfaces, transparent liquids and air because UV light is readily absorbed by the surface of opaque bodies. The unit used to characterize PL treatment regimens is fluence (J/cm^2), which is the amount of energy impinging a target per surface unit. A more formal definition of fluence states that it is "the total radiant energy traversing a small transparent imaginary spherical target containing the point under consideration, divided by the cross section of this target" [47]. The lack of reporting treatment conditions in terms of fluence makes difficult to compare and reproduce results published by different research groups and makes many results only reproducible using the same PL device model under the exactly the same treatment conditions, which is a severe limitation that has been previously discussed [48]. In many cases, results are reported based on treatment time and lamp-target distance, but devices vary in fluence per pulse, emission spectra and pulse repetition rate. Difficulties shared by UV generating devices of different types used in health care facilities have been recently discussed [49]. The bulk of the research about the use of PL in hospital environments has been addressed to the inactivation of bacteria, many of them targeting specifically methicillin-resistant *Staphyloccocus aureus* and *Clostridioides difficile* and carried out as case studies. While most of the evidence has been recently classified as weak due to experimental procedures [50], PL technology is a firmly accepted although not widespread technology in food industries, and the weaknesses of the experimental approaches used to test it for healthcare purposes can not underrate its potential. The need of additional evaluation by independent investigators has been previously recommended [51].

5. Pulsed Light Equipment

PL devices work by taken energy from the plug, storing it in capacitors and releasing it to a xenon lamp at fixed time intervals, typically 1–3 pulses per second. The charging time of the capacitors is longer than the releasing time, which amplifies the power received by the lamp. This not only allows generating a powerful blast of light but also enriches the UV component of the emission. The inert gas (xenon) that fills the lamp lacks of the potential danger of using conventional UV lamps that are filled with mercury and as consequence is more environmentally friendly.

Three basic devices can be distinguished for the purposes of this review. One is a benchtop device used in basic research. It consists in a treatment chamber were the experimental sample is loaded and subjected to the treatment. The second is a mobile robot manufactured by the American company Xenex™ and the Russian company Melitta™. The third is a handheld device powered by batteries manufactured by the Japanese company Comet™.

The robot is the type of PL system more tested in hospital environments. A typical test using this device includes moving the system to a hospital ambient and placing the potentially contaminated surfaces assuring its exposure to light, programing the robot and letting it work for several minutes in absence of people. The lamps, initially located inside the device, move automatically to the exterior and treatment starts. The procedure is repeated turning upside down potentially contaminated surfaces (TV remote in rooms, phone, blood pressure cuffs, etc.) and/or placing the robot in another part of the room. This treatment is sometimes combined with a previous conventional hand cleaning of surfaces with disinfectants. The cost of one unit of this equipment has been

