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Current Opinion in
Environmental Science & Health

Efficacy of frontline chemical biocides and disinfection approaches for inactivating SARS-CoV-2 variants of concern that cause coronavirus disease with the emergence of opportunities for green eco-solutions

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Abstract

The emergence of severe acute respiratory disease (SARS-CoV-2) variants that cause coronavirus disease is of global concern. Severe acute respiratory disease variants of concern (VOC) exhibiting greater transmissibility, and potentially increased risk of hospitalization, severity and mortality, are attributed to molecular mutations in outer viral surface spike proteins. Thus, there is a reliance on using appropriate counter-disease measures, including non-pharmaceutical interventions and vaccination. The best evidence suggests that the use of frontline biocides effectively inactivate coronavirus similarly, including VOC, such as 202012/01, 501Y.V2 and P.1 that have rapidly replaced the wild-type variant in the United Kingdom, South Africa and Brazil, respectively. However, this review highlights that efficacy of VOC-disinfection will depend on the type of biocide and the parameters governing the activity. VOC are likely to be similar in size to the wild-type strain, thus implying that existing guidelines for use and re-use of face masks post disinfection remain relevant. Monitoring to avoid injudicious use of biocides during the coronavirus disease era is required as prolonged and excessive biocide usage may negatively impact our receiving environments; thus, highlighting the potential for alternative more environmental-friendly sustainable biocide solutions. Traditional biocides may promote cross-antimicrobial resistance to antibiotics in problematical bacteria. The existing filtration efficacy of face masks is likely to perform similarly for VOC due to similar viral size; however, advances in face mask manufacturing by way incorporating new anti-viral materials will potentially enhance their design and functionality for existing and potential future pandemics.

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[a] Given his role as Guest Editor Neil J. Rowan had no involvement in the peer-review of this article and has no access to information regarding its peer-review. Full responsibility for the editorial process for this article was delegated to Damia Barceló Culleres.

Current Opinion in Environmental Science & Health 2021, **23:**100290

This review comes from a themed issue on **Environmental Toxicology 2021: Disruptive Green Deal Innovations**

Edited by **Neil J. Rowan** and **Robert Pogue**

For a complete overview see the Issue and the Editorial

https://doi.org/10.1016/j.coesh.2021.100290

Keywords
COVID-19, Disinfection, PPE, Biocides, SAR-Cov-2 variants, Healthcare, Environment.

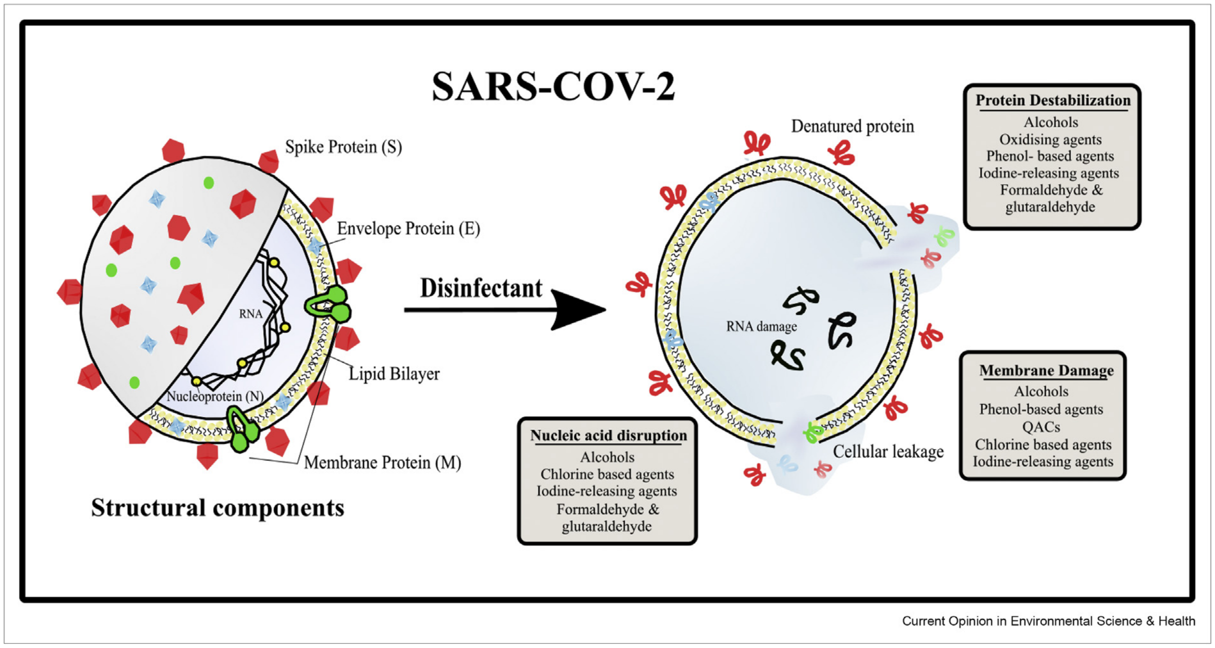
Introduction — coronavirus and its implications for maintaining healthcare provision

