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New food safety challenges of viral contamination from a global perspective: Conventional, emerging, and novel methods of viral control

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Abstract

Food- and waterborne viruses, such as human norovirus, hepatitis A virus, hepatitis E virus, rotaviruses, astroviruses, adenoviruses, and enteroviruses, are major contributors to all foodborne illnesses. Their small size, structure, and ability to clump and attach to inanimate surfaces make viruses challenging to reduce or eliminate, especially in the presence of inorganic or organic soils. Besides traditional wet and dry methods of disinfection using chemicals and heat, emerging physical nonthermal decontamination techniques (irradiation, ultraviolet, pulsed light, high hydrostatic pressure, cold atmospheric plasma, and pulsed electric field), novel virucidal surfaces, and bioactive compounds are examined for their potential to inactivate viruses on the surfaces of foods or food contact surfaces (tools, equipment, hands, etc.). Every disinfection technique is discussed based on its efficiency against viruses, specific advantages and disadvantages, and limitations. Structure, genomic organization, and molecular biology of different virus strains are reviewed, as they are key in determining these techniques effectiveness in controlling all or specific foodborne viruses. Selecting suitable viral decontamination techniques requires that their antiviral mechanism of action and ability to reduce virus infectivity must be taken into consideration. Furthermore, details about critical treatments parameters essential to control foodborne viruses in a food production environment are discussed, as they are also determinative in defining best disinfection and hygiene practices preventing viral infection after consuming a food product.

KEYWORDS
bioactive compounds, chemical and physical disinfection, heat, irradiation, pulsed light, ultraviolet, virucidal surface, virus

1 | INTRODUCTION

The World Health Organization estimated that about 21% of all foodborne illnesses worldwide were caused by food- and waterborne viruses, such as human norovirus, hepatitis A virus, hepatitis E virus, rotaviruses, astroviruses, adenoviruses, and enteroviruses. About 8.3% of the deaths associated with foodborne illness were due to these viruses (WHO, 2015), with emerging and re-emerging viral strains (e.g., hepatitis E virus, Nipah virus, and Aichi virus) found to be more life threatening to the elderly and immune-compromised (Harrison & DiCaprio, 2018; Luby et al., 2006; Rivadulla & Romalde, 2020). Human norovirus, hepatitis A virus, rotaviruses, enteroviruses (e.g., polioviruses and coxsackie viruses), sapoviruses, astroviruses, and adenoviruses can cause foodborne viral illness in infants and children, often with high mortality rate in developing countries (O'Shea et al., 2019). Solis-Sanchez et al. (2020) and Vasickova et al. (2005) reported that human noroviruses are the most potent food viruses and responsible for 85%–90% of all nonbacterial gastroenteritis cases, with estimated 200,000 deaths annually worldwide, including 70,000 child deaths in developing countries. The number of cases caused by other major viral food pathogens, such as rotaviruses, hepatitis A virus, and astroviruses, are rated by their significance at second, third, and fourth places, respectively.

Foods can be contaminated with foodborne viruses anywhere along the supply chain from farm to fork (Duizer & Koopmans, 2009). For instance, in production of fresh produce viral contamination can occur in a field during growth, harvesting, postharvesting, and storage due to the use of contaminated irrigation water and manure of animal or human origin, via children or pets, farm animals, and wildlife (e.g., rodents, birds, and so on), contaminated field workers' hands, washing water, and the application of unsanitary equipment. During processing, preparation, distribution, and servicing, infected food handlers, contaminated water, and fomites are the main causes of viral contamination. Poor personal and environmental hygiene practices may further catalyze the spread of foodborne viruses (Vasickova et al., 2005). The common transmission routes of viruses and some surrogates via foods that are frequently associated with virus poisoning are summarized in Table 1 (Miranda & Schaffner, 2019; Pexara & Govaris, 2020).

Typically, food- and waterborne viruses implicated in outbreaks are small, nonenveloped particles, rather than large, fragile, enveloped viruses (Koopmans & Duizer, 2004). Dried to inanimate surfaces (Terpstra et al., 2007) or in the presence of inorganic or organic soils (Pottage et al., 2009), viruses can be challenging to eliminate. Viral clumping may further reduce the effectivity of disinfection protocol (McDonnell, 2017). Finally, the structure of the virus itself (enveloped vs. nonenveloped; structure of the viral proteins) determine the susceptibility of a virus to chemical, physical, or biological methods of disinfection or decontamination (Eterpi et al., 2010).

Obviously, the practices to prevent contamination of food and water were preferred over processes aimed at inactivating the viruses present in the foods or water. Food safety must be maintained throughout the food chain by adhering to good agriculture, good manufacturing, and good hygienic practices. Viruses should be included in food safety/quality control and management systems (HACCP), as well as microbial food safety guidelines (Koopmans & Duizer, 2004). However, effective mitigation strategies to control foodborne and waterborne viruses on food contact and food surfaces are needed, and their efficiency must be regularly evaluated.

The use of clean water with minimal fecal contamination is essential during the growth, washing, preparation, or packing of produce especially in the developing world, and it requires appropriate disinfection techniques to reduce the viral load of water. Soap and effective virucidal hand disinfectants are essential in the implementation of good hand washing practices for food and food service workers. Of equal importance is the disinfection of inanimate surfaces (e.g., equipment, utensils, and working environment) with traditional chemical disinfectants, bioactive substances, or physical means. In this context of the necessity to preserve the marketability and quality (e.g., consistency, taste, and odor) of fresh produce and other products, the effectiveness of various disinfection methods to reduce viral food pathogens must be an area of active investigation (O'Shea et al., 2019).

In this paper, traditional and emerging chemical and physical disinfection and decontamination control methods, novel virucidal surfaces and biological control to remove and inactivate viruses on food contact surfaces (tools, equipment, hands, etc.) or the surfaces of fresh produce or other foods are reviewed in relation to the structure, genomic organization, and molecular biology of viruses, and taking into account the antiviral mechanism of action of the method employed to reduce their infectivity. Examined traditional wet and dry disinfection include chemicals and thermal treatment of foods, whereas emerging technologies are nonthermal and nonchemical methods such as irradiation, ultraviolet (UV), pulsed light, high hydrostatic pressure, cold plasma, and pulsed electric field (PEF). The details about efficiency, advantages, disadvantages, and critical treatment parameters to control viruses in food production environment are discussed. This knowledge will assist food producers and providers in

TABLE 1 Transmission route of food-, water-, and airborne viruses and some surrogates in foods

Foodborne viruses	Transmission route			Associated foods	Surrogate
	Fecal-oral	Wateror environment	Aerosolization		
Enteroviruses	✓	✓	✓	Shellfish (mainly oysters)	Poliovirus-1, enterovirus EV-A71, coxsackievirus, bacteriophage PRD-1, bacteriophage φx174
Human norovirus	✓	✓	✓	Shellfish, oysters, fish, buffet meals, vegetables	FCV, FCV-1, FCV-F9, FCV 2280, TV, bacteriophage MS2, MNV-1, MNV-2, MNV-4
Hepatitis A virus	✓	✓	✓	Sandwiches, fruits, vegetables, milk, shellfish	HAV
Hepatitis E virus	✓	✓		Raw/undercooked boar, deer and pork meat, livers, and liver sausages	HEV
Aichi virus	✓	✓		Raw shellfish	Bacteriophage T4
Astrovirus	✓	✓	✓	Bivalve molluscs, fruits, and vegetables	Astrovirus
Human rotavirus	✓		✓	Clams and oysters, fruits, and vegetables	Simian rotavirus SA-11, rotavirus WA
Human sapovirus	✓		✓	Shellfish (oysters and clams)	PoSaV

Abbreviations: FCV, feline calicivirus; HAV, hepatitis A virus; HEV, hepatitis E virus; MNV, murine norovirus; PoSaV, porcine sapovirus; TV: Tulane virus.

defining and selecting the best control disinfection method and hygiene practices to prevent viral infection after consuming a food product.

2 | CHEMICAL CONTROL METHODS: MODE OF ACTION AND EFFICIENCY

2.1 | Chlorine-based disinfectants

Chlorine-based compounds, as the most broadly applied disinfectants in the food sector, have been used in solid (e.g., calcium hypochlorite), liquid (e.g., sodium hypochlorite), and gaseous form (Cl_2) (DiCaprio et al., 2017). Elemental chlorine, chlorine dioxide (ClO_2), or one of the hypochlorites have been applied to treat potable water or wastewater (Dandie et al., 2019), to decontaminate the surfaces of fruits and vegetables, and to disinfect food contact surfaces (WHO, 1998). They have the capacity to inactivate a broad spectrum of microorganisms (Table 2), including viruses, in particular enteric ones (Moyle, 2016).

2.1.1 | Chlorine/hypochlorite

Chlorine/hypochlorite exerts its antimicrobial activity by mechanisms such as oxidation, enzyme inhibition, and physical disruption of cell walls. Maillard et al. (2013) reported that the capsid is the primary target of hypochlorite, with the inhibition of the transcription and/or amplification of RNA in viruses (e.g., hepatitis A virus) as second target. DiCaprio et al. (2017) emphasized that the impact of chlorine on various viruses strongly depends on environmental parameters, requiring the collection of inactivation data for every pathogenic virus, independently from others.

In the study of Butot et al. (2008), several berries and herbs inoculated with hepatitis A virus, strain HM-175

TABLE 2 The efficacy of sodium hypochlorite/calcium hypochlorite or chlorine dioxide against foodborne viruses/ surrogates

Concentration	Virus or surrogate	pH	Temperature (°C)	Time (min)	Food contact surface orsuspension	Method of analysis	Log_{10} reduction	Reference
200 ppm free chlorineNaOCl	NoV	NDA	18	NDA	Blueberry, raspberry, strawberry, basil, parsley	RT-PCR	>3.4	Butot et al. (2008)
	FCV[c]	low	18	NDA	Blueberry, raspberry, strawberry, basil, parsley	RT-PCR	2–4	
						$TCID_{50}$	2.7–3.5	
	HAV	NDA	18	NDA	Blueberry, raspberry, strawberry, basil, parsley	RT-PCR	0.7–2.2	
						$TCID_{50}$	0.6–2.4	
	RV	NDA	18	NDA	Blueberry, raspberry, strawberry, basil, parsley	RT-PCR	0.4–4.1	
						$TCID_{50}$	1–3	
0.1 mg/L free chlorineNaOCl	MNV[c]	7.2	20-25	30	Drinking water	Plaque assay	1.69	Kitajima et al. (2010)
						rRT-PCR	0.03	
0.5 mg/L free chlorineNaOCl	MNV[c]	7.2	20-25	30	Drinking water	Plaque assay	>4.41	
						rRT-PCR	2.88	
0.1 mg/L free chlorineNaOCl	PV-1[c]	7.2	20-25	30	Drinking water	Plaque assay	1.27	
						rRT-PCR	0.02	
0.5 mg/L free chlorineNaOCl	PV-1[c]	7.2	20-25	30	Drinking water	Plaque assay	2.88	
						rRT-PCR	3.21	
15 ppm free chlorineNaOCl	FCV[c]	6	NDA	2	Butter lettuce	qRT-PCR	2.9	Fraisse et al. (2011)
	MNV-1[c]				Butter lettuce	qRT-PCR	1.4	
	HAV				Butter lettuce	qRT-PCR	1.9	
200 ppm free chlorineNaOCl	MNV-1[c]	NDA	RT	2	Strawberry, raspberry, cabbage, romaine lettuce	Plaque assay	<1.2	Predmore and Li (2011)
10 ppm free chlorine NaOCl	TV[c]	10	NDA	10	Suspension	$TCID_{50}$/RT-PCR	<1	Tian et al. (2013)

(Continues)

TABLE 2 (Continued)

Concentration	Virus or surrogate	pH	Temperature (°C)	Time (min)	Food contact surface orsuspension	Method of analysis	Log_{10} reduction	Reference
25 ppm free chlorineNaOCl					Suspension	$TCID_{50}$/RT-PCR	<1	
50 ppm free chlorineNaOCl					Suspension	$TCID_{50}$/RT-PCR	<1	
200 ppm free chlorineNaOCl					Suspension	$TCID_{50}$/RT-PCR	2	
300 ppm free chlorineNaOCl					Suspension	$TCID_{50}$/RT-PCR	3	
500 ppm free chlorineNaOCl					Suspension	$TCID_{50}$/RT-PCR	>4	
10 ppm free chlorineNaOCl	MNV-1[c]	6.5	NDA	1	Strawberry	Plaque assay	1.3	Huang and Chen (2015)
					Raspberry	Plaque assay	2.2	
50 ppm free chlorineNaOCl	NoV GII	NDA	NDA	10	Suspension	IMS/qRT-PCR	<1	Ha et al. (2016)
100 ppm ree chlorineNaOCl					Suspension	IMS/qRT-PCR	<1	
200 ppm ree chlorineNaOCl					Suspension	IMS/qRT-PCR	1.55	
500 ppm free chlorineNaOCl					Suspension	IMS/qRT-PCR	1.85	
1000 ppm free chlorineNaOCl					Suspension	IMS/qRT-PCR	2.45	
50 ppmNaOCl	HAV	NDA	RT	2	Strawberry	$TCID_{50}$	3.4	Zhou et al. (2017)
	MNV-1[c]	NDA	RT	2	Strawberry	Plaque assay	1.5	
	MS2 [c]						2.1	
100 ppmNaOCl	HAV	NDA	NDA	1	Blueberry and mixed berries	MPN	3	Takahashi et al. (2018)
MNV-1[c]	NDA	NDA	1	Blueberry and mixed berries	Plaque assay	3.8		
100 ppm*NaOCl	NoV GII.4	NDA	NDA	10	Rubber, glass, stainless steel, ceramic tile, wood, and polyvinyl chloride	IMS/qRT-PCR	0.26–0.66	Lee et al. (2018)
500 ppm *NaOCl					Rubber, glass, stainless steel, ceramic tile, wood, and polyvinyl chloride	IMS/qRT-PCR	0.27–0.86	

(Continues)

TABLE 2 (Continued)

Concentration	Virus or surrogate	pH	Temperature (°C)	Time (min)	Food contact surface orsuspension	Method of analysis	Log_{10} reduction	Reference
700 ppm *NaOCl					Rubber, glass, stainless steel, ceramic tile, wood, and polyvinyl chloride	IMS/qRT-PCR	1.04–1.53	
1000 ppm*NaOCl					Rubber, glass, stainless steel, ceramic tile, wood, and polyvinyl chloride	IMS/qRT-PCR	1.35–1.98	
150 ppm[a] $Ca(OCl)_2$	MNV[c]	7.5	4	0.67	Green onion	Plaque assay	0.5–2.8	Hirneisen and Kniel (2013)
	HAV				Green onion	RT-PCRMPN	0.4–2.6	
	AdV41				Green onion	RT-PCRMPN	0.2–3.1	
5 ppm[b] ClO_2 (l)	NoV	NDA	RT	10	Raspberry, Parsley	RT-PCR	0.58–0.71	Butot et al. (2008)
	FCV[c]	NDA	RT	10	Raspberry, Parsley	RT-PCR	<0.43	
						$TCID_{50}$	<0.7	
	HAV	NDA	RT	10	Raspberry, Parsley	RT-PCR	0.4–0.7	
						$TCID_{50}$	0.97–1.05	
10 ppm[b] ClO_2 (l)	NoV	NDA	RT	10	Raspberry, Parsley	RT-PCR	0.5–1.19	Butot et al. (2008)
	FCV[c]	NDA	RT	10	Raspberry, Parsley	RT-PCR	<0.81	
						$TCID_{50}$	<1.31	
	HAV	NDA	RT	10	Raspberry, Parsley	RT-PCR	0.3–0.72	
						$TCID_{50}$	0.79–1.75	
ClO_2 (g) generated by acidifying 0.1 mg NaOCl[b]	TV[c]	NDA	NDA	15	Blueberry	Plaque assay	0.5	Kingsley et al. (2018)
ClO_2 (g) generated by acidifying 1 mg NaOCl[b]	TV[c]	NDA	NDA	15	Blueberry	Plaque assay	2.5	

Abbreviations: AdV41, human adenovirus, type-41; FCV, feline calicivirus; HAV, hepatitis A virus; IMS, immuno-magnetic separation; MNV, murine norovirus; MPN, most probable number; NDA, no data available; NoV, norovirus; PV-1, poliovirus, type-1; TV, Tulane virus; qRT-PCR, quantitative reverse transcription-polymerase chain reaction; rRT-PCR, real-time reverse transcription-polymerase chain reaction; RT, room temperature; RV, rotavirus; $TCID_{50}$, 50% tissue culture infective dose. *Organic load: Stool sample.