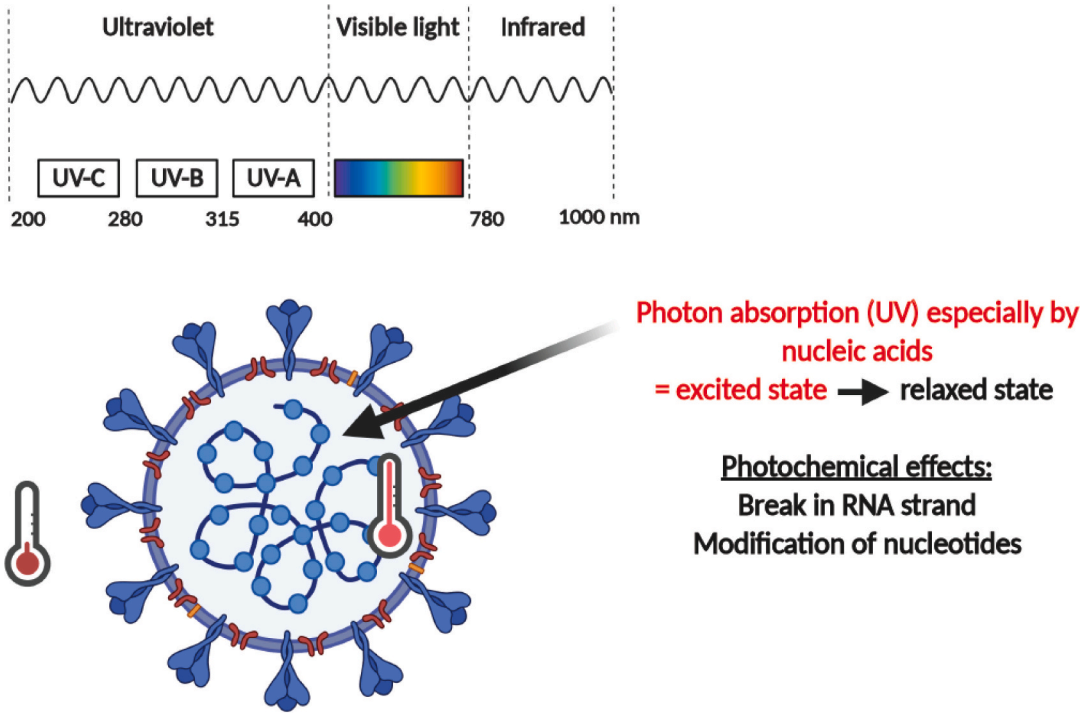

Fig. 1. Schematic representation of the mechanism of inactivation of coronavirus inactivation by pulsed light.

reported to be 102,300 USD in 2017 [50]. PL is harmful to humans and rooms must be evacuated during treatment. PL robots are equipped with movement sensors that stop them from working if someone enters accidentally to the treatment area.

6. Pulsed Light Inactivation Mechanism

All viruses are formed by nucleic acids and proteins, which absorb UV light and are the expected targets of PL action.

MNV-1 is a murine norovirus, with a single strand RNA virus like SARS-CoV-2. The effect of PL on MNV-1 was studied by Vimont et al. (2015) [52] by using transmission electron microscopy, gel electrophoresis under reduced conditions and ultra-performance liquid chromatography-tandem mass spectrometry. PL caused single-strand breakage, damage to the virion structure and breakage of proteins (Fig. 1); photoproducts were not detected but their formation in small quantities was not ruled out. Different from the SARS-CoV-2, MNV-1 is a non-enveloped virus. However, this should not suppose a significant difference for inactivation since PL has also been shown to be effective against Sindbis, which is a single strand RNA enveloped virus [53].

The spectral sensitivity of MS2 coliphage, a single-stranded virus, across the 210–290 nm range has been studied using a tunable laser [54]. The results indicate that RNA damage is the main cause of MS2 inactivation. The loss of infectivity had a peak at about 260 nm, which closely matches RNA absorbance and genome damage measured by reverse transcription-quantitative PCR. The loss of infectivity decreased at 240 nm but then dramatically increased up to the lowest wavelength assayed (210 nm), keeping a close relationship with genome damage but not with RNA absorbance. The relative spectral sensitivities at 260, 240 and 210 nm as compared with that at 253.7 nm (which is the usual reference wavelength because it corresponds to the emission of conventional monochromatic UV light) were respectively 1.4, 0.7 and 4.1. The finding suggests that RNA damage at 210–240 nm occurs due to energy transfer from proteins to RNA or protein-RNA cross-linking.

7. Susceptibility of Viruses to PL

RNA viruses seem more susceptible to PL inactivation than DNA viruses based on results found studying nine types of viruses [53]. This hypothesis is further supported by the higher susceptibility of poliovirus (RNA virus) to PL in comparison with that of adenovirus (DNA virus) reported by Lamont et al. [55]. Relatively low fluences are effective against viruses, with >3 log reductions for 3.45 J/cm^2 for MNV-1 [52] and 4 log reductions for 0.2–1.1 J/cm^2 for nine different viruses studied by Roberts and Hope [53]. As a reference point, the US Food and Drug Administration allows a maximum fluence of 12 J/cm^2 for food treatment [56]. Table 1 gives an overview of PL efficacy against viruses.

