Trends in Food Science & Technology 138 (2023) 551–563

Contents lists available at ScienceDirect

Trends in Food Science & Technology

journal homepage: www.elsevier.com/locate/tifs

Antiviral edible coatings and films: A strategy to ensure food safety

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ARTICLE INFO

Handling Editor: AR Jambrak

Keywords:
Viruses
Foodborne illnesses
Antiviral compounds
Active films
Active coatings
Food safety

ABSTRACT

Background: Pathological viral transmission via food has been a problem throughout humankind's evolutionary history, impacting food safety and public health. Fresh produce can be contaminated at any stage from pre- to post-harvest and frequently goes through little to no processing, imposing a high risk for contamination by foodborne viruses. Also, due to the globalization of the food industry and supply networks, the spread of enteric virus-related foodborne disorders has worsened. The current understanding of the transmission of viruses through contaminated foods needs more information regarding the potential infectivity, and it is essential to have effective ways to prevent viral transmission and minimize its adverse effects on human and animal health.
Scope and approach: This review addresses the global public health issue related to foodborne viruses and the current challenges of food safety. It provides an overview of food-grade and naturally occurring antiviral compounds with good antimicrobial activity and emphasizes how edible films and coatings with embedded antiviral agents can reduce the transmission of foodborne illness.
Key findings and conclusions: Antiviral edible films and coatings can be developed using plant-based compounds and their derived-products, like essential oils and extracts, with bioactive properties. Their use in food products and food contact materials can contribute to developing strategies to contain infectious outbreaks. Results show that these compounds interact with the viral particle, causing some damage to the virus integrity and affecting its infectivity. The development of antiviral edible films and coatings containing these bioactive compounds showed great potential against enteric viruses that cause foodborne illness, specifically norovirus and hepatitis A virus. However, some antiviral agents have also been shown to be very effective against other pathogenic viruses of great importance, some of which are not typically foodborne but can also be dangerous to humans.

1. Issues and challenges in the food supply chain

Throughout human history, viruses have been a major cause of infectious diseases and food poisoning, being responsible for global public health issues. For example, globally, there are thought to be 600 million cases of gastroenteritis each year (World Health Organization, 2015). More than 200 foodborne illnesses are currently recognized, with the potential for lifelong sequelae and symptoms from moderate gastroenteritis to fatal illnesses. Food and waterborne viruses are one of the main etiological agents in foodborne infections, and researchers, food hygienists, and policymakers are paying close attention to them. These pathogens differ from foodborne pathogenic bacteria in several ways. They are more likely to spread infection and survive in food environments and are harder to detect accurately and rapidly (World Health Organization, 2015).

Foodborne virus infections are predominantly associated with enteric viruses. These are shed in high concentrations in faeces and vomit and remain infectious in the environment for several days or months (Cliver, 2014). Viruses cannot reproduce independently and only do so in the host cells of people, other animals, plants, or microorganisms. As a result, unlike foodborne bacteria, foodborne viruses cannot multiply in food, and their potential to spread infection through contaminated food depends on both the virus's viability and the host's vulnerability (Miranda & Schaffner, 2018). Viruses can contaminate food at any point along the supply chain and persist for a long time in food. They can come, for example, from hands and surfaces that come into contact with food. Therefore, foods that are handled manually and not further treated with effective treatments (e.g., temperature,

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https://doi.org/10.1016/j.tifs.2023.06.038
Received 31 January 2023; Received in revised form 22 June 2023; Accepted 30 June 2023
Available online 4 July 2023

pressure, radiation) before consumption may maintain the foodborne viruses until consumption (World Health Organization & Food and Agriculture Organization of the United Nations, 2008).