(ATCC VR-1402), human rotavirus, WA strain (ATCC VR-2018), and human noroviruses GI and GII were washed with nonchlorinated tap water and chlorinated water (200 ppm free chlorine), respectively (test conditions: 30 s stirring of 15 g portions in 200 ml wash water at 18°C). In blueberries, for all viruses, reductions after washing with chlorinated water were about 1.5-2 log_{10} higher than those obtained after washing with nonchlorinated tap water. In raspberries, for all viruses, reductions achieved after washing with chlorinated water were only <0.5 log_{10} higher than those obtained after washing with nonchlorinated tap water, due to crevices and hairlike projections that may shield the viruses from environmental challenges. In strawberries, reductions in enteric virus titers achieved after washing with chlorinated water were 1-1.5 log_{10} higher than those obtained

after washing with nonchlorinated tap water. Chlorinated water also had limited effect on enteric virus titers when used to decontaminate basil and parsley. Chlorination of the wash water only provided a 0.5-1 $\log_{10}$ higher reduction for all viruses. Obviously, virus inactivation by washing produce with chlorinated water containing 200 ppm free chlorine varied with both the type of virus and the type of product. According to Predmore and Li (2011), to decrease the load of murine norovirus, type-1 in fresh produce by >1 $\log_{10}$, producers should use a concentration of 50–200 mg/L chlorine for a contact time >1 min.

Girard et al. (2016) reported how organic material like feces may affect viruses and the efficacy of chemical disinfectants such as chlorine. Also, food residues may reduce the virucidal effect of chlorine and hypochlorite (Cook et al., 2014). Based on their experiments, Park and Sobsey (2011) suggested that 5000 ppm of hypochlorite may be reasonably effective against norovirus on surfaces, if any organic soil is removed prior to the application of the disinfectant. The disinfectant should be applied for longer than 3 min to try to obtain a 3 $\log_{10}$ inactivation of the virus. Also, Barker et al. (2004) emphasized the need of precleaning to ensure that 5000 ppm of hypochlorite is effective in removing norovirus.

Birmpa et al. (2016) studied the antiviral effect of chlorine on human adenoviruses, and compared it with emerging disinfection technologies like ultrasound and UV light. Although human adenoviruses were inactivated faster by chlorine, these authors recommended the replacement of chlorine by new disinfection technologies that do not put a burden on human health.

2.1.2 | Chlorine dioxide

Fresh producers are using ClO_2 (Gil et al., 2009) due to its lower corrosiveness and reduced reactivity toward organic compounds and nitrogen/ammonia, and because no disinfection by-products like trihalomethanes are formed (Meireles et al., 2016).

López-Gálvez et al. (2010) revealed that 3 mg/L ClO_2 in fresh produce provided the same antiviral effect as 100 mg/L sodium hypochlorite (NaOCl). In gaseous form, ClO_2 reduced Tulane virus in fresh blueberries up to 2 $\log_{10}$ (Kingsley et al., 2018). Butot et al. (2008) demonstrated that ClO_2 had low effectiveness (<1 $\log_{10}$) against feline calicivirus F9 and hepatitis A virus after 10 min exposure to ClO_2 concentrations ≤5 mg/L, as is allowed by the FDA. According to Girard et al. (2016) murine norovirus, type-3 was in general resistant to ClO_2 when utilized in solution to disinfect fruits and vegetables.

2.2 | Alcohol-based disinfectants

Alcohol-based solutions have shown to be suitable for disinfecting various surfaces due to their disinfecting and antiseptic properties. They are also affordable and leave no residues on the surface after disinfection. Alcohols affect a wide range of microorganisms, and above all, their antiviral activity is considered. Among several alcohols, ethanol (EtOH) and isopropyl alcohol (IPA) are the most commonly used (Boyce, 2018).

At a proper contact time, alcohol-based disinfectants are highly effective at an optimum concentration of 60–90% (v/v) solution in water. At these concentrations, EtOH is a potent virucidal agent inactivating all of the enveloped (lipophilic) viruses and many nonenveloped (hydrophilic) viruses (Kampf, 2018; Kampf & Kramer, 2004; Rutala & Weber, 2019). IPA is fully active against enveloped viruses (e.g., hepatitis B virus and herpes simplex virus) and is sometimes even more active than EtOH (e.g., SARS-CoV-2) due to its higher lipophilicity (Singh et al., 2020). Due to its more lipophilic nature, IPA interacts more favorably with and disrupts more effectively the envelope of lipophilic viruses. But being more lipophilic than EtOH, IPA is consequently less active against the hydrophilic naked viruses such as enteroviruses (Kampf, 2018; Kampf & Kramer, 2004; Singh et al., 2020). Taken all together, EtOH has stronger and broader antiviral effect than IPA (Golin et al., 2020) as illustrated in Table 3.

Alcohols may inactivate enveloped viruses by targeting their envelope (by dissolving the lipid bilayer membrane, destabilization, and denaturation of proteins in the envelope) and their nucleocapsid (capsid protein denaturation) (Golin et al., 2020). Considering the fact that lipolysis is the main underlying mechanism for the germicidal effect of alcohols, their efficacy on nonenveloped viruses (due to the lack of a lipid bilayer membrane) is much lower (Sato et al., 2020; Singh et al., 2020). Where alcohols are successful in denaturing some nonenveloped viruses, denaturation of the capsid protein is the main reason for their virucidal effect (Golin et al., 2020).

Rabenau, Cinatl, et al. (2005) reported a >3.30 $\log_{10}$ reduction of the 2003 SARS coronavirus by 70 and 100% IPA (v/v) after 30 s contact time, and a >5 $\log_{10}$ reduction of the same 2003 SARS coronavirus by 78% EtOH (v/v) in the same time interval. Rabenau, Kampf, et al. (2005) also investigated the antiviral efficacy of four hand rubs (after 30 s contact time) and three surface/instrument disinfectants (after 15–60 min contact time) against the same 2003 SARS coronavirus. Irrespective of the load of organic material, all tested alcohol-based disinfectants had efficient antiviral activity (mainly ≥4 $\log_{10}$ reduction). Hulkower et al. (2011) examined the virucidal effect of 62, 70, and

TABLE 3 The efficacy of alcohol-based disinfectants against foodborne and airborne viruses, as well as their surrogates[a]

Disinfectant	Concentration (%)	Virus or surrogate	Temperature (°C)	Time (min)	Food contact surface or suspension	Method of analysis	Log_{10} reduction	Reference
EtOH	0	TV[a]	NDA	0.33	Suspension	$TCID_{50}$	<1	Tian et al. (2013)
	20						<1	
	30						<1	
	40						<2	
	50–70					$TCID_{50}$/RT-PCR	>5	
	10[**]	NoV GII	NDA	10	Suspension	IMS/qRT-PCR	0.12	Ha et al. (2016)
	30[**]						0.17	
	50[**]						0.35	
	70[**]						0.71	
	50[**]	NoV GII	NDA	10	Rubber, glass, stainless steel, ceramic tile, wood, PVC	IMS/qRT-PCR	0.04–0.32	Lee et al. (2018)
	70[**]						0.18–0.42	
	20	SARS-CoV2	NDA	0.5	Suspension	$TCID_{50}$	≤5.9	Kratzel et al. (2020)
EtOH-based hand rub[*]	80	SARS-CoV	RT	0.5	Suspension	$TCID_{50}$	≥4.25	Rabenau, Kampf, et al. (2005)
	85						≥5.5	
	90						≥5.5	
EtOH-based formula	30	SARS-CoV2	NDA	0.5	Suspension	$TCID_{50}$	≤5	Kratzel et al. (2020)
Propanol	20						5.9	
Iso-propanol based formula (75%)	30[***]	MERS-CoV	NDA	0.5	Suspension	$TCID_{50}$	≥4	Siddharta et al. (2017)
20	SARS-CoV2	NDA	0.5	Suspension	$TCID_{50}$	≤5.9	Kratzel et al. (2020)	
Hand rub[*] Iso-propanol (45%), n-propanol (30%), mecetronium ethyl sulfate (0.2%)	Undiluted	SARS-CoV	RT	0.5	Suspension	$TCID_{50}$	≥4.25	Rabenau, Kampf, et al. (2005)

Abbreviations: EtOH, ethanol; IMS, immuno-magnetic separation; MERS-CoV, Middle East Respiratory Syndrome Coronavirus; NDA, no data available; NoV, norovirus; SARS-CoV, 2003 severe acute respiratory syndrome coronavirus; SARS-CoV2, severe acute respiratory syndrome coronavirus 2; TV, Tulane virus; qRT-PCR, quantitative reverse transcription-polymerase chain reaction; RT, room temperature; RT-PCR, reverse transcription-polymerase chain reaction; $TCID_{50}$: 50% tissue culture infective dose.

**Organic load: stool sample; ***organic load: MEM (minimum essential medium: 0.3% albumin and 10% fetal calf serum/or 0.3% albumin with 0.3% sheep erythrocytes); ****organic load: EMEM (Eagle's minimum essential medium); DMEM (Dulbecco's modified minimal essential medium) and fetal calf serum,

*pH: 7.2;

71% EtOH (v/v) solutions on transmissible gastroenteritis virus and mouse hepatitis virus dried on stainless steel discs. A 2-4 $\log_{10}$ PFU reduction in these two surrogates of 2003 SARS-CoV was achieved within 1 min. Siddharta et al. (2017) assessed the virucidal effect of an 80% EtOH (v/v) based formulation (recommended by WHO) against MERS-CoV. MERS-CoV was reduced by >4 $\log_{10}$ PFU/ml in 30 s.

In the study of Tung et al. (2013), MNV-1 showed a high sensitivity to EtOH, with the lowest resistance being observed at 70% EtOH (v/v), followed by the concentrations of 90% and 50% EtOH (v/v). In the study of Steinmann et al. (2010), an 80% EtOH (v/v) solution supplemented with 1.45% glycerol (v/v) and 0.125% H_2O_2 (v/v) reduced MNV-1, adenovirus, type-5, and poliovirus, type-1 by, respectively, 5.5 $\log_{10}$, 5.2 $\log_{10}$, and 2.8 $\log_{10}$ PFU/ml over a contact period of 120 s. Tian et al. (2013) revealed that Tulane virus was inactivated within 20 s when the EtOH concentration increased from 40% to 50%–70% (v/v). Kampf (2018) conducted a literature review on the efficacy of EtOH disinfectant solution on various viruses. He found out that in all research reports, murine norovirus and adenovirus, type-5 usually were inactivated by EtOH at a concentration of 70% and 90% (v/v) after a contact period of 30 s. He further figured out that 80% EtOH (v/v) is unlikely to be sufficiently effective against poliovirus, feline calicivirus, and hepatitis A virus. But all these nonenveloped viruses could be inactivated by 95% EtOH (v/v). When EtOH at sufficient high concentration was supplied with additional ingredients like citric and phosphoric acid, poliovirus and feline calicivirus F9 could be inactivated, while hepatitis A virus remained too resistant. Kramer et al. (2006) reported that a formulation of 55% EtOH (w/w) supplemented with propan-1,2-diol, butan-1,3-diol, and phosphoric acid sufficiently inactivated (>4 $\log_{10}$) hepatitis A virus in suspension after 30 s exposure.

Steinmann et al. (2010) reported that 75% IPA (v/v) solution supplemented with 1.45% glycerol (v/v) and 0.125% H_2O_2 (v/v) reduced MNV-1, adenovirus, type-5, and poliovirus, type-1 by, respectively, 2.75 $\log_{10}$, 5 $\log_{10}$, and <0.5 $\log_{10}$ PFU/ml after 120 s of contact. Sato et al. (2020) demonstrated that 70% EtOH or IPA (v/v) could effectively suppress HuNoV GII.4, but no significant effect was observed on the HuNoV genotypes GII.3, GII.6, GII.17, and GI.7 tested in their study. The capsid protein of HuNoV GII.4 may be more sensitive to the protein denaturing effects of alcohol as compared with the other genotypes of HuNoV. Note that 70% EtOH or IPA (v/v) containing 1% citric acid (pH ~ 3.1) was sufficient for the inactivation of all of the above-mentioned HuNoV genotypes, with denaturation of the capsid protein as common cause. No impact on the RNA genome was observed. The acid–alcohol solution even could inactivate HuNoV GII.4 and GII.17 within 30 s, while no information was provided for the other genotypes of HuNoV. The authors postulated that acid-mediated changes in ionic and/or hydrogen bonds between alcohol and water are needed for 70% alcohol (v/v) to exert its virucidal effect on HuNoVs, except for the GII.4 genotype. Organic substances reduced the effect of acid–alcohol solutions.

In dry food processing environments, dry methods of equipment disinfection are preferred. Besides wiping with high-alcohol wipes (usually impregnated with quaternary ammonium compounds [QACs]), alcohol-based disinfectants can be applied as a fine spray onto the surface to be disinfected. Due to their fast evaporation, alcohol-based disinfectants can be sprayed just prior to resuming the operation. A contact time of 5 min is normally sufficient to disinfect the process line. But because the alcohol is potentially flammable, wiping and spraying with alcohol only is allowed for use far away from any sources of ignition (e.g., ovens). To reduce the fire risk, spray-based alcohol products could use carbon dioxide gas as the propellant (Moerman & Mager, 2016). Prolonged and repeated usage of alcohol also may compromise the integrity of equipment and construction materials such as plastics, causing them to discolor, crack, and swell (Nikoleiski et al., 2021).

2.3 | Peroxygenes

Hydrogen peroxide (H_2O_2), peracetic acid (PAA; CH_3COOOH), and ozone (O_3) are the most important peroxygens (McDonnell, 2017).