PL has been tested against MERS-CoV, which is a betacoronavirus like SARS-CoV-2. PL reduced MERS-CoV by 1.54 log cycles while VSV and Ebola virus exhibited >5 and 7 log reductions respectively. These results do not mean that the efficacy of PL on coranoviruses is low because these tests were carried out under different conditions. While MERS-CoV, vaccinia virus and IBDV were in a liquid suspension and no more than 1.54 log inactivation was measured for none of them, VSV and Ebola virus were dry and their titre decreased below the detection limit upon PL treatment [57]. The liquid used to suspend some of these viruses may have attenuated light transmission.

8. Factors Limiting PL Efficacy

The two main factors limiting the efficacy of PL in environments such as hospital rooms are the shadowing effect and the distance lamp-target [3]. The shadowing effect implies that any hurdle that generates a shadow to the light emitted by a PL device will give place to an area that will remain untreated. The second factor is that light intensity decreases with the square of the distance, which implies that the further the target is from the lamp, the lower the inactivation effect will be. It has also been reported that the presence of organic matter reduces PL efficacy. For example, the inactivation of murine norovirus and hepatis A virus is 5 log in absence of organic matter and about 3 logs in presence of 5% fetal bovine serum [60].

Table 1
Efficacy of pulsed light against different viruses on diverse matrices.

Nucleic acid	Family	Virus	Matrix	Log reduction	Fluence (J/cm$^{2)}$	Reference
(+)ssRNA	Coronaviridae	Middle East respiratory syndrome-related coronavirus (MERS-CoV)	Liquid	1.54	*NR	[57]
	Caliciviridae	Murine norovirus	Groundwater	3.35	4.30	[58]
			Blueberry	3.8	22.5	[59]
			Strawberry	0.9	22.5	[59]
			PBS	6.69	3.43	[58]
				5.8	2.47	[59]
			Alginate	3.58	0.69	[52]
			Hard water	3.9	4.84	[52]
			Turbid water	3	3.45	[52]
			Stainless steel	5	0.060	[60]
				2.6	8.98	[52]
			PVC (plastic)	5	0.060	[60]
				3	2.07	[52]
		Recovirus A (Tulane virus)	PBS	6	4.94	[59]
		Feline calicivirus	Swine Liver	2.8	60	[55]
		(FVC)	Ham	2.2		
			Sausage	2.3		
	Picornaviridae	Hepatovirus A	Stainless steel	5.0	0.060	[60]
			PVC (plastic)	5.0	0.091	
		Cardiovirus A (Encephalomyocarditis)	PBS	4	0.3	[53]
		Polio virus type 1	PBS	4	0.3	[55]
	Togaviridae	Sindbis virus	PBS	4	0.4	[53]
	Leviviridae	Escherichia virus MS2	Black pepper	0.61	28.2	[61]
			Garlic	0.40	18.8	
			Chopped mint	1.28	18.8	
			Culture Media	6.5	0.06	[62]
			Swine liver	1.6	60	[63]
			Ham	0.97	60	
			Sausage	1.3	60	
			Water	3	0.04	[64]
(−)ssRNA	Rhabdoviridae	Indiana vesiculovirus (VSV)	Culture medium	5	NR	[57]
	Filoviridae	Ebola virus	Culture medium	7	NR	
dsRNA	Birnaviridae	Infectious bursal disease virus (IBDV)	Culture medium	0.86	NR	
dsDNA	Adenoviridae	Human mastadenovirus A	Drinking water	4	0.174	[65]
		Human mastadenovirus F	Culture Medium	4	0.12	[66]
		Human mastadenovirus C	Culture Medium	2	0.06	
	Poxviridae	Vaccinia virus	Culture medium	1.38	NR	[57]
			PBS	4	0.5	[4]
	Myoviridae	Enterobacteria phage T4	Culture medium	3	0.0036	
	Autographiviridae	Escherichia virus T7	Culture medium	3	0.0034	
	Herpesviridae	Human alphaherpesvirus 1	PBS	4	0.8	[53]
	Polyomaviridae	Simian virus 40	PBS	4	1.1	[53]
ssDNA	Parvoviridae	Canine parvovirus	Plastic face shield/Surgical gown	4	NR	[67]
			Glass slide			
			PBS	4	0.2	[53]
		Deltapapillomavirus 4 (BPV)	PBS	4	0.9	[53]
Circular ssDNA	Microviridae	Enterobacteria phage phiX174	Swine Liver	2	60	[63]
			Ham	1.6		
			Sausage	1.6		