According to the World Health Organization (WHO), norovirus (NoV) and hepatitis A virus (HAV) are the leading causes of foodborne infections worldwide which have been linked to the bulk of outbreaks (World Health Organization, 2022). Nevertheless, additional viruses, not typically of food origin, can also be a danger to humans. Regarding the latter, the biggest epidemic outbreaks of the 21st century were primarily caused by coronaviruses, more notably SARS-CoV-1, MERS-CoV, and SARS-CoV-2. Coronaviruses and other respiratory viruses spread primarily through direct and indirect encounters. There has been much controversy about the possible transmission of SARS-CoV-2 through food. In particular, SARS-CoV-2 has been found to spread through food cold chains, also known as refrigerated and frozen supply chains, which are utilized to retain perishable goods during manufacture, storage, and transportation. Some authors have hypothesized that contaminated cold-storage foods may facilitate SARS-CoV-2 transmission between countries and regions (Han, Zhang, He, & Jia, 2021). For example, Qian et al. (2022) identified 45 COVID-19-related food cold chain incidents in China. However, according to the WHO there is no evidence that people can become infected by swallowing the virus in food (World Health Organization, 2020). Thus, further research will help to gain a more comprehensive understanding of this issue and to address the risks as thoroughly as possible (González et al., 2021).

Outbreaks of viral foodborne illness have often been attributed to unprocessed, uncooked, or lightly cooked foods, such as seafood, fruits, and fresh vegetables. Fresh produce, which usually undergoes little or no processing and can be contaminated at any stage of the production, storage, and distribution chain, presents a high risk of contamination by foodborne viruses, mainly enteric viruses. Additionally, the transmission of foodborne diseases related to enteric viruses has worsened due to the globalization of supply chains and production (World Health Organization, 2015; Miranda & Schaffner, 2018). Also, detecting viruses in food can be more difficult than detecting culturable bacteria. Given that the viral loads found in food samples are often significantly lower than those in clinical samples, highly sensitive detection techniques are required (Huang et al., 2021). A recent report suggested that the chain's temperature monitoring systems may play a significant role in the rapid identification of the sources of contamination responsible for the SARS-CoV-2-related food safety incidents (Qian et al., 2022).

Even though numerous antivirals are already on the market, their effectiveness is often constrained by issues such as low efficacy because of their reduced solubility and low stability under harsh conditions (Chen et al., 2021). Advanced antiviral delivery methods, such as nanoparticles, can solve some of these challenges (Delshadi et al., 2021). The use of antiviral films and coatings, similar to antibacterial control agents in food packaging systems, is another possibility. In this regard, edible films and coatings with antiviral compounds embedded into their polymer matrix are starting to get attention for their potential as delivery systems. It can be applied directly to foods subject to human handling, prevent viral transmission and consequently reduces foodborne illness (Mallakpour et al., 2021; Priyadarshi et al., 2022; Sharif et al., 2021).

There is still very limited information in the literature about the direct applications of edible antiviral coatings on food (Fabra et al., 2018; Falcó et al., 2018; Mayorga et al., 2018). In this sense, in addition to summarizing the current state of knowledge in quantitative microbial risk assessment related to foodborne viruses, this review presents an overview of the major classes of food-grade and natural antiviral compounds available with great antimicrobial potential. It also highlights the role of edible films and coatings with those antiviral compounds embedded in reducing foodborne illnesses transmission.

2. Edible films and coatings

Edible films or coatings are generally based on a mixture of biopolymers and other additives dispersed in aqueous solutions (Díaz-Montes & Castro-muñoz, 2021). Edible coatings are defined as a thin layer of material formed directly on the surface of a material, which can be a food product or food contact material. When applied directly to a food product, it can act as a semi-permeable barrier to gases, extending shelf life and protecting food integrity. Furthermore, the coating can also be used as a carrier of bioactive compounds such as probiotics, antimicrobials, antioxidants, and antiviral agents that can act on the food surface or in the human gut (Guimarães et al., 2018; Yekta et al., 2021). The edible films are made separately from the food as a result of drying of a solution (or extrusion) that is made separately from the food and only then adhered to the product (Kumar et al., 2021).

Fig. 1 shows the difference between film and coating production. Despite the different denominations, they are both rigid matrices with similar properties.