2.3.1 | Hydrogen peroxides

H_2O_2 is an oxidant that, by releasing hydroxyl radicals (•OH), affects basic cell constituents, such as lipids, nucleic acids, and proteins, and attacks the capsid and genome of viruses (Nasheri et al., 2021). It is an environmentally friendly disinfectant as it decomposes to safe by-products, such as water and oxygen. H_2O_2 is commercially available in a concentration range of 3%–90% (v/v), but is more effective as a vapor (McDonnell, 2017). The efficacy of H_2O_2 against various viruses/surrogates has been studied previously (Table 4). Becker et al. (2020) studied the virucidal effect of vaporous H_2O_2 (up to 260 ppm) against MNV-1 present on the surface of several fruits and vegetables (60-min exposure time). Depending on the smoothness/roughness of the surface of these fruits and vegetables, the inactivation of MNV-1 by vaporous H_2O_2 varied significantly. A ˂4 $\log_{10}$ reduction was found for apples and blueberries having a smooth surface, while a

TABLE 4 The efficacy of peroxygenes, quaternary ammonium biocides,[a] and other chemicals[b] against foodborne and airborne viruses/surrogates[c]

Disinfectant	Concentration (ppm)	Virus or Surrogate	Organic load	Temperature (°C)	Time (min)	Food contact surfaceor suspension	Method of analysis	Log_{10} reduction	Reference
H_2O_2*	100	NoV G.ll	NDA	NDA	10	Suspension	IMS/qRT-PCR	0.30	Ha et al. (2016)
	500					Suspension	IMS/qRT-PCR	0.41	
	1000					Suspension	IMS/qRT-PCR	0.57	
	2000					Suspension	IMS/qRT-PCR	0.71	
Peroxyacetic acid based disinfectant*	100	FCV [c]	NDA	NDA	2	Butter lettuce	RT-PCR	3.2	Fraisse et al. (2011)
		MNV-1[c]				Butter lettuce	RT-PCR	2.3	
		HAV				Butter lettuce	RT-PCR	0.7	
Ozone (g)	6.25	MNV[c]	NDA	20	10	Green onions	Plaque assay	1.5–2.5	Hirneisen and Kniel (2013)
		HAV				Green onions	MPN-qRT-PCR	1.5–2.9	
		AdV41				Green onions	MPN-qRT-PCR	0.9–4.3	
Magnesium monoperphthalate	5000	SARS-CoV	MEM 10%	RT	30-60	Suspension	$TCID_{50}$	≥4.5	Rabenau et al. (2005)
Benzalkonium chloride and laurylamine[a]	5000	SARS-CoV	MEM	RT	30-60	Suspension	$TCID_{50}$	≥6.13	
Benzalkonium chloride, glutaraldehyde and didecyldimonium chloride[a]	5000	SARS-CoV	MEM	RT	30-60	Suspension	$TCID_{50}$	≥3.75	
Alkyl dimethyl benzyl ammonium chloride (2.37%) [a]	Diluted in water (1:64)	NoV GI.1	Stool sample	21-23	2-10	Suspension	IMS-qRT-PCR	0.06	Liu et al. (2015)
		NoV GII.4	Stool sample	21-23	2-10	Suspension	IMS-qRT-PCR	−0.02	
Alkyl benzyl ammonium chloride (0.145%), isopropanol (1-5%) [a]	Undiluted	NoV GI.1	Stool sample	21-23	2-10	Suspension	IMS-qRT-PCR	−0.01	
		NoV GII.4	Stool sample	21-23	2-10	Suspension	IMS-qRT-PCR	−0.95	
ClO_2 (0.2%) Alkyl dimethyl benzyl ammonium chloride (0.125%) [a]	Undiluted	NoV GI.1	Stool sample	21-23	2-10	Suspension	IMS-qRT-PCR	−0.98	
		NoV GII.4	Stool sample	21-23	2-10	Suspension	IMS-qRT-PCR	−0.8	

(Continues)

TABLE 4 (Continued)

Disinfectant	Concentration (ppm)	Virus or Surrogate	Organic load	Temperature (°C)	Time (min)	Food contact surfaceor suspension	Method of analysis	Log_{10} reduction	Reference
Alkyl dimethyl benzyl ammonium chloride (0.07%) [a]	Undiluted	NoV GI.1	Stool sample	21-23	2-10	Suspension	IMS-qRT-PCR	−0.44	
		NoV GII.4	Stool sample	21-23	2-10	Suspension	IMS-qRT-PCR	−0.87	
Alkyl dimethyl ammonium chlorides (17.5%), ethylene diamine tetra acetic acid (5%) [a]	Diluted in water (1:500)	NoV GI.1	Stool sample	21-23	2-10	Suspension	IMS-qRT-PCR	−0.13	
		NoV GII.4					IMS-qRT-PCR	−0.12	
Alkyl dimethyl benzyl ammonium chloride (0.0216-0.086%); lactic acid (3.2%) [a]	Undiluted	NoV GI.1	Stool sample	21-23	2-10	Suspension	IMS-qRT-PCR	2.29	
		NoV GII.4				Suspension	IMS-qRT-PCR	0.21	
Alkyl dimethyl benzyl ammonium chloride (0.07%) [a]	Undilute	NoV GI.1	Stool sample	21-23	2-10	Suspension	IMS-qRT-PCR	3.19	
		NoV GII.4				Suspension	IMS-qRT-PCR	1.38	
Alkyl dimethyl benzyl ammonium chloride (40%)[a]	1000	NoV Gll.4	Stool sample	NDA	10	Rubber, glass, stainless steel, ceramic tile, wood, and polyvinyl chloride	IMS-qRT-PCR	0.02–0.12	Lee et al. (2018)
	2000						IMS-qRT-PCR	0.22–0.41	
Glutaraldehyde and (ethylenedioxy) dimethanol[b]	40,000	SARS-CoV	MEM	RT	15	Suspension	$TCID_{50}$	≥3.25	Rabenau et al. (2005)
	30,000				30	Suspension	$TCID_{50}$	≥3.25	
	60,000				60	Suspension	$TCID_{50}$	≥3.25	
SDS[b]	50	MNV-1[c]	NDA	RT	2	Strawberry, raspberry, cabbage, romaine lettuce	Plaque assay	3.14	Predmore and Li (2011)
Chlorine+ SDS[b]	200+50						Plaque assay	3.36	

(Continues)

TABLE 4 (Continued)

Disinfectant	Concentration (ppm)	Virus or Surrogate	Organic load	Temperature (°C)	Time (min)	Food contact surfaceor suspension	Method of analysis	Log_{10} reduction	Reference
Silver (0.003%), citric acid (4.84%)[b]	NDA	NoV GI.1	Stool sample	21-23	2-10	Suspension	IMS-qRT-PCR	−0.67	Liu et al. (2015)
		NoV GII.4				Suspension	IMS-qRT-PCR	−0.73	
Sodium metasilicate[b]	1000	NoV GII.4	Stool sample	NDA	10	Rubber, glass, stainless steel, ceramic tile, wood, and polyvinyl chloride	IMS-qRT-PCR	1.17–1.83	Lee et al. (2018)
	3000						IMS-qRT-PCR	1.51–2.71	
HDL[b*]	10,000	HAV	NDA	NDA	1 min	Blueberry and mixed berries	MPN	3.9	Takahashi et al. (2018)
		MNV-1[c]				Blueberry and mixed berries	Plaque assay	4.1	

Abbreviations: AdV41, human adenovirus type 41; FCV, feline calicivirus; HAV, hepatitis A virus; HDL, heat-denatured lysozyme; IMS/qRT-PCR, immuno-magnetic separation/quantitative reverse transcription-polymerase chain reaction; MEM, minimum essential medium (0.3% albumin and 10% fetal calf serum or 0.3% albumin with 0.3% sheep erythrocytes);
MNV-1, murine norovirus strain CW1; MPN, most probable number; NDA, no data available; NoV Gll.4, norovirus genotype GII.4; NoV GI.1, norovirus GI.1; RT, room temperature; RT-PCR, reverse transcription-polymerase chain reaction; SARS-CoV2, severe acute respiratory syndrome coronavirus 2;SDS, sodium dodecyl sulfate; TCID50, 50% tissue culture infective dose.
*pH: 6.8; **pH: 4; ***pH: 6.5.

1.9 $\log_{10}$ reduction was seen in cucumbers and no significant reduction at all in strawberries, both having a textured exterior. In other words, cracks, crevices, and openings on the outside of fruits and vegetables might reduce the virucidal effect of H_2O_2, because these are the places where viruses may find protection against H_2O_2 (Nasheri et al., 2021). Eterpi et al. (2009) investigated the antiviral effect of H_2O_2 against various viruses dried on surfaces. After 10 min contact time, H_2O_2 (7.5%) was 100% effective against vaccinia virus, while moderately effective against poliovirus, type-1 and adenovirus, type-5. In the same study, the parvoviruses showed high resistance to H_2O_2. Zonta et al. (2016b) studied the effect of nebulized H_2O_2 on infectivity of murine norovirus, type-1 and feline calicivirus F9 dried on surfaces of cover glasses and stainless steel discs. To this, a nebulizing machine aerosolized a solution of 7% H_2O_2 for 90 s at a dose of 6.6 ml/m^3, which achieved a varying H_2O_2 concentration inside the treatment chamber with a maximum of 77 mg/L. The treatment chamber was kept closed during 1 h. H_2O_2 decreased the infectivity of murine norovirus, type-1 and feline calicivirus F9 by, respectively, ≥4.84 and 4.85 $\log_{10}$ PFU on cover glasses. Lower PFU reduction up to ≥3.90 and 5.30 $\log_{10}$ for norovirus, type-1, and feline calicivirus F9 were observed on stainless steel. Genetically murine norovirus, type-1 is more related to human norovirus than feline calicivirus F9, as it belongs to the norovirus genus (Wobus et al., 2006).

2.3.2 | Peracetic acid

An equilibrium mixture of acetic acid and H_2O_2 known as peroxyacetic acid, peracetic acid, or PAA (Zoellner et al., 2018) has been approved by the FDA as a disinfectant for food contact surfaces and as a decontaminant for various foods (US FDA, 2017a, 2017b, 2017c). With an oxidation potential of 1.81 eV, PAA has high oxidative and antimicrobial properties (Dagher et al., 2017). At low concentrations, <0.3% PAA (v/v), it is an effective antiviral agent that decomposes to safe by-products: water, oxygen, and acetic acid (Kitis, 2004). PAA likely oxidizes S-H and N-H groups in the viral protein capsid (Wutzler & Sauerbrei, 2000). Maillard et al. (1996a, 1996b) and Sauerbrei et al. (2007) claimed that PAA affected nucleic acid and proteins in F116 bacteriophage and respiratory adenovirus. In the study of Wutzler and Sauerbrei (2000), 15 min exposure to 0.2% PAA (v/v) partially destroyed the envelope of vaccinia virus, while its core lost its typical biconcave structure. In the same study, PAA effectively disrupted adenovirus, type-2 leading to appearance of virus-derived debris.

Weng et al. (2018) found a low reduction in infectivity of MNV-1 when a practical concentration of 1.5 mg/L PAA was used for wastewater treatment. As a disadvantage, the breakdown products of PAA may increase the organic content in effluent, leading to microbial regrowth (Dandie et al., 2019).

Due to the increasing interest in peracetic acid as a disinfectant in water treatment processes, Dunkin et al. (2019) studied the effect of PAA on HuNoV GI.3, HuNoV GII.2, bacteriophage MS2, and MNV-1 in phosphate buffer solution, pH range of 6.5–8.5. The reductions in bacteriophage MS2 and MNV-1 infectivity observed after 120 min exposure to 1.5 mg/L and 10 mg/L of PAA were >4 $\log_{10}$ PFU/ml. A <1.3 $\log_{10}$ and 2.3–2.5 $\log_{10}$ reduction in gene copies of HuNoV GI.3 was observed at concentrations of, respectively, 1.5 mg/L and 10 mg/L of PAA, whereas reductions in gene copies of HuNoV GII.2 were 0.4 $\log_{10}$ and 0.6–1.6 $\log_{10}$ at the same concentrations of, respectively, 1.5 mg/L and 10 mg/L PAA. However, the authors proved that gene copy reductions were not robust predictors of reductions in infectivity. The reductions in HuNoV gene copies as measured by RT-qPCR underestimate the reductions in infectivity of both human noroviruses. Overall, water treatment with PAA at pH between 6.5 and 7.5 appeared to be better than a pH of 8.5 for achieving a substantial viral reduction.

PAA is an alternative for chlorine in the fresh-cut industry (Guix et al., 2019) (Table 4). Sánchez, Elizaquível, et al. (2015) reported that 80 mg/L PAA rapidly and thoroughly inactivated MNV-1 in lettuce process water. Although hepatitis A virus on lettuce was not susceptible to 100 mg/L PAA, a 3.2 $\log_{10}$ reduction in feline calicivirus F9 and a 2.3 $\log_{10}$ reduction in MNV-1 were obtained after 2 min exposure to 100 mg/L PAA (Fraisse et al., 2011). At a concentration of 250 mg/L PAA, Baert et al. (2009) observed a 1 $\log_{10}$ PFU/g reduction of MNV-1 in shredded iceberg lettuce, and this inactivation was not negatively influenced by organic material. Todd and Grieg (2015) suggested the use of PAA to minimize viral cross-contamination between fresh produce and washing water.

Eterpi et al. (2009) studied the effect of 0.2% PAA (v/v) on several viruses dried onto surfaces. After 10 min exposure, porcine parvovirus, minute virus of mice, poliovirus, type-1, adenovirus, type- 5, and vaccinia virus were effectively inactivated. Rabenau et al. (2014) reported a concentration-dependent reduction in various animal parvoviruses (bovine, canine, murine, and porcine), when 50-1500 mg/L PAA was tested against these viruses, both in suspension and dried on the surface of stainless steel.

2.4 | Ozone

Ozone (O_3) is a potent disinfectant to decontaminate fresh produce (Table 4), food contact surfaces, and the food processing environment (Khadre et al., 2001), as well as to treat water (von Gunten, 2007). Pascual et al. (2007) demonstrated that water containing 0.5–3.5 mg/L ozone was suitable to disinfect food processing equipment. They considered ozone as an eco-friendly disinfectant that does not form deleterious by-products detrimental to health. Ozone and its reactive by-products may attack proteins in the viral capsid, allowing leakage of the viral genome (Khadre et al., 2001). According to Brié et al. (2018), 3 ppm ozone (3 g/m^3 of air) inactivated MNV-1 (>3.1 $\log_{10}$ PFU/ml) on raspberries after 1 min contact time, whereas 5 ppm ozone (5 g/m^3 of air) was not effective in reducing hepatitis A virus after 5 min contact time. To inactivate hepatitis A virus on raspberries, higher concentrations of ozone in air should be tested. Meanwhile, the probable detrimental effect of ozone on the nutritional and sensory properties of the product should be monitored. Regardless of the O_3 concentration in the air and the product matrices tested (phosphate buffered saline and raspberries), the genome of the viruses remained intact. Shin and Sobsey (2003) studied the inactivation of human norovirus, poliovirus, type-1, and coliphage MS2 in ozonated water (0.37 mg/L, pH 7, 5°C and ≤5 min contact time). Note that 99.9% of all viruses tested were inactivated after 10 s exposure to the ozonated water.

2.5 | Quaternary ammonium compounds

Due to their lipophilic hydrocarbon chain, QACs have effect on enveloped viruses (McDonnell, 2017), but they are not very effective against nonenveloped viruses (Zonta et al., 2016a). QACs exert their activity by solvating and disrupting lipid envelopes. QAC-based disinfectants have a relatively high tolerance toward the presence of contaminating organic matter (Lin et al., 2020).