The coronavirus disease (COVID-19) pandemic, caused by the severe acute respiratory coronavirus 2 (SARS-CoV-2), has imposed tremendous challenges on healthcare systems globally [1–3]. At the time of writing (30th March, 2021), there have been 127,628,928 cases of COVID-19 worldwide, including 2,791,055 deaths [4]. COVID-19 elicits a broad infection spectrum ranging from very mild, non-respiratory symptoms to severe acute respiratory illness, sepsis with organ dysfunction and death; however, some infected people can be asymptomatic [1]. Evidence highlighting the contributions of super-spreaders of infectious airborne viral particles, including the more transmissible SARS-CoV-2 variants of concern (VOC), has also contributed to the occurrence of third and fourth waves of COVID-19 infections [5–7]. Addressing the ongoing COVID-19 pandemic has created unprecedented logistical challenges to maintain critical supplies of single-use personal and protective equipment (PPE) [8,9], where reuse and disinfection occurred under emergency use authorization. At the outset of COVID-19, there was a void in knowledge to effectively counter this disease; however, there is an increasing understanding of the potential role of different strategies to address COVID-19, including adopting non-pharmaceutical interventions (NPIs, such as correct wearing of face masks, hand hygiene, use PPE, maintaining social distancing, detection testing, contact tracing), along with delivering new vaccines [8,9]. Data generated from predictive mathematical modelling of multiple-contributing factors influencing the occurrence of COVID-19, and commensurate efficacy of disease counter-measures, is increasing, such information is translated to calculating risk probability to monitor and manage the basic reproduction number R_0 in the following [9]. It is challenging to appreciate the actual efficacy of specific COVID-19 disease interventions in real-time given the swiftly moving pace of this pandemic. This current opinion focuses on understanding the efficacy of frontline biocides and disinfection approaches against SARS-CoV-2 variants of concern.

Coronaviruses and implications for meeting personal and protective equipment supply chain shortage and disinfection reprocessing

SARS-CoV-2 is a large positive-stranded RNA virus with an outer lipid envelope containing glycoprotein spikes (Figure 1) [10]. In general, enveloped viruses, such as coronaviruses, are more sensitive to environmental deleterious stresses, such as chemical biocides, than similarly-treated naked viruses, due to the presence of a lipid membrane [9,11,12]. Coronaviruses range from 60 to 140 nm in size, which is below the 300 nm pore diameter used in multiple layers of material used to make face masks. However, the use of multiple layers in single-use plastic face mask reduces the probable risk of penetration and transmission by acting as a barrier to respiratory droplets [13,14], which is likely to apply similarly to mitigating against VOC transmission. The effectiveness of single-use plastic filtering-face piece respirators face masks varies based on type and certification that is defined across three levels of protection depending upon leakage of particles into the interior of the mask that are 22% (FFP1, such as medical and procedural masks), and 8% (FFP2, such as N95-type respirators), and 2% for non-disposable FFP3-type respirators [2]. Use of non-thermal biocidal and disinfection approaches, such as vaporized hydrogen peroxide (30–35% VH2O2) and moist heat (60–65 °C for 30 min), and ultraviolet light at 254 nm (or fluence at 2000 mJ/cm^2), has been applied for reprocessing FFP1 and FFP2 type respirators, such as under emergency use authorization [2,25–27]. Non-thermal disinfection approaches of FFPs have been selected to enable retention of filtration performance, material compatibility, comfort fit, and pressure drop. In addition, there has been increased usage of alternative, cost-effective, home-made, cloth or fabric face coverings by the general public, where particle penetration efficacy was improved by using more than one layer of cotton-polypropylene and by introducing pleats when compared to testing using a fitted