* NR: non-reported.

9. Use in Health Care Facilities

Different studies avail the use of PL in health care facilities. These studies have been carried out mainly against bacteria, which hints about its potential effectivity against viruses. The efficacy of PL, alone or as a complement of standard cleaning with disinfectants, has been proved on personal protective equipment [67], respirators [67], touching surfaces of hospital units (surgical sites, isolation units, hematology and bone marrow transplant units) [69–72], hospital rooms [69,73–79], post-discharge patient isolation rooms [80] clinical laboratories [81], human milk feed preparation areas [82], operating rooms [83], intensive care units [80] and burn units [84]. Table 2 gives an overview of these studies which compiles results of case studies of heterogeneous nature where a PL system was used to disinfect a room. No fluence data was reported in these tests and rooms had a wide variety of dimensions, furniture and appliances. The most common feature of these tests was the use of two cycles of disinfection of five minutes. While PL has not been tested to disinfect contaminated air in hospital rooms, it should be able to do it according to the evidence collected when testing the disinfection of air in ambulances [85].

There are many reports of the disinfection efficacy of PL in hospitals. These kind of studies are typically designed for disinfecting discharges and transfers, alone or after standard cleaning, and prior to occupation of the room by the next patient. For example, a PL robot used in a prospective study at Queen Hospital demonstrated the efficacy of a PL device in disinfecting 40 hospital rooms, for which the device was deployed for three cycles, one cycle on each side of the bed, and another cycle in the bathroom, all lasting five minutes. This study demonstrated a significant reduction in the microorganisms on the high contact surfaces in the patient rooms when PL was incorporated into the hospital room cleaning protocols. With this disinfection protocol carried out in the hospital, a 0.66 log reduction in the biological load has been

Table 2
Efficacy of pulsed light in health care facilities.