Gulati et al. (2001) examined two pure QACs and one QAC formulated with 2% sodium bicarbonate as disinfectant/cleaner to decontaminate food contact surfaces, lettuce, and strawberry. Albeit feline calicivirus F9 dried on stainless steel was not effectively inactivated (˂3 $\log_{10}$ PFU reduction) by none of the two pure QACs after 10 min exposure time, the virus was effectively inactivated by the QAC formulated with 2% sodium bicarbonate when used at concentrations of 1560 and 3120 mg/L (99.99% reduction). None of the QACs (also not the QAC formulated with 2% sodium bicarbonate) were effective against feline calicivirus F9 on lettuce and strawberry.

Whitehead and McCue (2010) determined the antiviral activity of QAC alone and in formulation against feline calicivirus F9 dried on a dry, hard, and inanimate carrier. It was observed that only the formulated QAC showed antiviral activity against feline calicivirus F9. The reductions obtained with 0.3% pure alkyl dimethyl benzyl ammonium chloride (pH 8.1) and 0.1% formulated alkyl dimethyl benzyl ammonium chloride (pH 11) were found to be, respectively, 1.2 and >3 $\log_{10}$ after 1 min contact. Feliciano et al. (2012) assessed the efficacy of QAC against MNV-1 on various contaminated ceramic plates, drinking glasses, and stainless steel forks. After washing and sanitizing with a mechanical dishwasher, reductions in MNV-1 were 2.7, 1.6, and 1.4 $\log_{10}$ on ceramic plates, drinking glasses, and stainless steel forks, respectively.

2.6 | Electrolyzed water

Electrolyzed oxidizing water (EOW) is produced by electrolysis of brine (sodium or potassium chloride solution) in a chamber with a cathode and an anode isolated by a membrane (Dandie et al., 2019). The biocide activity of EOW is due to its pH, oxidation-reduction potential, and the free available chlorine (Rahman et al., 2016). The solution obtained at the anode is called acidic EOW (abbreviated AcEOW), the solution produced at the cathode is known as alkaline EOW (abbreviated AlEOW), and neutral EOW (NEOW) is obtained from a single-cell chamber or is a mixture of the anodic solution and hydroxide ions (Cheng et al., 2012; Hricova et al., 2008). Acidic EOW that contains HCl, HOCl, Cl_2, OCl^-, and O_2 acts as a disinfectant, while alkaline EOW can be used as a cleaning solution (Kim et al., 2000).

The efficacy of electrolyzed water against viruses depends on the concentration of free available chlorine. Organic matter negatively affects the virucidal effect of electrolyzed water. As an example, in the study of Fang et al. (2016), AcOW as well as NEOW had the capacity to reduce titers of MNV-1 and HAV in suspensions. At a free chlorine concentration of 50 mg/L, the EO waters provided at least 4.7 $\log_{10}$ PFU/ml and 4.4 $\log_{10}$ PFU/ml reductions in, respectively, MNV-1 and HAV after 1 min contact time. Higher free chlorine concentrations and longer treatment times were needed to reduce the same viruses in the presence of organic matter and when dried on stainless steel surfaces.

In the study of Moorman et al. (2017), NEOW containing 250 mg/L free available chlorine could not inactivate HuNoV GII.4 strain Sydney dried on a stainless steel surface (only 0.4 $\log_{10}$ reduction), but could successfully inactivate this HuNoV in suspension (4.8 $\log_{10}$ reduction) (in both cases, 1-min contact time). Increased soil

load drastically reduced the antiviral efficacy of NEOW against HuNoV GII.4 strain Sydney, both in suspension and when dried on a stainless steel surface. The antiviral effect of neutral EOW (30-min exposure under a low load of organic material) was probably due to a loss in the structural integrity of the viral capsid. NEOW was also efficient in reducing titers of several viruses inoculated onto the surface of fresh blueberries: MNV-1 (>4 $\log_{10}$ after 1 min), MS2 phage (>4 $\log_{10}$ after 3 min), HAV (>4 $\log_{10}$ after 1 min), and bovine rotavirus (>5 $\log_{10}$ after 10 min) (Leblanc et al., 2021).

2.7 | Combined chemical disinfection methods

Liu et al. (2011) assessed the inactivation of three HuNoV strains by means of five commercially available gel sanitizers and two hand rubs containing 62%–95% EtOH (v/v) further combined with citric acid, peroxyacid, QACs, or copper gluconate. After 15-s exposure, HuNoV RNA was reduced by 0.1 $\log_{10}$ when the mixtures of 95% EtOH (v/v) with additives such as alkane/cycloalkanes, glycerin, myristyl alcohol, and hexane were used, and by 3.75 $\log_{10}$ when the mixtures of 70% EtOH (v/v), water, IPA, copper gluconate, diisopropyl sebacate, PEG/PPG-20/6 dimethicone, pentaerythrityl tetra-di-t-butyl hydroxyhydrocinnamate, and polyquaternium-37 were used.

Uzuner et al. (2018) investigated the antiviral effect of alcoholic hand antiseptics on adenoviruses. Note that 70% EtOH (v/v) or 70% IPA (v/v) along with 0.5% chlorohexidine-digluconate only provided a 1.6 $\log_{10}$ reduction in adenovirus serotypes 19 and 37. The highest reduction (2.5–3 $\log_{10}$) was achieved with a solution of 60% EtOH (v/v), 10% IPA (v/v), and 1% n-butanol.

Recently, the WHO specified two alcoholic hand disinfectants. Using the hand disinfectant with 85% EtOH (v/v), 0.725% glycerol (v/v), and 0.125% H_2O_2 (v/v) in diluted form (40%–80% in concentration), a ≤5.9 $\log_{10}$ reduction in SARS-CoV-2 and MERS-CoV was obtained in suspension. In the diluted form (30% concentration), the other hand rub containing 75% IPA (v/v), 0.725% glycerol (v/v), and 0.125% H_2O_2 (v/v) gave similar results, but not without cytotoxicity (Kratzel et al., 2020).

In the study of Malik and Goyal (2006), the virucidal effect of bicarbonate alone and in combination with H_2O_2 or aldehydes was evaluated against feline calicivirus F9 dried on stainless steel surfaces. Sodium bicarbonate at a concentration ≥5% and without additives effectively reduced feline calicivirus F9 dried on stainless steel (≥4 $\log_{10}$) after 1-min contact time. The virucidal effect was the same when sodium bicarbonate was used at a concentration ≤2.5% in combination with H_2O_2 or aldehydes.

Nozomu et al. (2020) investigated the antiviral effect of ozone stabilized in alcohol against 14 types of human adenoviruses (exposure time in a range of 3 s–5 min). Although ozonated alcohol inactivated all types of human adenoviruses with ≥4 $\log_{10}$ after 60 s, complete inactivation was only observed after 3-min contact time.

3 | PHYSICAL CONTROL MEASURES: MODE OF ACTION AND EFFICIENCY

3.1 | Heat

Dry and wet heats are effective means to inactivate viruses in foods and on food contact surfaces. According to Pollard (1960), structural changes in viral proteins are the main mechanism responsible for heat inactivation of viruses. The study of Brié et al. (2016) on the thermal inactivation of MS2 phages supports this theory. Furthermore, Ausar et al. (2006) have detected changes in different structural levels of the capsid protein of HuNoV upon heating.

Thermal processes are characterized by temperature–time combinations that must be respected and controlled to achieve the desired effect of virus inactivation in the current treatment. A thermal treatment to a core temperature of at least 90°C for 90 s is considered adequate to destroy viruses in most foods, although the effects of a heat treatment depend on the virus subtype, the initial viral population, and the food matrix (CAC, 2012). This temperature–time combination is part of the European Union criteria for the heat treatment of some bivalves, which are an important source of viral infections. However, some researchers have recently advised to replace this temperature–time combination by the classical lethality *F*-value used in thermal processing (Messens et al., 2018). Some countries have specific legislation for some food products. For example, the Danish legislation requires professional catering establishments to heat frozen raspberries at 100°C for 1 min before serving in order to avoid Norovirus outbreaks (Müller et al., 2015). A recent study suggests that heating at 70°C for 20 min, 80°C for 10 min, or 90°C for 5 min can inactivate human HuNoV GII.4 in mussels, with the last temperature–time combination rendering a product with the best sensory quality (Jeon et al., 2020). Determination of the decimal reduction time (*D*-value, min) and resistance (*z*-value, °C) is an established approach to characterize the thermal resistance of viruses using linear models. A compilation of *D*- and *z*-values for different foodborne enteric viruses and their viral surrogates in cell culture media, seafood samples, fruit, vegetables, herbs, and dairy and meat products can be found in Bozkurt et al. (2015c) and et al. (2017).

Food matrices can affect the lethality parameters. For example, the *D*-value for the inactivation of Tulane virus at 54°C is 2.91 min in cell culture media, but increases up to 4.09 min in spinach (Ailavadi et al., 2019). In the study of Croci et al. (2012), viruses were also protected by mussel matrix components. In model suspension, the titer of Feline calicivirus F9 was reduced by 4 $\log_{10}$ after 3 min treatment at 80°C, whereas only a 2 $\log_{10}$ reduction was seen in identical samples spiked with mussel debris after 15 min treatment at the same temperature. Bidawid et al. (2000) saw how an increase in dairy fat content protected hepatitis A virus from heat inactivation. Also, pH and salt may affect the thermostability of viruses, as demonstrated by Seo et al. (2012). Meister et al. (2020) proved that sodium chloride (NaCl) may enhance the thermal resistance of viruses due to an increase in van der Waals forces at different protein subunits in the viral capsid.

The kinetics of viral inactivation are important for the proper design of inactivation methods. It is important not to assume that the inactivation always follows log-linear kinetics. While there are cases of log-linear kinetics such as the thermal inactivation of Tulane virus and MNV-1 in strawberry puree (Bartsch et al., 2019), there are numerous examples of non-log-linear heat inactivation. For instance, this is the case for MNV-1 and coliphage MS2 (Seo et al., 2012) as well as hepatitis A virus (Bozkurt et al., 2015a) in clam meat (*Mercenaria mercenaria*). Non-log-linear heat inactivation kinetics were also observed for MNV-1, feline calicivirus F9, and hepatitis A virus in turkey deli meat (Bozkurt et al., 2015b), and for feline calicivirus F9, MNV-1, and hepatitis A virus in homogenate of blue mussel (*Mytilus edulis*) (Bozkurt et al., 2014; Bozkurt, D'Souza, et al., 2014).

Since the bacteriophages PRD-1 and φX174 seem to be more heat resistant than pathogenic viruses, Bertrand et al. (2012) proposed to use them as model viruses when studying the thermal inactivation of viruses under a worst-case scenario. According to these authors, it is not easy to identify the most resistant virus due to the high variability in virus types, types of treatments and matrices, and the limited number of studies. Differences in the experimental approach to determine virus resistance make it difficult to compare results reported by different research groups. For example, Hewitt Rivera-Aban and Greening (2009) reported a $D_{63} = 0.6$ min for HAV in water, while Gibson and Schwab (2011) reported a $D_{60} = 74.6$ min for the same virus in phosphate buffer saline. This difference of two orders of magnitude is hardly attributable to the slight differences in temperature and matrix composition. In their review, Peng et al. (2017) identified hepatitis A virus as the most heat-resistant virus, with D_{50} values as variable as 56.2 min in buffer and 385 min in phosphate buffer saline. The most heat sensitive virus might be MNV-1, with D_{50} values of 36.3 min in buffered medium and 106 min in phosphate buffer saline (Table 5). As for the SARS-CoV-2, a temperature–time combination of 92°C during 15 min can decrease the viral titer by >6 $\log_{10}$ (Pastorino et al., 2020). Despite the fact that dry and wet heats are readily available at relatively low cost, they may negatively impact the nutritional and organoleptic properties of foods. Moreover, energy requirements to produce heat are high.

3.2 | Irradiation

Irradiation is the process of exposing food to ionizing radiation, such as gamma rays, X-rays accelerated electrons, or e-beams, without direct contact with the food product (Farkas, 1998). Gamma and e-beam radiation could disrupt the virion structure of MNV-1 and Tulane virus by degrading the viral proteins and RNA genome (Predmore et al., 2015). In the study of Feng et al. (2011), similar destructive effects were seen in MNV-1 and vesicular stomatitis virus present in hard-shelled clams exposed to gamma irradiation. Although irradiation has broad spectrum activity, viruses are highly resistant to irradiation. The resistance of viruses against irradiation is compared by using decimal reduction dose values (*D*-values) in kGy. Because high irradiation levels may compromise the quality of the food being irradiated, food cannot be exposed to high irradiation levels. Taking into account the results of many studies, at the irradiation levels at present allowed, pathogenic viruses probably cannot be destroyed (O'Bryan et al., 2008; US FDA, 2019). Molina-Chavarría et al. (2020) studied the effect of gamma irradiation on HuNoV in strawberry. They found that high doses of radiation (20 kGy) were necessary to detect a significant reduction of up to 1.25 $\log_{10}$ in viral copy number. Pimenta et al. (2019) examined the inactivation of MNV-1 and human adenovirus, type-5 in strawberries and raspberries. A 2 $\log_{10}$ PFU/g reduction in MNV-1 and human adenovirus, type-5 was obtained after treatment with a dose of 4 kGy for both fruits. Still infective viral particles were detected at a dose of 11 kGy. The estimated gamma radiation dose needed to attain food safety (>7 kGy) would compromise the food quality. Similar results were published by Praveen et al. (2013) who studied the e-beam irradiation of HuNoV and hepatitis A virus in oysters. The e-beam dose required to reduce the titer of MNV-1 and HAV strain VR-1402 by 90% (*D*-value) in whole oysters was 4.05 kGy and 4.85 kGy. The study further revealed that e-beam processing of oysters cannot completely eliminate the risk of viral illness. Espinosa et al. (2012) studied the e-beam irradiation of poliovirus, type-1 (chat strain) and simian rotavirus SA-11 in iceberg lettuce and spinach. *D*-value (dose required to reduce virus titers by 90%) of

TABLE 5 Summary of effects of physical disinfection methods on food viruses

Physical method	Heat	Irradiation	UV light	Pulsed light
Inactivation mechanism	Targets proteins	Disrupts virion structure, degrades viral proteins, and genomic RNA	Targets nucleic acids and proteins	Targets nucleic acids and capsid
Processing parameters	Temperature, °C Time, min	Radiation dose, kGy	Light dose, mJ/cm^2	Light dose, J/cm^2
Values of decimal resistance parameter	*D*-value (min) at *T* (°C)	*D*-dose, kGy	*D*-dose, mJ/cm^2	*D*-dose, J/cm^2
The most resistant virus (family)	Parvoviridae(e.g., Parvovirus B19)	Parvoviridae,4–21.05 kGy	Adenovirus, type-4,92.1 mJ/cm^2	Bovine parvovirus,0.18 J/cm^2
The most sensitive virus (family)	Orthomyxoviridae(e.g., Avian influenza virus)	Caliciviridae0.01–3.3 kGy	Newcastle disease virus, 0.8 mJ/cm^2	Canine parvovirus,0.04 J/cm^2

simian rotavirus strain SA-11 (VR-1565) on spinach and lettuce was 1.3 kGy and 1.0 kGy, respectively. The *D*-value of poliovirus, type-1 on spinach and lettuce was 2.35 kGy and 2.3 kGy, respectively. The authors emphasized that e-beam irradiation technology can reduce the risks of infections, but only at the conditions that the starting levels of virus contamination are kept low by good agricultural and postharvest practices. High viral resistance to irradiation was also reported in the research work of DiCaprio et al. (2016) in which HuNoV GII.4 present in fresh whole strawberries was irradiated. No HuNoV GII.4 RNA was detected following e-beam treatment at a dose of 28.7 kGy. To achieve complete inactivation of HuNoV GII.4, gamma irradiation was more effective than e-beam irradiation, although still a dose of 22.4 kGy was required. At the currently approved levels of irradiation, gamma irradiation and e-beam treatment were thus not suitable to eliminate HuNoV GII.4 in fresh whole strawberries.