Figure 1



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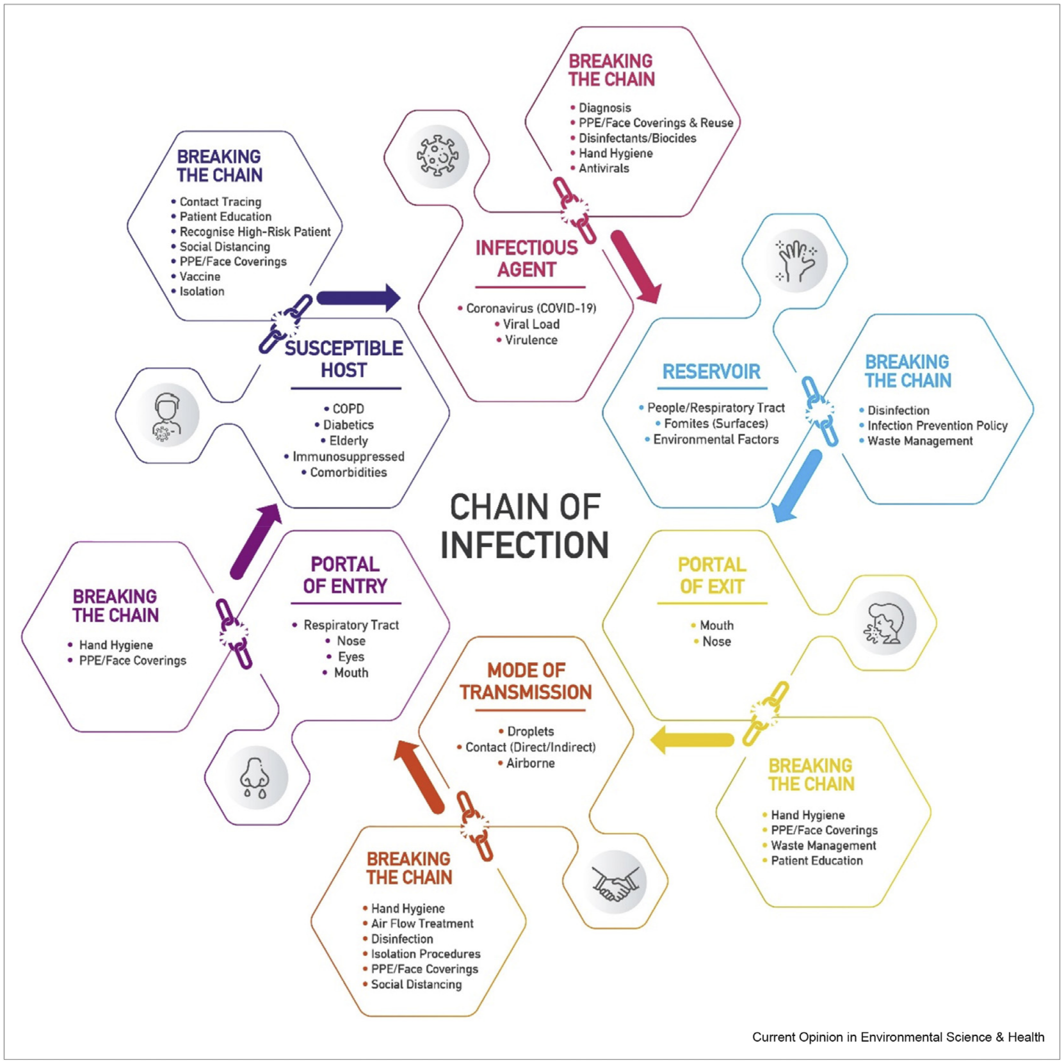
Structural components of SARS-COV-2 (left) and effective biocidal agents known to deactivate the virus (right).

N95 FFP2-type control [15–17]. Combining similar mild heat conditions, along with the use of detergent, for reuse of face coverings is theoretically plausible for coronavirus-disinfection; however, there remains a lack of information on disinfection and efficacy for informing the frequency of reuse that maintains filtration functionality [2,9]. Post COVID-19, it is likely that the changes in medical practice will drive sustaining or increasing high demand for PPE.

Understanding coronaviruses and the role biocides in breaking cycle of COVID-19 infection

Coronaviruses are typically inactivated on different surfaces within 4–5 days at ambient room temperatures on different surfaces, such as tissue, wood, glass, plastic, stainless steel, surgical masks, and paper, that can be influenced by humidity, viral load, presence of organic matter [9,18]; for example, colder conditions, such as refrigeration (4 °C), may extend SARS-COV-2 viability on surfaces beyond 14 days [19,20]. It took 14 days at 20 °C to reduce SARS-CoV-2 on nitrile gloves by 5 log orders using simulated typical infectious body fluids from infective patients; however, viral persistence was evident up to 21 days on plastic face shields, N100 FFPs, and polyethylene overalls [21]. These observations imply that the colder conditions associated with winter may support longer survival of SARS-CoV-2 on contact surfaces and when suspended in aerosols. There is a pressing need to understand the role of different interventions in breaking the cycle of SARS-CoV-2 infection (Figure 2) to protect frontline healthcare workers and patients [9]. This includes generating data over a longitudinal period to evaluate and harmonize deployment of these interventions (singly or combined) to prevent or reduce the risk of COVID-19 with a focus on

Figure 2



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Use of chemical biocides and other disinfectants to break cycle of COVID-19 disease.

infections agent (SARS-CoV-2 and co-infections), reservoir, portal of exit, mode of transmission, portal of entry, and susceptible host (Figure 2). The efficacy of such data will be informed by mathematical modelling and randomized control studies [9]. The use of disinfectants or chemical biocides and disinfection approaches will feature strongly as key disease countermeasures in breaking the cycle of infection (Figure 2). Factors that influence the efficacy and performance of different types of biocides are varied and complex [22,23]; however, the parameters governing selection and performance of different biocide types are generally well-established, where the degree of application depends upon categories of risk to patients aligned with a commensurate level of treatment required to be achieved on contact surfaces and in the environment (Table 1). ‘COVID-19 fatigue’ of citizens is likely to play a contributing role in meeting compliance with deploying disease counter-measures to effectively manage new cases to protect frontline healthcare workers [24].