Center	Virus/Bacteria	log reduction	Surface / Room type	Reference
NHS hospital in the Barking, Havering, and Redbridge University Hospitals group in North London	Aerobic bacteria, including methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, and carbapenemase-producing Enterobacteriaceae	1.05	Toilet seat Bathroom faucet	[86]
Veterans Affairs facility, Temple, Texas	Aerobic bacteria	0.74 0.81 0.61 0.58 0.30	Call button Bedrail Tray table Bathroom handrail Toilet seat	[67,74]
Central Texas Veterans Health Care System	Methicillin-resistant *Staphylococcus aureus*	1.08 0.68 1.54 0.37 1.29	Bathroom handrail Bedrail Call button Toilet seat Tray table	
Yamagata University Hospital	Methicillin-resistant *Staphylococcus aureus, Acinetobacter baumannii*	1.08	Bed rail, cardiopulmonary monitor touch panel, ventilator control panel, intravenous fluid pump control panel, glove hook, workstation keyboard, workstation trolley handle	[72]
The University of Texas MD Anderson Cancer Center	Methicillin-resistant *Staphylococcus aureus*, *Clostridium difficile*	>0.52	Monitors, electrocautery unit, anesthesia cart, bedside table controls	[83]
Short-term acute care facilities and ambulatory surgical center	Biological load	0.42 0.44 1.05 1.40 0.82	Anesthesia machine Nurses document station Back table OR table Supply cabinet doors	[70]
The Mayo Clinic large tertiary care hospital	*Clostridium difficile*	0.33	Hematology and bone marrow transplant units and one medical-surgical unit	[71]
Netcare Blaauwberg hospital	*Acinetobacter baumannii*, *Enterobacter cloacae*, *Stenotrophomonas maltophilia, Aeromonas hydrophilia, Enterococccus casseliflavus, Falvimonas oryzihabitans, Klebsiella pneumoniae pneumoniae, Serratia marcescens, Serratia liquifaciens*	1.00	The NICU prewash EHM bottle area, the Neonatal intensive care unit post-wash expressed human milk bottle area, fridge door handle and single counter surface	[82]
Veterans hospitals	Methicillin-resistant *Staphylococcus aureus* or aerobic bacteria colonies	0.61	Toilet seat Toilet handrail Bedrail Tray table Call button or telephone	[76]
University Hospital of Hiroshima, Japan	Methicillin-resistant *Staphylococcus aureus* or aerobic bacteria colonies	1.28 1.24	Bed rail Bed control panel Over table Vital sign monitor control panel Infusion pump control panel Bedside table Door handle Sink counter Toilet seat	[79]
Enrique Garcés General Hospital, Quito, Ecuador	Methicillin-resistant *Staphylococcus aureus*, *nterococcus. faecium* (Van B), *Pseudomonas aeruginosa* (VIM), *Klebsiella pneumoniae*	0.62–0.89	4 operating rooms, 8 intensive care units, 2 rooms for internal medicine, 1 neonatal intensive care unit, 1 neoInfectology unit, 1 microbiology laboratory	[77]
Department of Laboratory Medicine, the Third Xiang-Ya Hospital	*Staphylococcus haemolyticus, Micrococcus luteus, Staphylococcus epidermidis, Staphylococcus hominis, Klebsiella pneumonia, Staphylococcus condiment, Staphylococcus sciuri ssp sciuri, Staphylococcus capitalis, Staphylococcus xylosus, Aircoccus urethrae, Staphylococcus cohnii, Lactobacillus serratiae, Bacillus cereus, Bacillus plateau, Bacillus megatherium, Bacillus nisseni, Bacillus firmus, Bacillus licheniformis, Bacillus huanghai, Klebsiella pneumonia, Moraxella Oslo, Sucrose burkholderia. Stenotrophomonas maltophilia, Pseudomonas Moses, Sphingobacterium multivorum, Pseudomonas syringae, Paracoccus Histogenes, Timothy masai, Delftia acidovorans, Rhizobium radiobacter, Aspergillus nidulans, Aspergillus fumigatus, Aspergillus flavus, Aspergillus niger, Curvularia lunata, Streptomyces purpureus, Agromycetes salundinae, Bacillus pumilus, Rhizoma lemoniae*	1.00-"full inactivation"	Central laboratory, clinical microbiology laboratory and clinical immunology laboratory	[81]
Animal laboratory	*Revibacillus centrosporus, Flavobacterium gelidilacus, Hydrogenophaga pseudoflava, Lactobacillus brevis, Lactobacillus paracasei* ssp. *paracasei, Microbacterium lacticum*	"Full inactivation"	Research tables, weighing scales, doorknobs, handles of trolleys, and simultaneously the air	[87]

achieved, especially in the areas of the toilet seat and the tap in the bathroom [86].