According to the Commonwealth of Australia (2014), members of the Caliciviridae may have high (*D*-value = 3.3 kGy) or low (*D*-value = 0.01 kGy) resistance to irradiation (Table 5), while some members of the Parvoviridae are among the most resistant (4 up to 21 kGy). According to the same source, coronaviruses have a *D*-value up to 3.6 kGy. For SARS-CoV-2, the *D*-value is low, that is, 1.6 kGy (Leung et al., 2020).

3.3 | Ultraviolet light

Ultraviolet light (UV) has wavelengths in the 200–400 nm region of the electromagnetic spectrum. It is conventionally divided into UV-A (315–400 nm), UV-B (280–315 nm), and germicidal UV-C (200–280 nm). The UV light targets of action against viruses are the nucleic acids and proteins, which have to absorb light photons. UV-C light at 253.7 nm generates thymine-dimers between adjacent thymine residues, which may result in the inactivation of DNA viruses. However, because RNA viruses lack thymine, a different mechanism of inactivation may occur depending on the type of nucleic acid of the virus. When UV-C was used to inactivate nonenveloped feline calicivirus F9, damage to its ssRNA genome was identified as the major cause for the decrease in its infectivity. When Tanaka et al. (2018) studied the UV inactivation of feline calicivirus F9, no significant degradation of the capsid protein was observed, although oxidation of amino acids in the major capsid protein occurred. In the study of Araud et al. (2020), UV inactivation of Tulane virus proceeded by affecting both its RNA genome and capsid binding proteins.

The inactivation capacity of UV light varies with the wavelength. UV light is most effective in the 200–300 nm range, which includes the whole UV-C range and a part of the UV-B range. In the study of Mamane-Gravetz et al. (2005), ssRNA coliphase MS2 was inactivated by wavelengths lower than 300 nm, but the lethality at wavelengths near 214 nm was three times higher than at 254 nm, with a relative minimum at 240 nm. When Beck et al. (2016) used a tunable laser to study the spectral sensitivity of MS2 coliphage, they found similar results. The peak of UV sensitivity of MS2 coliphage was at about 260 nm, a wavelength where maximal absorption of UV-light by and damage to the RNA genome occurs. The effectiveness of the inactivation then decreased to a low at 240 nm to increase again up to 210 nm, keeping a close relationship with genome damage but not with RNA absorbance. The results suggest that RNA damage at 210–240 nm occurs due to protein–RNA cross-linking or energy transfer from

proteins to RNA. It has also been demonstrated that various viruses have distinctive responses to UV treatments and the action mechanism depends on the type of virus and the wavelength of the UV light. For example, during UV irradiation of rotavirus porcine strain OSU and Tulane virus different components of the virions are targeted, such as their genome and viral capsid (Araud et al., 2020).

The UV-C light resistance is estimated by the inactivation rate constant or decimal reduction dose (*D*, expressed in mJ/cm^2), along with the sensitivity of the specific virus in the applicable region of the spectrum. Because the UV sensitivity of MS2 coliphage is at its highest close to the quasi-monochromatic light output of low-pressure mercury-vapor lamps commonly applied in UV reactors (253.7 nm), it is also used as indicator virus for the validation of UV reactors in the United States. Adenoviruses were among the most resistant viruses being tested by Hijnen et al. (2006) and Tang and Sillanpää (2015). According to extensive data compiled by Kowalski (2009), in air, adenovirus, type-4 is the most susceptible to UV light (*D*-value = 0.8 mJ/cm^2), while Newcastle disease virus is the most resistant (*D*-value = 92.5 mJ/cm^2) (Table 5). Heilingloh et al. (2020) reported complete inactivation of SARS-CoV-2 at an infectious titer of 5 x 10^6 $TCID_{50}$/ml when treated with UV-C light (1048 mJ/cm^2) during 9 min.

UV light can inactivate viruses in liquid and solid food products, as well as on food contact surfaces. Although UV-light is a dry nonthermal technology that leaves no residues in foods, food contact surfaces, and equipment, it also has low penetration capacity. It makes UV only effective to inactivate viruses in translucid liquid food and beverages with addition of mixing and on the surface of solid foods and equipment.

To achieve viral inactivation, the viral target must receive a sufficient amount of light (fluence). This can be controlled by taking into account the amount of germicidal light that the lamp emits, as well as the exposure time. To exert its virucidal effect, UV light must have direct access to the viral particles. Poor cleaning practices leaving food residues or biofilms on surfaces may counter the destructive effect of UV light, as they may hide viruses from direct exposure to UV light. Surface irregularities such as cracks, crevices, and high surface porosity also may reduce the efficacy of UV light, as they may create shadow effects shielding microorganisms (including viruses) from the action of UV light. In liquid foods, turbulence enhances the efficacy of UV light, but the liquid thickness, turbidity, and absorbance decrease it.

UV-C light could inactivate ssRNA coliphage MS2 and dsDNA coliphage T1UV in coconut water with, respectively, 1.85 $\log_{10}$ (at *D*-value of 40 mJ/cm^2) and 4.75 $\log_{10}$ (at *D*-value of 30 mJ/cm^2) (Bhullar et al., 2018). Ward et al. (2019) succeeded to inactivate the same viruses in skim milk: 2 $\log_{10}$ (at a *D*-value of 45 mJ/cm^2) and 5.8 $\log_{10}$ (at a dose of 30 mJ/cm^2) for, respectively, MS2 and T1UV. UV-C light alone could inactivate hepatitis A virus and feline calicivirus F9 inoculated on the surface of lettuce, strawberries, and green onions (Fino & Kniel, 2008). At a dose of 40 mJ/cm^2, reductions in hepatitis A virus were 3, 2.9, and 0.9 $\log_{10}$ for respectively lettuce, green onions, and strawberry. At a dose of 40 mJ/cm^2, reductions in feline calicivirus F9 were 2.45, 1.7, and 0.8 $\log_{10}$ for, respectively, lettuce, green onions, and strawberry. In the work of Li et al. (2011), a combination of UV-C light and H_2O_2 (UV-C at 254 nm, 2.5% H_2O_2) proved to be effective against MNV-1, coliphage φX174, and *Bacillus fragilis* phage B40-8 inoculated on lettuce. MNV-1, coliphage φX174, and *Bacillus fragilis* phage B40-8 gave a reduction of, respectively, 0.75, 1.5, and 0.65 $\log_{10}$ PFU (UV-C at 254 nm, 5 min), and 1.35, 2, and 1 $\log_{10}$ PFU (UV-C at 254 nm + 2.5% H_2O_2, 5 min). The additional inactivation was not due to the direct action of UV-C light but the oxidative effect of hydroxyl radicals (•OH) generated by the photolysis of hydrogen peroxide. Such a process is also called an advanced oxidation process. In the study of Park et al. (2015), MNV-1 and HAV inoculated on stainless steel were successfully inactivated by UV-C light: MNV-1 and HAV were reduced with, respectively, 2.6 and 0.9 $\log_{10}$ PFU/ml at *D*-value of 50 mJ/cm^2. *D*-value for MNV-1 and HAV was found to be, respectively, 33.5 mJ/cm^2 and 55.5 mJ/cm^2.

3.4 | Pulsed light

Pulsed light is the application of pulses of high-intensity polychromatic light (from the infrared to UV range). The UV portion is the most lethal, and therefore this technology has many properties in common with conventional UV light (Gómez-López et al., 2007). The major difference between both is that pulsed light is more effective due to a denser generation of photons with different energies. Although pulsed light lamps are filled with an inert gas (xenon) making them more eco-friendly, pulsed light systems are more expensive than conventional UV reactors.

The effect of pulsed light on MNV-1 was studied by Vimont et al. (2015). The pulsed light caused single-strand breaks in the RNA genome, damage to viral proteins, and fractures in the virion structure. In the work of Belliot et al. (2013), pulsed light affected the viral capsid of coliphage MS2. Pulsed light also demonstrated to be effective against Sindbis virus (enveloped ssRNA virus) (Roberts & Hope, 2003), poliovirus, type-1, and adenovirus Group D (Lamont et al., 2007).

Pulsed light is capable of inactivating viruses in food matrices and on food contact surfaces, although there are very few studies published. In their study, Roberts and

Hope (2003) reported that bovine parvovirus was the most resistant to pulsed light and canine parvovirus the least resistant. Pulsed light in the range of 45–60 J/cm^2 could inactivate *Escherichia coli* coliphage φX174 (1.6–2 $\log_{10}$), feline calicivirus FCV 2280 (1.5–2.3 $\log_{10}$), and feline calicivirus wild type/84 (SVA) (2.2–2.8 $\log_{10}$) on swine liver, dry-cured ham, and sausage. With a 1-1.6 $\log_{10}$ reduction, MS2 demonstrated to be the most stable virus on the test samples (Emmoth et al., 2017). In the work of Huang et al. (2017), MNV-1 and Tulane virus inoculated on the surface of blueberries and strawberries were inactivated, although with limited efficacy. The same low inactivation rate was observed for coliphage MS2 inoculated on chopped mint, pepper, and garlic (Belliot et al., 2013). Comprehensive data on the level of inactivation obtained for 22 different viruses treated with pulsed light recently has been published (Jean et al., 2021). The rather limited efficacy of pulsed light in real food matrices versus in vitro studies is typical for light-based inactivation technologies. Surface irregularities again cause shadow effects with microorganisms and viruses being shielded from the action of the pulsed light. On food contact surfaces, such as stainless steel and polyvinyl chloride, pulses of UV light were very efficient in the inactivation of MNV-1 and hepatitis A virus (Jean et al., 2011). A 2 s treatment in the absence of fetal bovine serum completely inactivated (5 $\log_{10}$ reduction) the viral load at different distances tested, whether in suspension (MNV-1) or on disks (MNV-1 and HAV strain HM-175). In the presence of 5% fetal bovine serum, the same treatment provided a 3 $\log_{10}$ reduction.

Pulsed light was able to inactivate SARS-CoV-2 inoculated on hard surfaces and N95 respirators, with >4 $\log_{10}$ reduction after 5 min exposure to an unspecified fluence of pulsed light (Simmons et al., 2021).

The use of pulsed light to inactivate microorganisms (including viruses) in foods has not been adopted to an industrial level yet. Pilot plant equipment to accelerate the scaling-up is lacking, as well as elaborated cost-assessment reports that may guide the industry in evaluating the economic feasibility of its actual implementation.

3.5 | Other methods

In addition to pulsed light, several emerging technologies have been investigated for their potential to inactivate viruses: high hydrostatic pressure processing (HPP), cold atmospheric plasma (CAP), and PEFs.

HPP is a nonthermal batch process that exposes foods already sealed in their final packaging to a high-pressure treatment (Koutchma et al., 2016). It has been suggested that HPP inactivates viruses by denaturing capsid proteins, rendering them unable to bind their receptor on the surface of their host cells (Kingsley, 2013). High hydrostatic pressure inactivation of viruses in several food matrices occurred with varying effectiveness. The efficacy of HPP against viruses depends on several factors such as water activity. The virucidal effect of HPP is reduced at low water activity. For example, high-pressure treatment of feline calicivirus in laboratory medium at 250 MPa and 20°C during 5 min resulted in insignificant inactivation of the virus at water activities <0.90, but 5 $\log_{10}$ reductions were obtained at a water activity of 0.99. The results also depended on the solute used to depress the water activity (Kingsley & Chen, 2008). Nasheriet al. (2020) studied the HPP treatment of hepatitis E virus, type-3 (HEV-3) in cell culture medium, and pork pâté. In the cell culture medium, they found 1.6 and 1.95 $\log_{10}$ reductions in the load of HEV-3 after a treatment at 400 MPa during 1 and 5 min, respectively. Reductions of 2.3 and 2.2 $\log_{10}$ were found when treating the samples at 600 MPa during 1 and 5 min. Reductions in the load of HEV-3 were limited to 0.4-0.5 $\log_{10}$, when treating ready-to-eat pork pâté samples at 400 MPa and 600 MPa during 1 and 5 min. Obviously, the inactivation efficiency of HPP depended on the surrounding matrix, with pork pâté protecting HEV-3 from HPP treatment. Food matrices may provide a protective effect against viral inactivation by HPP, with viral capsids becoming less prone to HPP denaturation. Even though HPP treatment could reduce the load of HEV-3, the degree of inactivation might not be sufficient to completely mitigate the food hazard burden brought about by HEV.

According to Sido et al. (2017), to obtain a >3 $\log_{10}$ reduction of HuNoV GII.4 in green onions and salsa treatment conditions of, respectively, 500 MPa and 300 MPa for 2 min are needed (treatment temperature of 1°C). In purees of blueberries, strawberries, and raspberries, to obtain >2.9 $\log_{10}$ reduction of HuNoV GI.1 strain and >4.0 $\log_{10}$ reduction of HuNoV GII.4, a pressure ≥550 MPa for 2 min at 0°C was needed (Huang et al., 2016). Selection of the most and least baroresistant virus is complex, since it depends on the pressure, treatment time, and temperature and food composition. Comprehensive tables on the inactivation of viruses by high hydrostatic pressure in laboratory media and in foods can be found in Govaris and Pexara (2021).

Plasma, as the fourth state of matter, is generated by subjecting certain gases to electric discharges. It goes together with the production of a wide variety of antimicrobial agents. Cold atmospheric plasma has proven to successfully inactivate viruses on the surface of food products. Its lethality is due to high-energy electrons, ionized atoms and molecules, as well as UV photons. This mixture of reactive compounds modifies and/or degrades nucleic acids, proteins, and the lipids of viral envelopes (Niedźwiedź

et al., 2019). Studies on bacteriophages T4, φ174, and MS2 have demonstrated that plasma damages both proteins and nucleic acids (Guo et al., 2018). Tulane virus inoculated on the surface of blueberries was reduced by 3.5 $\log_{10}$ after 120 s of treatment with cold plasma, while the titer of MNV-1 was decreased by 5 $\log_{10}$ after 90 s treatment (Lacombe et al., 2017). Roh et al. (2020) also inactivated Tulane virus inoculated on whey protein-coated boiled chicken breast cubes by 2.2 $\log_{10}$ after 3.5 min of treatment at 39 kV.