As mentioned before, edible films and coatings, when applied to food products such as fruits or vegetables, present various benefits such as (Pinheiro et al., 2010):

- Reduce water loss, i.e., decrease water vapour permeability;
- Reduce oxygen permeability to increase shelf life, delay oxidative decomposition, and reduce ethylene production (drives ripening in some fruits) of foods;
- Increase carbon dioxide permeability to prolong the lag phase and logarithmic growth of undesirable microorganisms (yeasts and moulds);
- Reduce spoilage, ripening, and aroma loss and delay browning and colour changes;
- Improve appearance and enhance colour and flavour;
- Improve mechanical resistance to prolong the integrity of the fruit;
- Reduce the incidence of light through high values of opacity since light promotes fat oxidation;
- Promote the transport and controlled release of agents that improve the texture and antioxidant capacity of volatile precursors and nutritional and functional compounds.

Edible films and coatings are based on polysaccharides, proteins, lipids, or a combination thereof. Plasticizers and surfactants can also be added to these materials to improve end-product characteristics such as flexibility and elasticity, barrier and optical properties, and active compounds can also be incorporated as a tool to increase the shelf life of food products and control the growth of pathogenic and spoilage microorganisms (Rawdkuen, 2018). A material with a good water vapour barrier is desirable to delay surface dehydration of fresh foods and control gas exchanges (e.g., reduce oxygen exchange to reduce oxidation and rancidity consequently) (Aliabbasi et al., 2021). Additionally, using raw materials from natural and renewable sources could help to reduce environmental impacts and promote more environmentally friendly and sustainable industrial production (Guimarães et al., 2018).

2.1. Materials for the production of films and coatings

Depending on the sources, the raw materials used in forming edible films and coatings can be grouped according to their animal, vegetable, or microbial origin. They can be classified into two categories: hydrophobic and hydrophilic. In general, hydrophobic substances (e.g., lipids) have better barrier properties against moisture transfer, while hydrophilic substances (e.g., proteins and polysaccharides) display a good barrier to oxygen and present better mechanical properties (Guimarães et al., 2020).

Polysaccharide-based coatings are transparent and homogeneous with good mechanical and structural properties. Due to the hydrophilic nature of most polysaccharides, their moisture barrier properties are