While some studies have been focused in using PL as lone disinfection method, others have assayed it as a complement of the standard cleaning procedures of concerned hospitals. The use of PL after a standard disinfection with the use of bleach was studied by Vianna et al. [80] in a standard hospital room with an integrated bathroom. The equipment was run one cycle in the bathroom and another cycle at each side of the bed, each lasting 5 min. If the room did not have a bathroom, only two cycles were applied. The impact of the PL treatment was significant, reducing the number of patients who developed infection with methicillin-resistant *Staphylococcus aureus* (MRSA), *Clostridium difficile* and vancomycin-resistant Enterococci (VRE), especially in areas of high flow of patients. These types of studies were also carried out by Jinadatha et al. [67,74] and both has shown that PL technology was effective in disinfecting rooms, managing to eliminate from aerobic bacteria to MRSA; and by Kovach et al. [75], who has shown that not only is the bacterial load of the rooms decreased, but also the rate of pneumonia infection during hospitalization of patients.

Other studies focused on the disinfection of intensive care units (ICUs) or operating rooms because patients could get nosocomial infections due to MRSA, or *Clostridium difficile*. For example, El Haddad et al. [83] applied PL after disinfection of the monitors, electrocautery unit, anesthesia cart, bed table controls in operating rooms, for 2 and 8 min; log reductions of 0.56 and 0.57 were achieved respectively. Likewise, Kitagawa et al. [79] use illumination cycles of 5 min, achieving a 1.28 log reduction in the areas of greatest contact such as bed rails and infusion pump control panels for MRSA and 1.24 for aerobic bacteria. Comparing these values with manual cleaning the disinfection efficacy increased by 14% for MRSA and 42.62% for aerobic bacteria. Similarly, Villacís et al. [77] applied PL for a 5-min cycle in bathrooms, two five-minute cycles in individual rooms and two 10-min cycles in operating rooms. The surface and environmental contamination was reduced by 75% compared to manual cleaning. It is more, in the case of operating rooms; it was reduced by 87% and in patient rooms by 76%.

The studies abovementioned used the PL device in individual rooms, but it is also considered necessary to carry out this type of study in multiple rooms, with an occupancy of about 4–6 patients, especially when there are outbreaks of any kind of microorganism like multi-drug resistant microorganisms (MDROs). Two studies have tested the efficacy of PL for this case. Morikane et al. [72] applied PL for the inactivation of MRSA and *Acinetobacter baumannii* in intensive care units (ICUs) applying two cycles of 5 min placing the device in two opposite points of the room. Inside the ICU wards, samples were taken from the bed rail, cardiopulmonary monitor touch panel, ventilator control panel, intravenous fluid pump control panel, glove hook, workstation keyboard and handle of workstation cart. In this case, after traditional cleaning, bacterial load was eliminated with 0.69 log reduction, however, after using the PL device, a 1.08 log reduction was achieved. Zeber et al. [76] carried out a study controlling some of the variables mentioned above, such as the relocation of the patient in shared rooms and reinforcing traditional cleaning with the use of PL (two cycles of 5 min). The study included four hospitals, two of them used manual disinfection and the other two used PL complementarily. PL reduced MRSA and aerobic bacteria counts by 0.61 and 0.80 log reductions respectively, versus only 0.12–0.15 for manual cleaning.

A focus on operating rooms was placed by Catalanotti et al. [69] and Simmons et al. [70]. Simmons et al. [70] carried out a study in 23 hospitals, and established that those operating rooms less than 120 m underwent 5-min cycles, but in those over 120 m the cycle was 10 min. Results demonstrated that 67% of the surfaces continued to maintain biological contamination after manual cleaning, but after using PL only 38% continued to test positive. Meanwhile, Catalanotti et al. [69] also perform the 10-min cycles, demonstrating that there is a relationship between cleaning the operating rooms with expert personnel and PL and the rate of wound infection of the patients.

Other studies have been carried out in different hospital areas such as hematology units, bone marrow transplant areas and food preparation areas for newborns [71,82]. In all cases, the duration of the cycles was 5 min. One log reduction in the biological load was obtained in the food preparation area. In the control samples, 10 different strains appeared, and after treatment with PL only three remained [82]. However, in the hematology units, only a reduction in the rate of *Clostridium difficile* infection was achieved from 0.77 to 0.55 [71].