SARS-CoV-2 VOC

The World Health Organization monitors public health events associated with SARS-CoV-2 VOC [3]. Key features for these VOC are presented in Table 2. VOC 202012/01, 501Y.V2, and P.1 have commonly demonstrated an increase in transmissibility compared to wild-type (non-VOC) variants and have demonstrated a propensity for rapidly replacing other circulating SARS-CoV-2 strains. Variants 202012/01, 501Y.V2, and P.1 rapidly replaced the wild-type variant in the United Kingdom, South Africa, and Brazil, respectively. However, it is highly likely that more transmissible and pathogenic VOCs will emerge during this pandemic as the virus has ample opportunity to mutate given the high numbers of infected hosts globally. However, in terms of existing VOC, the WHO deploys ‘a logistic model of competitive growth that highlighted additive increases in the effective reproduction number (Rt) relative to the wild-type variant that was estimated at 41% (95% CI: 41–42%) for 202012/01, 36% (95% CI: 32–40%) for 501Y.V2, and 11% (95% CI: 7–16%) for P.1’ [3]. The transmissibility of P.1 is such that it is rapidly replacing the wild-type variant at a local level. Recent studies have shown VOC 202012/01 may be associated with an increased risk of hospitalization, severity, and mortality. There is a growing body of evidence on vaccine-induced neutralizing antibody activity against VOCs (Table 2). The findings support that neutralizing activity is largely sustained against this variant. However, these findings highlight the importance of using combinational approaches, including the use of biocides for surface disinfection, as important to limit transmission of VOCs. Key mutations affect viral non-structural proteins that are unlikely to affect the efficacy of frontline biocides described in Tables 3 and 4. There is an increasing interest in the future proof design of face masks by also incorporating potentially new antiviral materials with the provision for more environmentally friendly non-metal nanomaterials [66].

Indication of biocide efficacy against coronavirus

Biocides encompass chemicals with antiseptic, disinfectant, and/or preservative activity (Table 3). Biocides are used for a broad range of purposes, ‘usually with inanimate objectives (hard surface disinfectants), externally on the skin (antiseptics and topical antimicrobials), to prevent or limit microbial infection for pre-operative skin infection or incorporated (preservatives) into pharmaceutical, cosmetic, or other types of products to prevent microbial contamination’ [28]. Desirable properties of biocides include virucidal within the time that can allow for it to be in contact with materials to be treated; effectiveness not diminished under conditions of disinfection; does not damage material treated, has a suitable spectrum of activity; low toxicity and resistance to it has not emerged; inexpensive. Biocidal efficacy is influenced by several, and sometimes, inter-related factors — notably concentration, period of contact, pH, temperature, presence of organic or other interfering or enhancing materials or compounds, nature, numbers (dose), location (planktonic, biofilm), and condition of microorganisms (recalcitrant endospores vs sensitive enveloped viruses) (Table 3). For example, concentration exponent (η) is particularly important as it measures the effect of concentration of dilution based on the activity of the biocide [22,23]. Biocides with high η-values (such as alcohols, phenols) rapidly lose efficacy when diluted, whereas those with low η-values (such as QACs, chlorhexidine, orthopthalaldehyde) retain considerable activity on dilution. This difference is highly relevant when considering both lethal disinfection activity and potential implications on receiving environment, where the potentially deleterious impact of biocide residues must be considered [28]. In addition, many frontline biocides have optimal pH activity, such as hypochlorite and phenolics are most effective at acid pH, whereas glutaraldehyde and cationic biocides (e.g. QACS) are most potent at alkaline pH. Several researchers have reported that biocide activity can be influenced by interaction with organic matter (e.g. dirt, blood, serum, vomit, the presence of biofilm), and non-ionic surfaces, and adsorption on containers and other contact surfaces (Table 3).

Coronaviruses are incapable of supporting independent life; thus, biocide disinfection is determined by using *in vitro* bioassays, where reduction of cytopathic effects in tissue culture monolayers are observed that is attributed to a reduction in viral infectivity compared with untreated controls. Surviving viral fractions are typically expressed through Log_{10} reductions enumerated either by determining the 50% titration reduction endpoint for infectivity (known as tissue culture infectious dose 50%,

Table 1

Factors governing anti-viral efficacy of biocides.