Of the emerging technologies, PEF is the most examined and developed. However, research reports dealing with the inactivation of viruses by means of PEFs are very scarce. This technology uses short pulses of electrical energy to inactivate microorganisms. In the study of Khadre and Yousef (2002), 20–29 kV/cm electric pulses applied to a suspension of human rotavirus did not result in a substantial reduction of the viral titer.

4 | VIRUCIDAL SURFACES

Cleaning and disinfection are the traditional means to remove viruses from surfaces. However, proper cleaning and disinfection can be laborious, time consuming, and is not always effective. Self-decontaminating surfaces could help in reducing indirect transmission of viral pathogens via surfaces. Up to now, virucidal surfaces are exclusively tested in the laboratory.

4.1 | Silver-containing materials

Nonionic silver (Ag°) has no antimicrobial effect. The virucidal activity relies on Ag^+-ions diffusing from the substrate material. Viral proteins are an important target, as Ag^+-ions may interact with thiol groups in proteins inducing conformational changes. Ag^+-ions also can bind viral DNA and RNA, more specifically the bases of the nucleic acids. Damage caused by Ag^+-ions is partially due to reactive oxygen species (ROS) providing nonselective antiviral activity (Moerman & Partington, 2016).

Martínez-Abad et al. (2013) prepared polylactide films with 0.1 and 1.0 wt.% of Ag^+-ions. After 24 h, feline calicivirus F9 was reduced by 2 and 4 $\log_{10}$ at, respectively, 0.1 and 1 wt.% Ag^+-ions. Under the same conditions, a 6 $\log_{10}$ reduction was seen in *Salmonella enterica*. The nonenveloped feline calicivirus F9 was thus more resistant. Contact with food components could reduce the effectiveness of the Ag^+ polylactide-films against both *S. enterica* and feline calicivirus F9.

Besides the direct interaction with viral surface glycoproteins, silver nanoparticles (AgNP) also interact with the viral DNA or RNA, especially once the AgNPs enter the host cell. Attached to the viral genome, the AgNPs prevent its replication. Castro-Mayorga et al. (2017) tested the effectiveness of AgNP/poly(3-hydroxybutyrate-co-3-hydroxyvalerate) films against feline calicivirus F9 and MNV-1. After 24-h exposure at 37°C and 100% RH, 2.26 and 0.86 $\log_{10}$ reductions in, respectively, feline calicivirus F9 and MNV-1 were observed. Differences in capsid structure and capsid composition may explain these results.

4.2 | Photocatalytic TiO_2

TiO_2—especially the nanosized anastase form—has proven to be successful in the photocatalytic inactivation of several viruses. The photocatalytic inactivation processes take place on or at nanometer size distance from the TiO_2 surface. Upon excitation by light with wavelength <380 nm, photons with energy excessing its valence band gap (3.2 eV for anatase) generate an electron–hole pair. The hole in the valence band can react with H_2O or hydroxide-ions (adsorbed on the surface) to produce especially hydroxyl radicals (•OH), while the electron in the conduction band can reduce O_2 to produce superoxide ions (O_2•–). In secondary reactions, other ROS are formed: hydrogen peroxide (H_2O_2), HOO•, and singlet oxygen ($^1O_2$). The most reactive species are the short lived •OH radicals which, due to their high oxidation potential (E° = 2.07 V), have the ability to oxidize viral constituents in a nonselective way (Blake et al., 1999). These •OH radicals can damage carbohydrates, nucleic acids (mutations due to strand breaks; chemical changes in deoxyribose/ribose moieties, as well as in purine and pyrimidine bases), lipids (lipid peroxidation), proteins (chemical attack on carbonyl and thiol-groups), and amino acids (conversion of phenylalanine in m-tyrosine and o-tyrosine).

Watts et al. (1995) observed a 3 $\log_{10}$ reduction in poliovirus, type-1 in secondary waste effluent after irradiation with a 40 W black light (UV) during 30 min. Inactivation of coliform bacteria was four times less effective. Viruses could be more susceptible to photocatalytic killing because of their much greater surface area to volume ratio. Bacteria also have a cell membrane and cell wall reducing the diffusion of •OH into these microbial cells (Burrows & Muller, 1998; Pogozelski & Tullius, 1998; Poormohammadi et al., 2021; Sang et al., 2007).

Guillard et al. (2008) studied the photocatalytic UV/TiO_2-based inactivation of A/H5N2 virus (a conventional research model for Avian A/H5N1 viruses) in air. Using an aerosol flow of about 40 m^3/h, the photocatalytic TiO_2 reactor achieved a 3.1 $\log_{10}$ inactivation.

Sang et al. (2007) used a platinum-doped TiO_2 that was also active in the visible light region. Visible light irradiation is more convenient, economical, and safer than UV catalysis. With this catalyst, •OH and O_2•− radicals were also generated. The Pt/TiO_2-mediated photocatalytic inactivation of human and simian rotaviruses (dsRNA, triple-layered capsid protein structure), human astrovirus, type-1 (ssRNA, single layered capsid protein), and feline calicivirus F9 (ssRNA, icosahedral capsid structure) was studied. White light irradiation at 30°C during 24 h gave 1.5 and 2.78 $\log_{10}$ reductions in, respectively, human and simian rotavirus, a 2.42 $\log_{10}$ reduction in human astrovirus and a 1.95 $\log_{10}$ reduction in feline calicivirus F9. The photocatalytic inactivation achieved with visible light is lower than with UV light. The capsid protein was the primary target of the ROS, with RNA as the second target. Due to the penetration of •OH radicals into the capsid protein, directly or indirectly, RNA degradation could occur.

Sang et al. (2007) have proven that protein residues may reduce the photocatalytic inactivation by adsorption on reaction sites and radical scavenging, being the proof that food residues may compromise the photocatalytic inactivation process.

4.3 | Copper and copper alloys

Rapid contact-mediated killing of viral pathogens by copper is due to its ability to accept and donate single electrons, when it changes oxidation state between Cu^+ and Cu^{2+}. These redox-properties allow copper to act as a catalyst in Fenton and Haber-Weiss reactions, generating ROS such as •OH radicals. Again, these ROS may damage vital viral constituents such as carbohydrates, proteins, lipids, and nucleic acids. The oxidative conversion of sulfhydryl-groups into disulfide functions induces lethal conformational changes in the structure of viral proteins (Weber & Rutola, 2013).

Noyce et al. (2007) inoculated 2×10^6 influenza A virus particles onto the surface of copper and stainless steel coupons. After 6 h incubation, still 10^6 infective virus particles were left on the stainless steel, whereas only 500 active viral particles were found on the copper alloy. After 24 h, still 5×10^5 infectious virus particles were found on stainless steel, but no influenza A particles could be detected on the copper surface.

Unpublished results of Keevil and Noyce demonstrated the inactivation of adenoviruses on the surface of C11000 copper alloy: 1.9 $\log_{10}$ and 5 $\log_{10}$ reductions within, respectively, 1 h and 6 h. During this same period, 50% of the infectious adenovirus particles survived on stainless steel (Lewis, 2009).

Issues about durability and corrosion-sensitivity limit the use of copper, copper alloys, or copper-impregnated surfaces. Alkaline detergents, sodium hypochlorite, acid and salt food may severely affect copper, increasing its surface roughness. It makes copper prone to fast attachment of food residues and microorganisms (biofilm formation). However, copper (alloys) may be suitable for nonproduct contact surfaces such as door knobs, tables, chairs, handrails, lavatories, toilets, dispensers, sinks, door push plates, computer keyboards, and so on (Moerman & Partington, 2016).

4.4 | N-halamine surfaces

N-halamine surfaces can be obtained by halogenation of amide-, imide-, or amino-containing heterocyclic rings attached to polymer backbones. Typically, one or more halogen atoms (Br or Cl, but usually the latter) are covalently bonded to the nitrogen atoms of the compounds. Because the N-Cl or N-Br covalent bonds are quite stable, release of free active halogen species occurs slowly. On direct contact with viruses, the covalent N-Cl or N-Br bonds are disrupted producing oxidative halogens (Cl^+ or Br^+) having the potential to bind thiol or amino groups in proteins (Moerman & Partington, 2016).

In the study of Panangala et al. (1997), N-chloro and N-bromo hydantoin derivatives of polystyrene provided, respectively, 4 $\log_{10}$ and 6 $\log_{10}$ inactivation of rotavirus in water flowing through a packed column (contact time 10 s). The presence of organic material was detrimental to the virucidal effect of the N-halamine resin. Cost restrictions limit large-scale application of N-halamine polymers.

4.5 | Surfaces immobilized with QACs

Because of their low toxicity and high effectiveness as disinfectants, amphiphilic QACs were immobilized on surfaces to study their potential as antimicrobial surfaces. The covalent binding on a substrate may provide nonleachable antimicrobial activity.

In the study of Tuladhar et al. (2012), surfaces were coated with quaternized ammonium compounds obtained by the alkylation of the tertiary amines present in commercial hyperbranched polymers. The coatings were tested for virucidal activity against enveloped (lipophilic) human influenza A virus H1N1 and nonenveloped (hydrophilic) enteric poliovirus Sabin, type-1. On the noncoated surfaces, the H1N1 virus showed a fast decay in the first 24 h, a slower decay up to day 5, and again a faster decay afterwards. The persistence of the poliovirus on the noncoated surface was high with less than 1 $\log_{10}$

decay in 10 days. Complete inactivation of the H1N1 virus was achieved within 2 min, while no significant reduction in poliovirus was detected after 6 h. Already from disinfection practices, we have learned that QACs have little virucidal activity against hydrophilic nonenveloped viruses. The authors suggest that hydrocarbon chains can attract viruses with a lipid envelope and embed themselves in this envelope, bringing the virus in close contact with the quaternary ammonium groups. The primary target of the n-alkyl ammonium groups is thus the virus envelope, causing its disruption and detachment. However, no profound effect was seen on the viral genome.

4.6 | N-alkylated polyethyleneimine coatings

Plastic coatings with polycationic polyethyleneimine (PEI) branches, consisting of a hydrophobic ethylene backbone with hydrophobic alkylated amino-functions, were also studied for their antimicrobial activity. Haldar et al. (2006) provided glass slides with a quaternized surface grafted PEI coating. The influenza A viruses H1N1 and H3N2 were for 98% inactivated after 30 min contact time and 100% inactivated (4 $\log_{10}$ reduction) after 2-h contact time. As with bacteria, smaller N-alkylated PEI derivatives resulted in slightly incomplete virucidal efficiencies. The lipid envelope of influenza viruses enables them to be damaged by means of the hydrophobic polycationic chains. Larson et al. (2011) studied the inactivation of the nonenveloped polioviruses and rotaviruses on PEI surfaces. N, N-dodecyl, methyl-PEI achieved to inactivate poliovirus for 100% after 30-min exposure. Using glass slides covalently modified with branched N, N-hexyl, methyl PEIs, both poliovirus and rotavirus were inactivated. Nonenveloped protein-coated viruses also can be inactivated by polycationic PEI coatings.

4.7 | Surface coating with photosensitizers

Light-activated inactivation of viruses in blood plasma with photosensitive dyes (e.g., methylene blue) is a well-established technique. When irradiated with light, excitation of the photosensitizing agent or mixture of photosensitizers takes place, leading to the production of $^1O_2$, O_2•−, •OH radicals, and H_2O_2. Due to their short-lived nature, only structures in close proximity to the photosensitizer(s) are directly affected. Viruses to some extents are more susceptible to photosensitized killing due to their relatively small size (10–300 nm), the absence of a protective envelope in many viruses and the exposure to attack of the viral capsid surface proteins essential for their binding to receptors on the surface of host cells (Brovko, 2010).

Decraene et al. (2006) studied the virucidal potential of a cellulose acetate coating containing toluidine blue and rose bengal as photosensitizers, with as test organism bacteriophage φX174 (host organism *E. coli ATCC 13706*). Used as model virus in transmission studies, its stability is comparable to resilient human-pathogenic viruses (e.g., parvoviruses and polioviruses). After 16-h exposure to light from a 25-W fluorescent lamp, a 2 $\log_{10}$ reduction in infectious viral particles was obtained.

In conclusion, although laboratory tests show medium to high virus reductions, the effect of virucidal surfaces in food environments is expected to be low. Food residues, scale, and biofilms may protect viral pathogens and prohibit their intimate contact with the surface. Virucidal nonfood contact surfaces could be of value on the condition that they are regularly cleaned. They will not be a substitute for standard cleaning and disinfection, as insufficient cleaning just impairs their virucidal effect (Moerman & Partington, 2016).

5 | NATURAL CONTROL METHODS: MODES OF ACTION AND EFFICIENCY

In the scientific community, the interest in natural methods (e.g., bioactive substances) to control foodborne and waterborne viruses is increasing. Natural control measures to combat foodborne viruses along the food chain may ensure food security, and increase food quality and safety. When combining several natural control techniques, they even may work synergistically increasing their effectiveness.

5.1 | Proteins

Takahashi et al. (2018) have demonstrated the antiviral effect of a 1% solution of heat denatured lysozyme against hepatitis A virus and MNV-1 on the surface of blueberries and mixed berries (strawberry and raspberry). Reductions were in the order of >3.1 $\log_{10}$ PFU/g and >4.1 $\log_{10}$ PFU/g for, respectively, hepatitis A virus and MNV-1 (contact time 1 min). The mechanism behind the inactivation of these viruses by means of heat denatured lysozyme is still unclear, especially because lysozyme has no antibacterial activity after complete denaturation. Transmission electron microscopy revealed that the particle diameter of MNV-1 was increased after exposure to heat-denatured lysozyme, while its viral capsid protein was

visibly destroyed. Lysozyme is accepted as a food additive (GRAS by the U.S. Food and Drug Administration; approved as E1105 in European Union), and therefore it can be used as an edible antiviral agent (Kamarasu et al., 2018).

5.2 | Polysaccharides

5.2.1 | Chitosan

Zhu et al. (2010) took out a patent on the use of chitin, chitosan, and their derivatives in antiviral preparations or disinfectants. Chitosan is a natural, nontoxic biodegradable polymer obtained by the deacetylation of chitin from the exoskeleton of crustaceans. It has proven to protect plants and animals from viral disease by reducing virus infectivity and inducing resistance of plants and animal organisms to viral infection (Badawi & Rabea, 2011; Friedman & Juneja, 2010). Chitosan containing hand rubs are available on the market, as well as chitosan-based formulations that can be sprayed or fogged on food and nonfood contact surfaces. At a concentration of 5%, the commercially available chitosan-based formulation ProtectUs Viridis (Residual Barrier Technology Ltd.) achieved a 4 $\log_{10}$ reduction in murine norovirus, Strain S99, and vaccinia virus within 2 min, even in the presence of 0.3 g/L bovine serum albumin (EN14476-test, performed by Sunway University, Malaysia). At a concentration of 3%, the formulation achieved a 4 $\log_{10}$ reduction in enterovirus EV-A71 and Sars-CoV-2 within 5 min. To inactivate enterovirus EV-A71 by 4 $\log_{10}$ with a solution containing 10% Clorox® (total amount of NaOCl in 10% Clorox solution is about 0.75%), time of 60 min was required.

Edible chitosan coatings impregnated with extracts from fruits or plants (containing polyphenols, proanthocyanins, components in essential oil, etc.) have the capacity to inactivate viruses in food (Amankwaah, 2013).