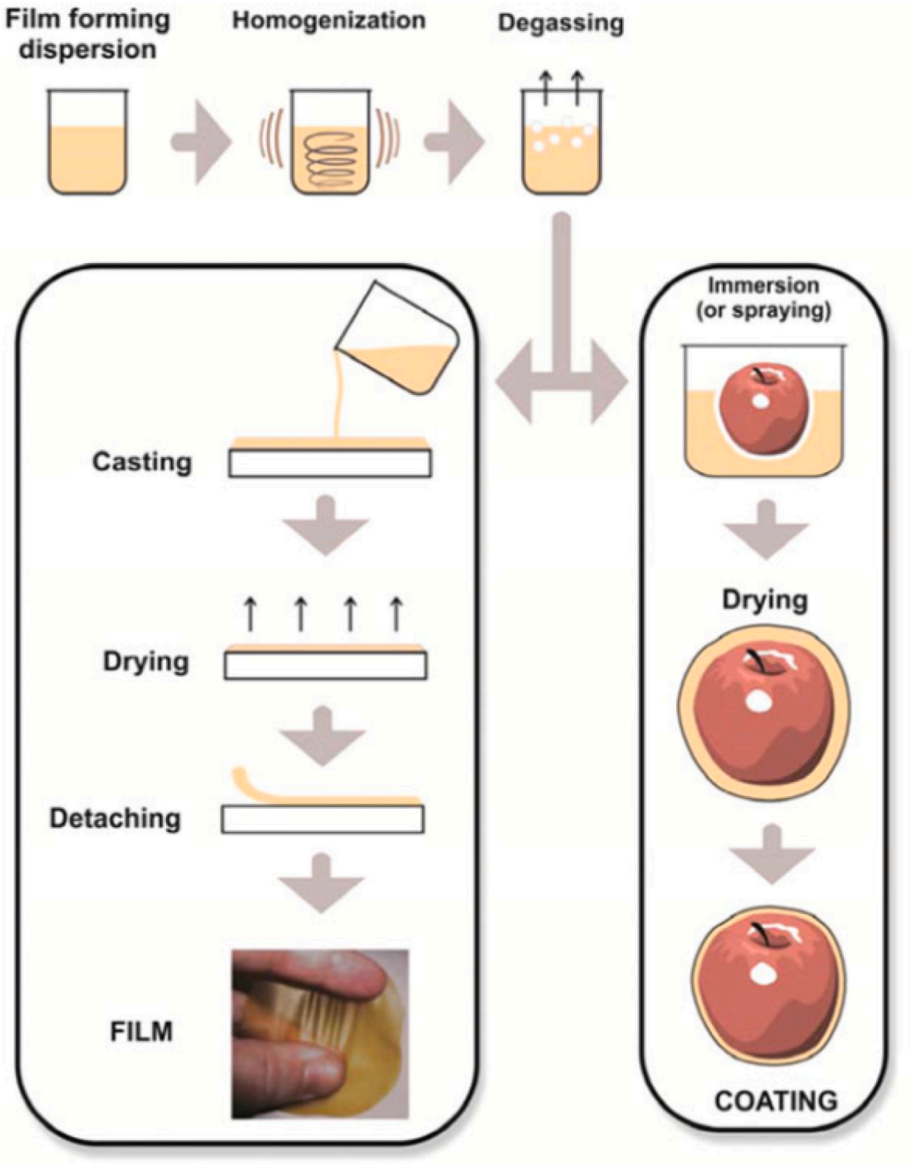

Fig. 1. Difference between film and coating production. Reproduced with permission from Otoni et al., 2017.

ineffective; however, they provide good barriers to oxygen, flavours, and oils. Amongst the most commonly used polysaccharides are alginate, cellulose, starch, chitosan, pectin, and polysaccharide gums, which are polymers usually derived from plants, microbial sources, insects, and crustaceans (Kocira et al., 2021; Kong et al., 2022).

The proteinaceous coating-forming materials can be derived from plant or animal sources. Animal proteins can be gelatin, casein, and whey, and the most explored vegetable proteins are corn zein, wheat gluten, and soy protein (Henriques et al., 2016; Mihalca et al., 2021). These coatings have numerous advantages ranging from reduced moisture loss, restricted oxygen uptake and reduced lipid migration, as well as good mechanical properties (i.e., elastic modulus, tensile strength, puncture resistance) and providing physical protection against the migration of contaminants into food (Suput et al., 2015). However, most proteins available are susceptible to moisture, presenting very high permeability to water vapour and high solubility in water, which can limit their application (Saklani et al., 2019).

Finally, the primary function of lipid-based coatings is to block moisture transport due to their low polarity. Due to their chemical characteristics, the structures formed by lipids are fragile and not very cohesive, which is why they should be associated with other coating-forming agents, such as proteins and polysaccharides, to improve their properties (Aguirre et al., 2016). In contrast, the main advantages of employing lipids in coatings are their ability to provide a good moisture barrier and improve the surface appearance of fresh foods in terms of sheen and gloss. However, lipid-based coatings can have an oily surface and undesirable organoleptic properties, such as a waxy taste and lipid rancidity. Hydrophobic substances potentially used for lipid-based edible coatings include neutral lipids, fatty acids, waxes, and resins (Debeaufort & Voilley, 2009; Milani & Nemati, 2022).

Plasticizers and surfactants can also be added to these materials to improve the final product's characteristics, such as flexibility, elasticity, barrier, and optical properties (Parreidt et al., 2018; Rodríguez et al., 2006). Films or coatings can also incorporate active compounds with functional properties that can improve food quality and extend shelf life (antioxidants and anti-browning agents), improve sensory properties, delay food decomposition resulting from the presence of bacteria (antibacterial agents) and viruses (antiviral compounds), and provide additional health benefits to consumers (nutraceuticals, such as vitamins, minerals, prebiotics and probiotics) (Hamed et al., 2022; Pedreiro

et al., 2021).