Factors[a]	Comments	Relevance and implication for usage in practice
Factors characteristic of biocide		
Concentration	Understand the effect of dilution upon activity — concentration must be 'cidal' to viruses	Appropriate staff training
Contact time	Length of exposure can often enhance biocidal efficacy	Appropriate staff training
Organic load	Diminish the activity of biocide and protect other contaminating bacteria of concern	Understand physicochemical factors governing biocidal action
Formulation	Influences inactivation performance against coronaviruses and intended surface or application for treatment	Understand nation of active agent and impact on intended contact material
Temperature	Increased activity against viruses can be achieved with higher temperatures and relevant for some devices (e.g. endoscopes)	Appropriate staff training
pH	Affects biocide (stability and ionization) and affects growth of co-infective microorganisms	Less relevant for healthcare environment
Biological and environmental factors		
Presence of biofilm	Provides protective menstrua or environment that can be found on equipment and in certain surfaces	Combine physical cleaning along with chemical action
Viral load	The greater the population number of viruses present the more difficult it can be to disinfect	Biocides often used in excess at high level concentration — SARS-CoV appear sensitive to low and moderate levels

Categories of risk as defined for patients and treatment of surfaces, equipment, environment	
High risk	Sterilization such as use of VH2O2
Intermediate risk	Disinfection
Low risk	Cleaning and drying usually sufficient; disinfection
Requirements of chemical biocides or disinfectants	
Spectrum of activity	'Cidal' as opposed to 'static' activity as latter is not appropriate
Efficacy	Rapid action, particularly on surfaces
Incompatibility	Should not be neutralized or diminished easily
Toxicity	Should be minimal
Damages to surfaces, or materials	Corrosiveness should be minimal, especially at dilution of use. Should not damage contact surface to be disinfected
Costs	Should be affordable, particularly to ensure supply chain

[a] Factors listed in order of importance – adapted from the study by Michie, West, and Harvey [24].

Table 2

Synopsis of key information on SARS-CoV-2 variants of concern, as reported by World Health Organization on 23rd March, 2021.

Emerging information[a]	Variant of concern (VOC)		
Next strain clade	20I/501Y.V1	20H/501Y.V2	20J/501Y.V3
PANGO lineage	B.1.1.7	B.1.351	B.1.1.28.1 (alias P.10
Alternate name	VOC 20201/01	VOC 202012/02	
First detected	United Kingdom	South Africa	Brazil
First appearance	20 September, 2020	Early August, 2020	December 2020
Key spike mutations	H69/V70 deletion; Y144 deletion; N501Y, A5700, P681H	L242/A243/L244 deletion; K417N E484K, N501Y	N417T, E484K; N501Y
Key mutation in common	5106/G107/F108 deletion in Non-Structural Protein 6 (NSP6)		
Transmissibility	Increased (36–75%), increased secondary attack rate (10–13%)	Increased (1.50 (95% CI: 1.20–2.13) times more transmissible than previously circulating variant	Increased, more transmissible than previous circulating variants
Severity	Possible increased risk of hospitalization, severity and mortality	Possible increased risk in hospital mortality by 20%	Under investigation, limited impact
Neutralization capacity	Slight reduction, but overall neutralising titres still remained above levels expected to confer protection	Decreased, suggesting potential increased risk of infection.	Decreased reinfections reported
Potential Impacts on vaccines	• No significant impact on post-vaccine neutralization by Moderna, Pfizer-BioNTech, Oxford-AstraZeneca, Novavax • No significant change in prevention of disease by Oxford-AstraZeneca, Novavax, and Pfizer-BioNTech • Evidence for prevention of infection evidence limited — reduced effect reported for Oxford-AstraZeneca	• Post-vaccine neutralization reductions range from minimal to moderate for Moderna and Pfizer; however, there is also some evidence of more substantial reductions • Substantial reductions found for Oxford-AstraZeneca products • There is no evidence to inform vaccine impact on asymptomatic infection by 501Y.V2	• Limited to modest reduction in post-vaccine neutralization by Oxford-Astrazeneca, Moderna, and Pfizer-BioNTech vaccines. • Preliminary suggestion of loss of neutralization following vaccination with Sinovac
Countries reporting new cases (newly reported in last week)	125 (7)	73 (11)	41 (3)

[a] Adapted from WHO [ ]; note, consult this reference report for more detailed information on emerging information on key VOC.

Table 3

General properties, strengths and limitations of frontline chemical biocides against coronaviruses.