Su et al. (2009) exposed feline calicivirus F9 and MNV-1 to different concentrations of chitosan for 3 h at 37°C. Water-soluble chitosan (MW = 53,000, with a degree of acetylation of 9%) could decrease feline calicivirus F9 (initial titer ~5 $\log_{10}$ PFU/ml) by 2.1 $\log_{10}$ PFU/ml, 2.55 $\log_{10}$ PFU/ml, and 4.2 $\log_{10}$ PFU/ml at concentrations of, respectively, 0.175%, 0.35%, and 0.7%. No titer reduction in MNV-1 (initial titer of 7 log PFU/ml) was observed at all test concentrations. Using chitosan oligosaccharide (MW = 5000), feline calicivirus F9 at an initial titer of ~5 $\log_{10}$ PFU/ml was reduced by 0.4 $\log_{10}$ PFU/ml, 0.8 $\log_{10}$ PFU/ml, and 1.4 $\log_{10}$ PFU/ml at concentrations of, respectively, 0.175%, 0.35%, and 0.7%. Once again, titers of MNV-1 remained the same at the above-mentioned concentrations of chitosan oligosaccharide in solution.

The antiviral activity is thus dependent on the molecular weight and concentration of chitosan in solution. The antiviral effect is higher at higher concentrations, and when exposed to soluble higher molecular weight chitosan. But chitosan with molecular weight ≥100,000 is no longer water soluble at pH higher than 6.3. Furthermore, the authors attributed the antiviral effect of chitosan to its charge effect. With an isoelectric point (p*I*) of 4.9, feline calicivirus F9 is negatively charged at pH 6, allowing the virus to bind to positively charged chitosan. This binding could weaken or disrupt the capsid structure of feline calicivirus F9. To achieve considerable titer reduction in MNV-1, higher molecular weight chitosan at higher concentrations as well as longer incubation times may be effective. But chitosan only can be an effective inhibitory agent for those foodborne viruses that have a p$I < 6$.

5.3 | Polyphenols (tannins, pseudo tannins, and proanthocyanidins)

Tannins are a class of polyphenolic molecules containing hydroxyls and other groups (such as carboxyl groups) having the capacity to form strong complexes with various macromolecules (e.g., proteins) and to bind various other organic compounds including amino acids. Condensed tannins (MW up to 20,000) are mainly polymers of flavan-3-ols, such as catechin, epicatechin gallate, epigallocatechin, epigallocatechin gallate, theaflavins, etc. Hydrolyzable tannins (MW 500–3000) have a central carbohydrate partially or totally esterified with phenolic groups such as gallic acid in gallotannins or ellagic acid in ellagitannins. Proanthocyanidins are condensed oligomeric tannins, made up of catechin and epicatechin and their gallic acid esters, while anthocyanidins are higher order polymers.

5.3.1 | Persimmon extract

Kamimoto et al. (2014) evaluated the use of an ethanol-based sanitizer containing persimmon extract (in their study labeled as NA-20). Extract of persimmon (*Diospyros kaki*) contains ~22% high-molecular weight condensed tannins, in which catechin, catechin gallate, gallocatechin, and gallocatechin gallate are condensed via carbon–carbon bonds at a ratio of approximately 1:1:2:2 (Matsuo & Itoo, 1981). The amount of residual viral genome of HuNoV and bacteriophage MS2 were significantly decreased when treated with NA-20. As an example, MS2 phage was reduced by 3.06 $\log_{10}$ PFU/ml. The same disinfectant without persimmon extract or a 50% EtOH (v/v) solution did not reduce the infectivity of the MS2 phage (less than 0.04

$\log_{10}$ reduction). Shimamoto et al. (2014) took out a patent on the use of persimmon extract in hand soap, disinfectant formulations, etc. Within this invention, the formulation may further contain an alcohol (EtOH or IPA), an organic acid or salt of an organic acid (e.g., citric acid or citrate), a surfactant (anionic or nonionic), bactericide, antioxidant, etc. Formulations containing 50% EtOH (v/v) and 0.5% persimmon extract (without citric acid and trisodium citrate) gave a 93% (<2 $\log_{10}$ reduction) reduction in norovirus RNA copies, a number increasing up to 99% (2 $\log_{10}$ reduction) when the formulation was supplied with 1.6% citric acid and 0.5% trisodium citrate. When the persimmon extract was replaced by 0.5% tannic acid (gallic acid esters of glucose) or 1% catechin, gallic acid, propyl gallate, or pyrogallol (all hydrolysable tannins), no decrease in the number of norovirus RNA copies was observed. The compositions containing hydrolyzable tannin, low-molecular weight tannin, or an analogous compound thereof had thus no efficacy against the norovirus. Hand lotions containing 15%–20% EtOH (v/v), 15% glycerin, 7% laurylglucoside, 0.3% glycerol monocaprate, 0.5% astringent juice of persimmon, and 1% citric acid reduced the number of norovirus particles with 4.5–4.7 $\log_{10}$ PFU/ml.

In the study of Ueda et al. (2013), persimmon extract suppressed the infectivity of all enveloped (influenza virus H3N2, H5N3, herpes simplex virus, type-1) and nonenveloped viruses (poliovirus, type-1 sabin strain, coxsachievirus, type-5 group B, adenovirus, type-5, rotavirus WA strain, feline calicivirus F9, and MNV-1) to less than the detection limit (4 $\log_{10}$ PFU/ml up to 5 $\log_{10}$ PFU/ml reduction depending from the initial titer, 5.5 $\log_{10}$ up to 7.5 $\log_{10}$ PFU/ml). The antiviral activity was due to the interaction/binding of the persimmon tannins with the virion proteins (tannin-induced viral protein aggregation).

5.3.2 | Cranberry proanthocyanidins

Proanthocyanidins with A-type linkages, as found in cranberries, have antiviral activity against some human enteric viruses. Therefore, Su et al. (2010a, 2010b) studied the potential of cranberry proanthocyanidin extract as a disinfectant against human noroviruses, with feline calicivirus F9 and MNV-1 as surrogates. Feline calicivirus F9 decreased from the original titer of 5 $\log_{10}$ PFU/ml to undetectable levels immediately upon mixing with the cranberry proanthocyanidin extracts (both 0.15 mg/ml and 0.30 mg/ml). A ~5 $\log_{10}$ PFU/ml reduction in feline calicivirus F9 titer was thus obtained instantaneously. Immediately after mixing MNV-1 (original titer of 5 $\log_{10}$ PFU/ml) in a 0.15 mg/ml cranberry proanthocyanidin extract, a 1.6 $\log_{10}$ PFU/ml reduction was observed. In total, a 2.25–2.65 $\log_{10}$ PFU/ml reduction in MNV-1 was seen after 1-h exposure to 0.15 mg/ml cranberry proanthocyanidins. The reduction in viral titer on exposure to 0.3 and 0.6 mg/ml cranberry proanthocyanidins was, respectively, 2.75–2.95 $\log_{10}$ PFU/ml and ≥2.95 $\log_{10}$ PFU/ml after 1 h at room temperature. These studies were in line with previous research, where MNV-1 also has shown to be the harder to inactivate HuNoV surrogate. At higher titers of feline calicivirus F9 and MNV-1 (7 $\log_{10}$ PFU/ml), the cranberry proanthocyanidin solutions were less effective. The authors postulated that viruses at higher concentrations probably have a tendency to aggregate in clusters, protecting the viruses inside the cluster. Higher concentrations of cranberry proanthocyanidins will be needed to reduce higher titers of viruses. Upon closer examination with a transmission electron microscope, loss of the typical icosahedral symmetry and surface features of feline calicivirus F9 were seen after treatment, an indication of structural damage in the viral capsid. Greater morphologic and structural change/damage were observed after treatment with the 0.30 mg/ml cranberry proanthocyanidin solution. A solution of proanthocyanidins sufficient in strength can thus be an effective disinfectant against human noroviruses.

5.3.3 | Grape seed extract

Su and D'Souza (2013) studied the virucidal effect of grape seed extract, rich in oligomeric proanthocyanidins, on hepatitis A virus, feline calicivirus F9, and MNV-1 with air-dried lettuce and jalapeno pepper as model produce. They were inoculated with high (~7 $\log_{10}$ PFU/ml) and low (~5 $\log_{10}$ PFU/ml) titers of the viruses. At high viral titer, after 1 min exposure to 0.25, 0.50, and 1 mg/ml grape seed extract, feline calicivirus F9 was reduced by, respectively, 2.3, 2.6, and 2.7 $\log_{10}$ PFU/g on lettuce and by, respectively, 2.20, 2.75, and 3.05 $\log_{10}$ PFU/g on jalapeno peppers. At low titer, feline calicivirus F9 could not be detected after 1-min exposure to all three grape seed extract concentrations, both in lettuce and jalapeno pepper. At the same low titer, MNV-1 was reduced by 0.2–0.3 $\log_{10}$ PFU/g on the lettuce and 0.8 $\log_{10}$ PFU/g on the peppers, but without reduction at the titer of ~7 $\log_{10}$ PFU/ml. After 1 min, the grape seed extracts at a concentration of 0.25–1 mg/ml achieved 0.7–1.1 $\log_{10}$ PFU/g and 1–1.3 $\log_{10}$ PFU/g reductions for, respectively, high and low hepatitis A titers on both commodities. The inactivation of hepatitis A virus, feline calicivirus F9, and MNV-1 was thus dependent on the exposure time and test compound concentrations. The increase in contact time and grape seed extract concentration could possibly result in higher reductions of viral titer (Bosch et al., 2018).

5.3.4 | Black raspberry seed extract

Lee et al. (2016) have proven that black raspberry seed extract and its cyanidine derivatives could be useful in the prevention of foodborne and waterborne virus outbreaks, by using them in ready-to-eat foods, edible films, etc., the disinfection of water or in the decontamination of food contact surfaces. Black raspberry, native to Korea, China and Japan, has seeds rich in polyphenolic compounds. These seeds make up approximately 10% of the black raspberry fruit weight. The authors studied the antiviral effect of black raspberry seed extract against feline calicivirus F9 and MNV-1 (initial virus titer of 5 $\log_{10}$ PFU/ml). Maximum inhibition was achieved for both viruses at 0.1–1 mg/ml, with reductions in a range 2.7–3 $\log_{10}$ PFU/ml after 1-h exposure. The catechins and ellagic acid present in black raspberry seed extract exhibited negligible and weak antiviral activities. Transmission electron microscopy revealed that the viral capsids of MNV-1 were enlarged or disrupted after exposure to the black raspberry extract.

5.3.5 | Green tea extract—epigallocatechin-3-gallate

Many authors have proven that extract of green tea (*Camellia sinensis L.*) possesses antiviral properties. In the study of Ueda et al. (2013), it was shown that green tea extract suppressed the infectivity of both foodborne and waterborne enveloped (influenza virus H3N2 and H5N3, herpes simplex virus, type-1) and nonenveloped viruses (poliovirus, type-1 sabin strain, rotavirus WA strain, feline calicivirus F9). The green tea extract contains tannin of hydrolyzable type. Catechins constitute around 40%–50% of the green tea extract, because 30% of the dry weight of green tea consists of catechins. Of the catechins present in green tea, epigallocatechin-3-gallate had the highest antiviral activity (EC_{50}, 12 mg/ml).

In the study of Randazzo et al. (2017), green tea extract was examined for its potential as disinfectant. A 15-min treatment with 5 mg/ml green tea extract could reduce MNV-1 and hepatitis A virus by, respectively, 0.85 $\log_{10}$ PFU/ml and 0.15 $\log_{10}$ PFU/ml on a clean stainless steel surface, and finally up to, respectively, 1.5 $\log_{10}$ PFU/ml and 0.6 $\log_{10}$ PFU/ml after 30 min. A 10 mg/ml green tea extract reduced MNV-1 and hepatitis A virus on clean stainless steel by, respectively, 1.25 $\log_{10}$ PFU/ml and 0.65 $\log_{10}$ PFU/ml after 15 min, further increasing up to, respectively, 3.3 $\log_{10}$ PFU/ml and >3.75 $\log_{10}$ PFU/ml after 30 min contact. When the green tea extract was used to disinfect dirt stainless steel discs inoculated with MNV-1 and hepatitis A virus (same concentrations and exposure time), reductions in MNV-1 were about 0.5–1 $\log_{10}$ PFU/ml lower while the reductions in the hepatitis A virus titer were not affected by the presence of protein on the test surface. Although hepatitis A virus was still well inactivated, dirty surface conditions decreased the antiviral disinfectant potential of green tea extract due to the binding and masking effects of the organic load (such as protein).

The same authors also examined the potential of green tea extract as antiviral disinfectant of leafy vegetables, lettuce, and spinach. After 30-min treatment with 10 mg/ml green tea extract, MNV-1 was reduced by 2.4 $\log_{10}$ PFU/ml and hepatitis A virus by >3.85 $\log_{10}$ PFU/ml in these leafy vegetables. Again, hepatitis A virus was more sensitive than MNV-1, which confirms the results obtained by Falcó et al. (2017). In their study, hepatitis A virus was more sensitive to epigallocatechin-3-gallate than MNV-1. Epigallocatechin-3-gallate has shown high affinity but nonspecific binding to viral surface proteins (Hsu, 2015).

In the study of Ueda et al. (2013), green tea extract was not effective against coxsackievirus, type-5 group B, adenovirus, type-5, and MNV-1 (all nonenveloped viruses). But the green tea tannin could not induce aggregation of virus proteins in the same way persimmon tannin did. With a molecular weight of 500–3000, green tea tannin is much smaller in size than persimmon tannin that has a molecular weight of 13,800. In order to have a potent antiviral effect, the tannins must have a large structure allowing intense binding with virus proteins.

The numerous examples demonstrate that plant polyphenols (hydrolyzable tannins, condensed tannins, and proanthocyanidins) have antiviral activity on a wide range of foodborne viruses (e.g., hepatitis A virus, rotaviruses, surrogates of norovirus), making them suitable to prevent foodborne viral outbreaks. They may denature the viral capsid protein (Su et al., 2010a, 2010b) or coat virus particles (De Oliveira et al., 2013). Used in a hurdle approach with or without other microbial reduction technologies, they can make food production safer. As a major benefit, they can be a low cost alternative for more expensive and rigorous decontamination techniques such as heat or high pressure, which often also compromise the visual, sensorial, or nutritional value (Su et al., 2010b, 2011).

5.4 | Essential oils

Essential oils are complex natural mixtures of lipophilic and volatile secondary metabolites isolated from plants via extraction (hydro- and steam distillation). Monoterpenes, sesquiterpenes, and phenylpropanoids including

carbohydrate, alcohol, ether, aldehyde, ketone, acid, and ester functions are responsible for the fragrant and biological properties of aromatic and medicinal plants. Used as flavoring agents for centuries, they are generally recognized as safe (GRAS) for consumption. Essential oils or their individual components are also used as biopreservatives reducing or eliminating pathogen populations, including many DNA and RNA viruses (Swamy et al., 2016).