2.2. Strategies for the incorporation of active compounds

The incorporation of functional compounds into edible films and coatings is one of the most attractive features of these edible structures. It can be achieved either by a simple dispersion of a mixture of active compounds in a film-forming solution or by prior encapsulation of the active compound followed by mixing it into this solution (Nogueira et al., 2020). Encapsulation of the functional ingredient in a suitable carrier provides a planned delivery and controlled release. The use of micro and nanoencapsulation systems in edible films and coatings can help improve the quality and extend the shelf life of food products (Fang & Bhandari, 2010).

Micro and nanoencapsulation are techniques in which solid, liquid and gaseous substances, compounds, or agents are coated with an encapsulating agent, resulting in particles of micro and nanometric dimensions (Guía-García et al., 2022). The most commonly used micro and nanoencapsulation systems for the incorporation of active compounds in edible films and coatings are nanoemulsions, nanoparticles and nanocapsules (Nogueira et al., 2020). These nanoencapsulation methods allow maintaining the stability of bioactive compounds in different environmental conditions, increasing the solubility of lipophilic ingredients, and controlling the release of compounds, providing new solutions for food products. Encapsulation focuses primarily on lipophilic compounds with low water solubility and stability (Assadpour & Mahdi Jafari, 2019). In fact, some studies report the production of nanoemulsions with essential oils to increase their functionality (Donsì et al., 2011; Liang et al., 2012; Salvia-Trujillo et al., 2014; Ziani et al., 2011). Moreover, previous research has demonstrated that nanoparticles and nanocapsules can enhance the antimicrobial activity of active compounds. For instance, adding titanium dioxide (TiO_2) nanoparticles and red apple pomace to a chitosan coating enhanced its antimicrobial activity (Lan et al., 2021). In the same way, the addition of TiO_2 nanoparticles and rosemary oil to a cellulose/wheat protein matrix greatly reduced microbial growth, lipid oxidation, and lipolysis, while also extended the shelf life of lamb meat from 6 to 15 days when stored in the refrigerator (Alizadeh-Sani et al., 2020).

3. Food grade and natural antiviral compounds

The incorporation of active and functional compounds in edible films and coatings is an interesting strategy that guarantees food safety, extends the shelf life of food, and inhibits the growth of unwanted microorganisms and pathogens. Currently, several studies have already proven the antimicrobial potential of various natural compounds such as organic acids, enzymes, plant-derived compounds and their byproducts, like essential oils, among others (Saklani et al., 2019); however, the information on antiviral compounds is still very limited; thus further research on this topic is needed. Some natural compounds with antiviral activity are listed in Table 1.

NoV, a human enteric pathogen, is an RNA virus from the Caliciviridae family that causes acute gastroenteritis and appears mainly in seafood and minimally processed and ready-to-eat foods. Nowadays, human noroviruses are considered the number one cause of foodborne illness and the fourth cause of foodborne deaths globally (Robilotti et al., 2015). Several studies showed that oregano oil and its primary active component, carvacrol, were effective in inactivating murine norovirus (MNV), the human norovirus surrogate. Gilling et al. (2014) proved that the oil and the purified active component reduced the MNV infectivity, especially carvacrol, which was effective at concentrations less than or equal to 0.5% (w/v). They observed that long exposure to carvacrol reduced the cell culture infectivity. This fact suggests that the antimicrobial compound causes some degradation in the viral capsid; however, the virus remains infectious after some time of exposure. Therefore, the total loss of virus infectivity is due to a second mechanism of action

Table 1
Antiviral natural compounds associated with the respective target virus.