On the other hand, Chen et al. [81] and Li et al. [87] studied not only the disinfection of various surfaces of different rooms, but also verified the effect of PL on air disinfection, since they achieved a log reduction of one to full reduction of the biological burden [81,87]. Furthermore, Song et al. [85] suspended *Escherichia coli* and *Staphylococcus albus* in a liquid that was aerosolized in two security booths, which were later treated with a PL device during 30 min. After the encouraging results obtained in the laboratory model, the same protocol was adapted to ambulances that had been used throughout a workday increasing the treatment time to 60 min. There was a 100% elimination of *E. coli* and 3 log reduction in *S. albus* with the protocol used in the safety cabinets and one log elimination in ambulances, which even though was lower, it still provides effective, real-time disinfection that could be used for virus disinfection.

10. Pulsed Light vs Continuous UV-C Light

Besides PL devices, there are continuous UV devices for use in healthcare [49]. There is conflicting evidence about the superiority of one of these technologies over the other. The higher efficacy of PL over conventional UV has been proved in other contexts. It is not clear if the lack of superiority of PL reported in some cases is due to the technology itself or to the way that commercial companies have adapted this technology for healthcare purposes. Comparisons of the efficacy of different light technologies must be carried out under controlled conditions where the only variable be the light source itself, such as in quasi-collimated set-ups [48,88]. Under controlled conditions, PL has been proved more efficient than low- and medium-pressure UV lamps for inactivation of *Escherichia coli* and phages T4 and T7, a result that has been correlated with a higher production of thymine dimmers in *E. coli* [4]. On the other side, it is true that many studies comparing both technologies in health-care facilities have been aimed to corroborate the merits of the equipment's alleged by the manufacturers and to select the best option among the devices currently marketed, which are not necessarily the best possible versions of each technology. The studies comparing the efficacy of both systems of UV delivery have been carried out on bacteria.

A hand-held PL device was more efficient that a continuous UV-C in attaining >2 log inactivation of eight species of critical nosocomial bacteria, it took five seconds to achieve the same effect that required 30 s with the UV-C treatment [89].

Different studies carried out on a PL robot have concluded that it is not better than continuous UV-C. This has been reported for the inactivation of *Clostridium difficile* spores, methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*; yet, each device was tested in a different hospital [49]. Another study using the same microorganisms showed that UV-C was much more effective than the PL robot in a radiology procedure room [49]; however, it is noteworthy that the log reductions found for PL were < 0.5, which is not consistent with other reports. This could be explained because the UV-C irradiance measured for this device was 10.8 $\mu W/cm^2$ while that for the continuous UV-C devices was 106.2–159.9 $\mu W/cm^2$. This pose the question whether these tests are valid to compare both technologies or just compare two devices in which the technology is not necessarily used in its best possible version. It is interesting that the peak irradiance of the PL robot is in the UV-A range, while the emission of the PL system used by Bohrerova et al. [4] was in the UV-C range, which is the most germicidal. It is known that the emission spectrum of the lamps used in PL

Table 3
Comparison of kinetic constants (k) for the inactivation of viruses by pulsed light and conventional UV light.

	Pulsed light			CW UV light			
Virus	Substrate	k (cm^2/J)	Reference	Substrate	k (cm^2/J)	# data	Reference
BPV	PBS*	5.6	53	Water	65.8	1	[91]
EMC	PBS	12.4	53	Water	36.5–46.4	3	
HAV	PBS	15.2–96.0	53, 60	Water	7.5–57.6	6	
HSV-1	PBS	7.2	53	Water	20.9–110.5	6	
MNV-1	Water	1.2	60, 52	Water	30.4	1	
Polio-1	PBS	14.8–347.8	53, 91	Water	9.6–40.1	12	
Sindbis	PBS	10.8	53	Water	20.3–46.1	3	
SV 40	PBS	8.0	53	Water	0.92–131.6	9	
Vaccinia	PBS	6.8	53	Water	3.22–349	8	

* phosphate buffered saline.

technology get richer in lower wavelengths as function of the operating voltage [90], therefore it is likely that a PL robot using a higher discharge voltage should yield a better performance.