5.4.1 | Carvacrol

As an alternative to more corrosive disinfectants, carvacrol was suggested as disinfectant of fomites (Gilling et al., 2014), and as virucidal agent in the decontamination of wash waters and vegetables in the vegetable industry (Sánchez, Aznar, et al., 2015). At an initial titer of 6–7 $\log_{10}$ PFU/ml, a 3.85 $\log_{10}$ reduction in feline calicivirus F9 was achieved when 0.5% carvacrol was used to decontaminate lettuce wash water, and this regardless of the chemical oxygen demand (COD) (Sánchez, Aznar, et al., 2015). In lettuce wash water treated with the same concentration of 0.5% carvacrol, a 4.35 $\log_{10}$ PFU/ml reduction in MNV-1 was achieved. But when the COD of the wash water was higher than 300 ppm, the carvacrol was no longer effective against MNV-1. After inoculation of lettuce with high titers (6 $\log_{10}$ PFU/ml), no significant reduction in infectivity of MNV-1 and feline calicivirus was observed after washing the lettuce with 0.5% carvacrol. But a 1 $\log_{10}$ PFU/ml reduction was observed for both norovirus surrogates at 1% carvacrol. In lettuce inoculated with low titers (3.85 $\log_{10}$ PFU/ml) of the viruses, reductions in both norovirus surrogates were negligible at 0.5% carvacrol. However, a 1.7 $\log_{10}$ PFU/ml reduction in MNV-1 was seen after washing the lettuce with 1% carvacrol, whereas for feline calicivirus F9 the titer fell below detectable limits (2.45 $\log_{10}$ reduction). Viral clumping at higher virion concentrations may protect the viruses inside the clusters against carvacrol. Pilau et al. (2011) demonstrated that carvacrol was also effective against human rotavirus.

Gilling et al. (2014) monitored the effect of carvacrol on MNV-1 under an electron microscope. The capsids of MNV-1 were substantially expanded in size, from ≤35 nm up to 800 nm in diameter. Further expansion of the capsid finally resulted in its disintegration. Carvacrol could disrupt and/or destroy the viral capsid within 30 min.

5.4.2 | Thymol

In the study of Sánchez and Aznar (2015), the potential of thymol as a disinfectant in food environments was examined. Feline calicivirus F9, MNV-1, and hepatitis A virus (initial titer 6 $\log_{10}$ PFU/ml) were incubated with thymol at concentrations from 0.5%, 1%, and 2% for 2 h at 37°C. A reduction of 3.4 $\log_{10}$ PFU/ml in feline calicivirus F9 was seen at concentrations above 0.5% thymol. MNV-1 was reduced by 0.3 $\log_{10}$ PFU/ml, 1.5 $\log_{10}$ PFU/ml, and 2.3 $\log_{10}$ PFU/ml respectively, at 0.5%, 1%, and 2% thymol. Thymol was thus effective in reducing the titers of the norovirus surrogates in a dose-dependent manner. No titer reductions in hepatitis A virus were observed for thymol at all test concentrations.

5.4.3 | *Lindera obtusiloba* leaf extract

In the study of Solis-Sanchez et al. (2020), MNV-1 was preincubated in increasing concentrations of *Lindera obtusiloba* leaf extract (1–12 mg/ml) during 1 h. The inactivation occurred in a dose- and time-dependent way, and was also influenced by the temperature (highest at 37°C and lowest at 4°C). As an example, preincubation of MNV-1 with 12 mg/ml of the extract at a treatment temperature of 25°C revealed reductions in infectivity of 35.5% and 69.5% after, respectively, 30 and 60 min. The authors also studied the antiviral effect of *L. obtusiloba* leaf extract on model food systems and stainless steel. Lettuce, cabbage, oyster, and stainless steel surfaces, known carriers in previous norovirus outbreaks, were spot-inoculated with MNV-1 (5 $\log_{10}$ PFU/ml). After 1-h incubation at 25°C, pretreatment with 12 mg/ml *L. obtusiloba* leaf extract significantly reduced MNV-1 plaque formation in lettuce (76.4%), cabbage (60.0%), oyster (38.2%), and stainless steel (62.8%). Even after 30-min incubation (12 mg/ml *L. obtusiloba* leaf extract), the antiviral effect was significant in all model food systems. Reductions in all samples pretreated with the extract were also dose dependent. The plaque reduction assay revealed that of the major chemical compounds in the *L. obtusiloba* leaf extract, β-pinene, α-phellandrene, camphene, and (+)-limonene could reduce the infectivity of MNV-1 by 49.7%, 26.2%, 18%, and 17%. Leaf extract of *L. obtusiloba* (blunt-lobed spice bush), as well as β-pinene, may thus effectively inhibit human norovirus on food and metal surfaces.

The effectiveness of essential oils largely depends on the composition of the individual components, the type of virus, the exposure time, and test conditions (such as temperature). Regarding the inactivation of enveloped viruses by essential oils, several mechanisms are proposed: (i) direct binding of the essential oil (or an ingredient) to the virus, likely inhibiting the adsorption of the virus to host cells, and (ii) disruption and/or disintegration of the envelope. Inactivation of nonenveloped viruses is mainly due to essential oils (or an ingredient) affecting

the viral capsid, but without irreversible binding to it. The antimicrobial might bind to the capsid or block epitopes required for virus adsorption to the host cells, or cause a conformational change in the capsid (Cliver, 2009; Gilling et al., 2014).

5.5 | Organic acids

If organic acids have some antiviral effect, then their biological activity is more important than their pH obtained in solution. MNV-1, which has greater similarity to human norovirus (such as size, capsid structure, genomic organization, molecular biology, replication cycle, pathological characteristics, resistance in the environment, and against rigorous treatment) than feline calicivirus F9, is more resistant to pH than the latter (Elizaquível et al., 2013). Referring to the many HuNoV outbreaks linked to fruits and fresh-cut vegetables, low pH cannot be a significant contributor to antiviral activity. However, sensitivity to pH may differ from one virus to another virus (Oh et al., 2012; Su et al., 2010a, 2010b).

5.5.1 | Citrate

Citric acid is found in many citrus fruits. Citric acid is also produced in large quantities by fermentation processes. As a food additive (citric acid; sodium, potassium, and calcium citrate), it is used as an acidifier and antimicrobial agent. However, it also may act as a chelating agent in acid detergent formulations and can be used in disinfectant formulations. The EPA-approved disinfectant silver dihydrogen citrate (brand name: Pure® Hard Surface, Pure Bioscience, El Cajon, CA, USA) was tested against GI.6 and GII.4 human norovirus by Manuel et al. (2017) using a virucidal suspension and stainless steel carrier assay according to, respectively, the ASTM E 1052-96 and ASTM E1053-11 standards. The suspension assay showed a 4 $\log_{10}$ reduction in RNA copies within 5 min, while the carrier assay showed a 2–3 $\log_{10}$ reduction in RNA copies after 30 min. A 5% soil load into the sample matrix significantly reduced the efficacy: only a 2.5 $\log_{10}$ reduction in RNA copies was observed in the suspension test and no statistically significant reduction in the surface assay. Treated norovirus GII.2 virus-like particles displayed deformation and aggregation, and an 80% reduction in histo-blood group antigen (HBGA) receptor-binding ability. Using X-ray crystallography, Koromyslova et al. (2015) failed to identify any conclusive effects from the silver ions on the structure of norovirus GII.10 virus-like particles, but citrate caused the norovirus virus-like particles to enlarge and change their morphology.

Hansman et al. (2012) found that citrate and other glycomimetics have the potential to prevent human norovirus from binding HBGAs. Citrate has the capacity to bind the HBGA binding pocket on the human norovirus capsid, because citrate and a water molecule can form a ring-like structure mimicking the pyranoside ring of fucose, being identical to the terminal HBGA fucose. The binding affinity of citrate for this HBGA binding pocket is similar to the binding affinity of HBGAs. Citrate may outcompete the HBGAs linked to the glycoproteins or glycolipids present in the epithelial cells of the intestinal mucosa (Almand et al., 2017). According to Koromyslova et al. (2015), the binding of citrate also triggers the virus particles to undergo a conformational change, disrupting the HBGA binding pocket and making it more accessible for other potentially less specific or previously sterically inhibited molecules. At high citrate concentrations, even disassembly of HuNoV particles seems to occur, exposing their vulnerable RNA or rendering the particles inactive. These findings suggest that it is possible to reduce norovirus infections with citrate. Several norovirus disinfectants therefore label citric acid as an active ingredient.

Natural antiviral compounds must have activity against a broad range of foodborne and waterborne viruses at a low minimum inhibitory concentration, even those with high genomic variability. Nonenveloped viruses generally seem less sensitive than enveloped viruses for biological substances, pure phytochemicals, and plant extracts (Witvrouw et al., 1991). Although of natural origin, natural compounds can still be toxic or even more toxic than artificial chemicals. To be acceptable for food, pure phytochemicals and plant extracts must have minimal toxicity, not cause adverse health effects, or engender undesirable sensory changes in the product. Rigorous testing and clinical trials will be needed before approval by the appropriate regulatory agencies will be granted (Randazzo et al., 2017; Su et al., 2010b).

6 | CONCLUSIONS

During the past century, foodborne diseases were mainly credited to bacterial pathogens. With better diagnostic techniques and surveillance capabilities, it is now accepted that nine enteric viruses are major contributors to foodborne infections as well. These foodborne viruses can be transmitted anywhere in the food supply chain during the growing, harvesting, postharvesting, storage, and retail stages via contamination of the environment, such as water, via wild life but also in combination with person-to-person contact or contaminated food.

Historically, the food industry used chemical disinfection methods and thermal treatment due to their

availability, low cost, and proven antiviral effectiveness. In this review, we analyzed the antiviral efficacy of traditional, emerging, and novel disinfection approaches and emphasized the need of food industry to utilize more of the natural physical means (e.g., UV light), as well as biological antiviral compounds. They are considered to have minimal effects on food attributes and to be more environmentally friendly.

Based on available data and industry experience, inactivation of viruses using chemical disinfectants is only successful when the surface is clean with no food residues. The antiviral effectiveness of chemical disinfection may decrease in the presence of food residues, because they may neutralize disinfectant chemicals or protect viruses from the destructive effect of disinfectants. Additionally, consumers dislike chemicals due to potential effects on health and sustainability considerations. The effectiveness of a given disinfectant largely depends on its mode of action, as well as the viruses that need to be destroyed. Some disinfectants such as QACs and alcohol-based disinfectants especially target the lipid bilayer membrane of enveloped viruses, but their activity is lower or minimal against naked viruses when concentrations are too low. Because oxidizing agents (chlorine-based disinfectants, peroxygenes, ozone, and electrolyzed water) target both the membrane (enveloped viruses) and the nucleocapsid (enveloped and non-enveloped viruses), they have broader antiviral effect.

Dry and wet heats are the other traditional methods used because of their effectiveness to reduce or eliminate viruses on contaminated surfaces and foods. According to reports, it is not easy to identify the most heat-resistant virus due to the high variability of virus types, types of treatments and matrices, the limited number of studies, and differences in methodologies used. Literature data can be used to develop and validate thermal processes with a virus as target organism. Also, the common concern of thermal treatments is the undesirable effect of heat on thermally labile food compounds, affecting the quality of produce and destroying health-promoting substances in foods. In response to the concerns of consumers, the food manufacturers are forced to be more open for the use of alternative pure physical nonthermal disinfection/decontamination technologies and biological mitigation strategies that are natural and similarly effective.

Food irradiation is approved worldwide but viruses can be quite resistant to irradiation, while consumers are erroneously suspicious about irradiated food. Parvoviridae are among the most irradiation-resistant viruses. Low-dose electron beams can be an alternative surface treatment method to traditional gamma irradiation and high-dose electron beams.

Foodborne, airborne, and waterborne viruses can be inactivated by light-based technologies using various UV sources at multiple wavelengths in UV-C range. Although UV light is an established technique for air and water disinfection, its limited penetration capacity to food, liquids, and beverages can be a hurdle to its broad use as virucidal technique for food treatment. To be effective, viruses must be directly exposed to the UV photons and absorb them, which is often hampered by shadowing effects caused by surface irregularities, cracks, crevices, and high surface porosity. As UV light also may discolor food or cause sensory changes at high doses, its current main value is in the inactivation of viruses on clean inanimate surfaces including packaging materials, as well as in transparent liquid foods and beverages. The fast development of UV LEDs offers the options to apply multiple wavelengths in UV-C, UV-B, and UV-A ranges to overcome the disadvantages of a single wavelength.

Pulsed light can be more effective than conventional monochromatic UV-light, but it also requires direct exposure of the viral targets to the light beam. The effectiveness of other emerging technologies such as high pressure, PEFs, and plasma treatment to inactivate viruses is still under study.

Antimicrobial surfaces have proven potential in inactivating both bacterial and viral pathogens at least in the laboratory, and especially on nonfood contact surfaces, but they are less effective in the presence of soil which is relevant in food environments. To be effective, antimicrobial materials must be regularly cleaned. Only then the benefits they offer will come to their fullest: more environmentally friendly than chemical disinfection methods, labor savings, lower operational costs due to reduced use of chemicals and water, and finally a healthier environment.

As alluded to in this review, consumers prefer natural means over artificial chemicals to control microbial pathogens, including foodborne and waterborne viruses. In fact, it is a revival of an old method of surface disinfection and food decontamination, because phytochemicals have been successfully used for that purpose since ancient times. Phytochemicals, either as pure compound or plant extract, can be used as disinfectant on both inanimate surfaces (e.g., equipment), food contact surfaces such as hands, and food surfaces (e.g., fresh-cut vegetables). Up to now, chlorine is the most commonly used decontaminant in the fresh-cut vegetable industry, although some European countries have limited its use because of the formation of by-products (e.g., trihalomethanes). Natural compounds being "generally recognized as safe" are already used as a component of the hurdle-concept against foodborne and waterborne viruses in the food industry. Biopreservatives with small ecological footprint are embraced by environmentally conscious consumers, and therefore food supplied with or processed with the aid of phytochemicals often has higher marketability. Furthermore, antiviral

phytochemicals abundantly present in indigenous plants and trees growing in developing countries may provide the poor native people with cheap bio-disinfectants able to inactivate viruses in their food and water, as well as on inanimate surfaces.

Preventing food from getting contaminated with microorganisms (including viruses) always comes at first place in the plethora of food safety control strategies that exist, especially because reducing and eliminating microbial contaminants is technically and operationally demanding, and as consequence also costlier. Protecting food consumers against foodborne viral infection starts with "good agricultural practices," with "good hygiene practices" and "good manufacturing practices" as additional requirements to be implemented along the food chain. The guideline CAC/GL 79-2012 of the Codex Alimentarius Commission considers "hazard analysis critical control point" as an essential instrument in the control of viruses along the food preparation, processing, and production continuum. Preferably sensitive semiquantitative detection methods for viruses should be used to monitor critical control points and the effectiveness of mitigation strategies.

Finally, there is an urgent need to harmonize regulations and the use of disinfectants globally. In many developing countries with usually low standards of hygiene, the approach to inactivate viruses may be different from the approaches in developed countries.

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7AUTHOR CONTRIBUTIONS

Ezzatpanah, H.: Conceptualization; Supervision; Writing – original draft; Writing – review & editing. **Gómez-López, V. M.**: Writing – original draft. **Koutchma, T.**: Conceptualization; Writing – original draft; Writing – review & editing. **Lavafpour, F.**: Writing – original draft. **Moerman, F.**: Conceptualization; Writing – original draft; Writing – review & editing. **Mohammadi, M.**: Writing – original draft. **Raheem, D.**: Writing – original draft.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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