Compound	Target virus	Mechanism of action	Reference
Oregano oil and carvacrol	MNV	Conformational changes in viral capsid (loss of integrity) or blocking of epitopes necessary for virus adsorption to host cells	Gilling et al. (2014)
Persimmon extract	NoV, MS2 bacteriophage and MNV	Astringent properties of the main active component - persimmon tannin	(Kamimoto et al., 2014) and (Méndez et al., 2021)
Houttuynia cordata	MNV	Deformation and inflation of virus particles and inhibition of virus entry into target cells.	Cheng et al. (2019)
GSE	MNV	Denaturation of the viral capsid protein	Li, Baert, et al. (2012)
Curcumin	HBV	Inhibition of gene expression and replication by down-regulation of the PGC-1α protein	Rechtman et al. (2010)
	HCV	Inhibition of entry of all HCV genotypes into hepatoma cells and primary human hepatocytes through alteration of the lipid bilayer properties of membranes that disrupt liposomes	Chen et al. (2013)
	HIV	Direct targeting and inhibiting of viral proteins such as proteases, integrases and the *trans*-activator of transcription (Tat) protein	(Vajragupta et al., 2005); (Mazumder et al., 1995) and (Ensoli et al., 1990)
	HSV	Inhibition of gene expression	Kutluay et al. (2008)
	SARS-CoV-2	Inhibition of virus entry into host cells as blocking the virus replicate in human cells	Chainani-wu (2003)
Cucumis melo pectin	HSV	Viral envelope alterations, blocking of viral attachment to cell surfaces, virion inactivation, and inhibition of HSV replication	Agostinho et al. (2021)
Isochlorogenic acid A	HBV	Blocking the translation step	Hao et al. (2012)

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Table 1 (*continued*)

Compound	Target virus	Mechanism of action	Reference
		of HBV replication	
DHCH	HBV	Reduction of extracellular and intracellular DNA levels and reduction of covalently closed circular DNA of HBV	Zeng et al. (2013)
Viscum coloratum (Kom.) *Nakai*	HBV	Inhibition of virus DNA replication and secretion of HBV antigens	Chai et al. (2019)
Radix isatidi	HBV	Activation of JAK/STat signalling pathway and induction of the anti-HBV protein expression	Wang et al. (2020)
Flammulina velutipes	HBV	Reducing the expression of hepatitis B surface antigen, hepatitis B e-antigen, and DNA replication	Zhang et al. (2018)
Heparosan-derived heparan sulfate and heparin-like compounds	HIV	Inhibition of HIV by electrostatic interactions with basic amino acid residues of Tat	Li, Baert, et al. (2012)
CHLA and PUG	HCV	Inhibition of HCV entry and attachment into the host cell by targeting viral glycoproteins that interact with cell surface heparin sulfate	Lin et al. (2013)
EGCG	HCV	Inhibition of the entry of HCV of all genotypes into hepatoma cell lines and primary human hepatocytes, preventing the virus from binding to target cells	Ciesek et al. (2011)
	HIV	Inhibition of replication and reverse transcription, destruction of virions by envelope binding, poor regulation of the CD4 receptor, and interference with gp120 binding	(Nakane & Ono, 1989); (Fassina et al., 2012) and (Kawai et al., 2003)
	HSV	Direct effect on virion inactivation and target cell incubation, leading to a binding of the compound to envelop proteins	Isaacs et al. (2008)
	HBV	Reduction of the expression of HBV-specific antigens, extracellular DNA levels, intracellular replicative intermediates, and covalently closed circular DNA	Xu et al. (2008)
GRFT	HCV	Inhibition of te cell-to-cell HCV transmission and interaction between viral capsid proteins and the viral receptor CD81	Meuleman et al. (2011)
Tannic acid	HCV	Blocking of virus entry and adsorption to the host cells by inhibiting cell-to-cell-transmission	(Tsao, 2010) and (Bourvellec & Renard, 2012)
CHLA and PUG	HSV	Inhibition of HSV-1 entry by inactivating viral particles, preventing binding and cell-to-cell spread	Lin et al. (2011)
Glucoevatromonoside	HSV	Inhibition of viral protein synthesis, blocking the release of the virus, reduction of the viral cell-to-cell spread, and changes in the cellular electrochemical gradient	Bertol et al. (2011)
Inga spp. pectin	HSV	Inhibition of replication, blocking the virus entry, or prevention of the conformational changes to bind to the cell membrane	Godoi et al. (2019)
Caesalpinia ferrea	HSV	Inhibition of replication, blocking the virus entry, or prevention of the conformational changes to bind to the cell membrane	Lopes et al. (2013)
Euchema gelatinae	HSV	Inhibition of replication, blocking the virus entry, or prevention of	Jin et al. (2015)