Biocide type and active igredient	Mechanism of virucidal Action	General usage	Limitations	Strengths
Alcohols Isopropyl alcohol (isopropanol) Ethyl Alcohol (Ethanol)	Disrupts cell envelope, coagulates and denatures proteins. Isopropyl alcohol is lipophilic disrupting lipid membrane.	Skin antisepsis (ca 70% v/v) Small equipment disinfection, for example, thermometers, critical tools, non-invasive probes	Not sporicidal Prolonged and repeat usage affects integrity of materials such as plastics. Flammable	No-staining, low toxicity, mild pleasant odour
Cationic surfactants — QAC such as BZK, MBAT, DDA	Mostly disrupt by solvating or disrupting cell envelope — cationic ammonium groups with hydrophilic heads	Fomites (200 ppm),	Require warmer temperature and longer periods for achieving MEC Low affinity against non-enveloped viruses	Nontoxic, colourless and odourless — retain activity in hard water, high tolerance to organic matter
Oxidising agent — Sodium hypochlorite	Oxidation of cell envelope	Household bleach — dissolves in water to form hypochlorous acid — used in clinical area for fomites, non-critical surfaces where there is blood spillage or vomit	Sensitive to presence of organic matter and porous material — can range from <1000 pm to 10,000 ppm depending on organic material — cleaning step and ventilation needed	Fast acting at low concentrations — inactivates envelope and non-envelope viruses
Oxidising agent Hydrogen peroxide	Hydroxyl free radicals cleave or crosslink biomolecules including proteins, nucleic acids, an lipids	Skin antisepsis (0.125% v/v); contact surfaces (35% v/v)	Limited information. Concentration of 0.5% effective against enveloped and non-envelop viruses.	Decomposes to form water and oxygen — effective against SARS-CoV-2 and surrogates — can be used on stainless steel
Halogenated compounds — Povidone iodine and Povidone Iodone (PVP-1)	Possibly blocking receptor for viral binding. Iodine can inhibit viral enzymes (neuraminidase) essential for viral release from host	PVP-1 (0.23%) used for rapid skin, oral cavity, nasal disinfection. Povidone iodine used at 7.5–10% pre-operative skin disinfection, antiseptic hand washes, scrubs, ointments	Can be cytotoxic and cause skin irritancy — Is an iodophor is mixture of iodine and carrier polymerpolyvinl pyrrolidone — not suitable for use with silicone products	PVP-1 water soluble, stains can be removed by washing. Substitute or used in combination with for alcohol-based disinfection products.
Aldehydes Glutaraldehyde. Formaldehyde and OPA	Chemically alkylating the amino and sulfhydryl groups of proteins and amino groups of nucleic acid bases	High level broad spectrum virucidal disinfection — vaccine production — decontaminates of surgical equipment, endoscopes, dialysers.	High reactivity, hazardous to health — irritant. Apart from OPE, more reactive at alkaline conditions. Pungent odour <1 ppm, monitoring.	Rubber, plastics, lensed instruments are tolerant. OPA chemically stable over pH 3–9, non-irritant, stains skin wear PPE.

QAC – Quaternary ammonium compounds; BZK - benzalkonium chloride; mon; MBAT - biz(tri-methyl ammonium methylene chloride)-alkaly (C_{9-15}) toluene; DDA – didecyldimethyl ammonium chloride; OPA – Ortho-phthalaldehyde or 1,2-dicarboxybenzaldehyde.

MEC –lowest concentration of biocide that reduces virus titre by 99.9% or greater compared to control reactions. Adapted from Lin [ ], Dev Kumar [ ].

Table 4

Use of different disinfection approaches for inactivating SARS-CoV-2 and its' surrogate indicators.