A third study have also concluded that UV-C treatment was better than a PL robot for the decontamination of N_{95} respirators inoculated with methicillin-resistant *Staphyloccocus aureus* and bacteriophages MS2 and Phi6 [68]. Yet, it is noteworthy that results were unexpectedly dependent on the exposed surface. For example, for *S. aureus*, the inactivation was >4 logs for continuous UV-C and > 2.5 logs for PL inoculated on outer top of the mask; while in the inner surface the inactivation attained by continuous UV-C light was also >4 logs but was negligible for the PL treatment.

When PL is compared to continuous UV-C light based on in vitro data from different bibliographical sources conclusive results are precluded. Table 3 shows a high variability in the kinetic data with differences even of three orders of magnitude for the same virus and technology, which is likely due to the variety of experimental approaches used to obtain them. An additional difficulty resides in the fact that except for data by Lamont et al. [55], PL fluence is reported in terms of total fluence, which includes a significant portion of non-germicidal wavelengths, while conventional UV light fluence is exclusively germicidal.

The most remarkable difference between both technologies becomes obvious when comparing in time basis the results shown in Table 3, where results corresponding to PL were obtained after few seconds of treatment while those of CW UV light required minutes. In order to compare with equivalent kind of data, the bibliography generically reported in Table 3 as Kowalski [91] was searched and analyzed. Only few of the original sources reported results in time units since most of them used fluence units. The kinetic data reported for Sindvis required >3 min of treatment [92]. Other data are, for HAV: 15 s-10 min [92–94], HSV-1: 7 min [95], SV40: 3–20 min [92,96,97], Vaccinia: 1–3 min [98–100] and Polio-1: 15 s-30 min [94,101–104]. In contrast, most of the results reported in Table 3 for PL were calculated from data by Roberts and Hope [53], who used a treatment time of <1 s (only one pulse). Jean et al. [52] and Vimont et al. [60] used ≤3 s for their PL experiments and Lamont et al. [55] 10 s. Therefore, PL technology is much faster than continuous UV light.

Apart from the antiviral efficacy of both types of technologies, the differences in their economic impact must also be taken into account. A detailed economic comparison was carried out by Health Quality Ontario [50] in 2018, concluding that purchasing and using two pulsed light units for hospital use would have a budget impact of 586,023 Canadian dollars over five years, compared to 634,255 Canadian dollars for conventional UV light. Therefore, the pulsed light technology seems to be more cost efficient than conventional UV light. This study did not include the potential cost saving from reduced hospital acquired infections.

The comparison of the electrical efficiency and lifetime between pulsed and continuous UV sources is not straightforward because unlike mercury lamps, PL performance depends on operating conditions. Low- and medium-pressure mercury lamps have an UV-C efficiency of 35 [90] and 5–15% [105] and a lifetime of 9000 h [106] and 3000–5000 h [90,105] respectively. On the other side, up to 60% of energy input can be converted to light in PL systems [106] but this includes wavelengths in the visible and infrared range. An UV efficiency of 9% was reported by Schaefer et al. [90] but this vary by more than a factor of 2.5 depending of operating conditions, with the highest efficiency corresponding to the shortest lifetime. The higher the pulse energy and repetition rate, the lower the lifetime, which is generally in the range of 10^6 to 10^8 flashes [106]. Furthermore, manufacturers of PL systems allege that they consume 80% less energy than mercury UV systems [107].

11. Conclusions

Pulsed light technology is virucidal and capable to inactivate microorganisms and viruses contaminating surfaces of hospital environments. It is a suitable candidate for testing to avoid hospital-acquired infections by SARS-CoV-2.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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