Disinfectant		Parameters	SARS-CoV-2 & Surrogate species	Reduction Assay used
Chemical	Ethanol	60–70%, 1 min, hard surfaces, ceramic and porcelain tiles -carrier test.	hCoV (HCoV-229e)	3 - 4 log, TCID$_{50}$ assay [53]
	H_2O_2	0.5%, 15 min, surface carrier test 1–6%, 30 s, suspension testing of oral mouth wash	SARS-CoV-2 SARS-CoV-2, USA–WA1/2020 strain	6 log plaque assay using Vero E6 cells [52] 1–1.8 log TCID assay using Vero 76 cells [54]
	QAC – BAC QAC – DDAC	0.04% w/v, 1 min, steel surface. quantitative carrier test 0.025%, 3 days, suspension test	Parainfluenzavirus type 3 (HPIV-3) and human coronavirus 229-E (HOV-229E) Canine Coronavirus	3 log Plaque assay using MA-104 line of rhesus monkey kidney cells 4 log TCID assay using A72 fibroma cell line [55]
	Sodium hypochlorite	0.1%, 1 min, suspension test. 6%, 30 s surface carrier test.	SARS-CoV-2	4 log [39] TCID assay [40]
	IPA	70–90%, 30 s 70–80%, 15 s, ceramic and porcelain tiles -carrier test.	SARS-CoV-1 hCoV (HCoV-229e)	4 log, TCID assay [53]
	Acetic acid	6%, 5 min, aqueous suspension test.	SARS-CoV-2 (Hu/DP/Kng/19–020 strain)	4 log TCID$_{50}$ assay using VeroE6-TMPRSS2 cells [43]
	Glutaraldehyde Formaldehyde	0.5%, 2 min, suspension test 0.7–1%, 2 min, suspension test	SARS-CoV isolate FFM-1	3 log TCID using human embryonic lung fibroblasts [23]
	Povidone iodine	1–2.5%, 15 s, suspension testing of oral mouth wash	SARS-CoV-2, USA-WA1/2020 strain	4 log TCID assay using Vero 76 cells [54]
Technologies	Steam sterilisation	121 °C, 5 min, medical masks, N95 respirators	Avian coronavirus (H120)	2 log inoculation of embryonated eggs, real-time TaqMan RT-PCR assay [56]
	Heat	56 °C, 30 min, 65 °C, 15 min, 98 °C 2 min, suspension test.	SARS-CoV-2	5 log TCID$_{50}$ assay using Vero E6 cells [57],
	Deep UV LED	265, 280, and 300 nm, 20 s, hard surfaces, carrier test	SARS-CoV-2	3.3 log Plaque assay using Vero E6 cells [58]
	Simulated sunlight	60 min on hard surfaces, carrier test on surface dried droplets.	SARS-CoV-2 USA-WA1/2020	4 log. TCID$_{50}$ assay using Vero cells (ATCC CCL-81) [60]
	UVC	254 nm, 4–9 s, wet and dried droplets	SARS-CoV-2	3 log Plague assay [61]
	Ozone	30 ppmv, 40 min 100 ppmv, 30 min, 1000 ppmv, 20 min on surfaces, carrier test.	hCoV 229E (HuCoV-229E)	95% reduction (1 log) HEK-293 cells and imaging using IncuCyte ZOOM system [36]
	Vapourised H_2O_2	0.5%, 60 s, surface of stainless steel disks, carrier test.	feline calicivirus, human adenovirus type 1, avian and swine influenza virus	4 log TCID50 assay using A-549 cells, MDCK cells [59]
	Chlorine dioxide gas (ClO2)	30–300 ppm, 25 °C to 30 °C, 1.5–3 h, in vivo.	avian infectious bronchitis coronavirus	infected chick embryos as models [62]
	Gamma radiation (cobalt-60)	1–5 MRads, suspension test.	arenavirus, bunyavirus, coronavirus, filovirus, flavivirus, orthomyxovirus, paramyxovirus	6 log TCID$_{50}$ assay Vero cells [63]

TCID$_{50}$ assay - Tissue Culture Infectious Dose assay, QAC quaternary ammonia compound, BAC benzalkonium chloride, DDAC didecyl dimethyl ammonium chloride.

or $TCID_{50}$ assay) or by performing a viral plague assay; however, reverse transcriptase - polymerase chain reaction (RT-PCR) using threshold (Ct value) is also used to determine viral load through detection of specific genes. Determining factors influencing biocides efficacy has traditionally been conducted to evaluate minimum inhibitory concentrations or lethal effects such as European suspension test, rate-of-kill test, and in-use test that are more suitable for anti-bacterial agents [29]. The Sterilization industry relies upon 12 $\log_{10}$ reductions of recalcitrant bacterial spores as biological indicators or surrogates, such as *Geobacillus stearothermophilus*, *Bacillus atrophaeus*, for determining sterility assurance levels for different sterilants where there is significant overkill to ensure validation of processes [25,30,31,32]. Thus, existing disinfection processes are ultimately based upon the probability of viral reduction where there is a pressing need to elucidate robust real-time inactivation enumeration methods [such as 31], which is likely to be informed by predictive modelling and may create opportunities for machine learning and artificial intelligence.

Disinfection of SARS-CoV-2

As an enveloped virus, SARS-CoV-2 is susceptible to commercial disinfectant chemicals, technologies, and physical disinfection methods [33,34] (Table 4). Recent studies have detected SARS-CoV-2 RNA on surfaces in isolation wards 28-days following exposure via RT-PCR methods [35], where the infectivity ability of viral RNA is unknown. However, it is unlikely that undamaged viral RNA realized on treated surfaces would remain a significant risk because of its inability to enter human lung cells as RNA only. Determination of biocidal efficacy against SARS-CoV-2 is not always feasible as the virus requires biosafety level 3 or higher; therefore, fewer pathogenic viruses as surrogate indicators of infectivity are frequently used [36]. Virucidal efficacy is determined by quantitative suspension tests, namely EN 14476 requiring 4 log reduction using surrogate enveloped species such as polio, adenovirus and murine norovirus, where efficacy against SARS-CoV-2 has yet to be elucidated experimentally. The framework of the European Committee for Standardization outlines surrogate species suitable for disinfection studies for many microorganisms. For virucidal activity against enveloped viruses, including SARS-CoV-2, the vaccinia virus has been specified as the relevant test organism according to this framework [37]. In clinical settings, SARS-CoV-2 has been detected on surfaces in intensive care units ($4.4-5.2 \log_{10}$), in isolation rooms, and on general wards ($2.8-4.0 \log_{10}$) [38]. While the viral load of SARS-CoV-2 on fomites directly following contact with infected persons is currently unknown, it is known that the virus remains infectious on surfaces for up to 9 days [39,40] depending on the surface material, pH, temperature, and humidity [40]. The suitability of suspension tests to determine efficacy on surfaces is unknown, particularly where the organic matter may be present such as in healthcare settings. ISO 18184 is a surface carrier test for virucidal activity; at present, no studies have demonstrated biocidal efficacy against SARS-CoV-2 using this method. The disinfection of surfaces and hand sanitation is of paramount importance in controlling viral transmission as recommended by the WHO. Disinfectant efficacy is affected by viral type, organic matter, viral titre, pH, viral clumping, biocide contact time and concentration. As such, cleaning is an essential prerequisite for disinfection to remove contaminating organic matter. In healthcare settings, disinfection agents in use include high-pressure steam sterilization, dry heat, UV-light, ethylene oxide (EtO) gas, hydrogen peroxide gas plasma, and biocidal chemicals [41] (Table 4).

The environmental protection agency (EPA) has approved various chemical biocide for use domestically and clinically to reduce coronavirus transmission, including quaternary ammonium (QACs), hydrogen peroxide (H_2O_2), peroxyacetic acid, isopropanol (IPA), ethanol, sodium hypochlorite, octanoic acid, phenolic, among others [41]. Viral inactivation is resultant from disruption of the cell structure, destruction of the lipid envelope, protein coagulation, nucleic acid, and protein denaturation [23] (Tables 3 and 4). Studies assessing disinfection efficacy are difficult to compare because of innate experimental variations and lack of standardized procedures, including test material, varied exposure times, viral load, test chemical or combinations and the organic inhibitor used [40] (Table 4). Studies report efficacy of 70–90% IPA with 30 s exposure against SARS-CoV with 1–3% H_2O_2 demonstrating efficacy after 1 min exposure [42], while 0.1% sodium hypochlorite was effective in 1 min [39] (Table 4). A concentration of 6% acetic acid reduced human coronavirus (hCo-V) viability by 3.5 $\log_{10}$ after 1 min contact time [43] on surfaces. 60–70% ethanol reduced surface viral load by $>3 \log_{10}$ after 1 min exposure in healthcare settings [44]. For the inactivation of SARS-CoV-2, the most common disinfectants used are 62–70% ethanol, 0.5% H_2O_2, and 0.1% sodium hypochlorite, which are effective with 1 min exposure via oxidative reactions [42]. Pulsed plasma gas discharge has also produced biocidal water comprising short-lived oxygenated free radicals that has potential contact surface disinfection leaving no unwanted chemical residues [45]. For hand disinfection, the WHO recommends the use of 75% IPA or 80% ethanol hand rubs for 30 s to inactivate SARS-CoV-2 [46]. However, there is increasing opportunities to exploit advances in digitization and modelling to inform the future efficacy of disinfectants, including combining biocidal approaches and to hurdle limitations for broad applications [9,47]. Material compatability and functionality are important factors to consider when using new eco-alternatives to conventional biocides that includes combinational treatments [64].

Conclusion

Variant strains of SARS-CoV-2 are constantly emerging due to innate mutagenic changes in the viral genome, primarily altering structural components such as spike proteins. Although the efficacy of vaccinations program against these variants is unknown, such structural changes are unlikely to confer disinfection resistance as non-specific destruction of proteins and lipids of the viral capsid occur. Frontline biocides appear to be affective against VOC, but factors governing usage needs careful consideration. Vigilance is needed to protect our environment during the COVID-19 era, particularly by avoiding injudicious use of biocide that may negatively impact our agroecosystems [48]. Prolonged and excessive biocide use may give rise to situations that potentially promote cross-antimicrobial resistance in problematical bacteria to frontline antibiotics [49]. Adaptive resistance to frontline biocides has been reported since the early 1990s such as against bisphenol, triclosan, glutaraldehyde, and oxidising agents [22]. Paul et al. [48] highlighted that extensive application of biocides affects microbial flora that may lead to a decrease in the number and diversity of beneficial microbes that may directly affect the functioning of nutrient cycles; thus, careful considerations should be given to biocide neutralization, environmental management and sustainability [50,51]. Understanding these factors is important for the training of end-users, (e.g. healthcare, industry and community), to ensure the efficacy of biocidal product is maintained and effectively neutralized, along with monitoring policy for effective and responsible deployment of biocides. This current opinion supports Article 18 of the European Union's biocidal products regulation that directs the European Commission to issue a report on how the biocidal products regulation contributes to the sustainable use of biocidal products to reduce the risks posed to human health, animal health, and the environment by biocidal products. The aforementioned also recommends a series of actions to be completed by 2024, including investing additional resources in enforcement activities; developing the best available techniques reference documents that can be relevant for biocidal products used in industrial processes, and encouraging the development and implementation of standards that could contribute to the sustainable use of biocidal products and alternatives to biocidal products.

Funding

No funding.

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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Papers of particular interest, published within the period of review, have been highlighted as:

* of special interest
* * of outstanding interest

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