(*continued on next page*)

Table 1 (*continued*)

Compound	Target virus	Mechanism of action	Reference
		the conformational changes to bind to the cell membrane	
Basella rubra	HSV	Interference of the virus absorption into host cells	Dong et al. (2011)
Sugiol	SARS-CoV-2	Inhibition of virus replication and SARS-CoV3C protease (3CLpro)	Zhang et al. (2020)
Lignan	SARS-CoV-2	Inhibition of virus replication and SARS-CoV3C protease (3CLpro)	Zhang et al. (2020)
Betulinic acid	SARS-CoV-2	Inhibition of virus replication and SARS-CoV3C protease (3CLpro)	Zhang et al. (2020)
Fortunes bossfern rhizome	SARS-CoV-2	Inhibition of virus replication and SARS-CoV3C protease (3CLpro), and entry	Zhang et al. (2020)
Lepidii semen descurainiae semen	SARS-CoV-2	Inhibition of SARS-CoV3C protease (3CLpro)	Zhang et al. (2020)
Resveratrol and emodina	SARS-CoV-2	Inhibition of binding of the SARS-CoV-2 protease spike to the ACE2 receptor, blocking the virus entry into host cells and inhibition of viral RNA replication	Paraiso et al. (2020)
Ocimum sanctum and *Azadirachta indica*	SARS-CoV-2	Inhibition of attachment and replication of the SARS-CoV-2 virus by binding to the spike glycoprotein, RNA polymerase, and/or its protease	Kumar (2020)
Melia azedarach L., *Camellia sinensis (L.) Kuntze, Laurus nobilis* L., *Salvia officinalis* L., and *Thuja orientalis* L.	SARS-CoV-2	Inhibition of replication of the SARS-CoV-2 virus and RNA polymerase or RNA-dependent proteases.	Llivisaca-contreras et al. (2021)
Glycyrrhiza glabra L. (licorice)	SARS-CoV-2	Inhibition of SARS-CoV virus replication by interfering with the ACE-2 receptor	Ali et al. (2021)
Allium sativum L.	SARS-CoV-2	Interaction with the ACE-2 receptor	Ali et al. (2021)
Alnus japonica (Thunb.) (Diarylheptanoids)	SARS-CoV-2	Inhibition of papain-like protease, an enzyme required for SARS-CoV replication	Ali et al. (2021)
Houttuynia cordata Thunb.	SARS-CoV-2	Inhibition of SARS-CoV3C protease (3CLpro) and RNA-dependent RNA polymerase (RdRp)	Ali et al. (2021)
Lactoferrin	SARS-CoV-2	Inhibition of SARS-CoV-2 replication in a dose-dependent manner by blocking cell surface HSPG (Heparan sulfate proteoglycans) receptors at the viral binding stage	(Carvalho et al., 2020) and (Hu et al., 2021)

Note: GSE, grape seed extract; DHCH, dehydrocheilanthifoline; EGCG, epigallocatechin-3-gallate; CHLA, chebulagic acid; PUG, punicalagin; GRFT, griffithsin; MNV, murine norovirus; NoV, Norovirus; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HSV, herpes simplex virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus.

(Cliver, 2009). The authors postulated two potential explanations for this secondary mechanism: a) the antimicrobial compound induces a simple conformational change in the capsid, compromising its structural integrity and subsequently impeding the virus-host cell interactions, or b) the antimicrobial compound blocks the epitopes required for the viral adsorption process.

In addition, Kamimoto et al. (2014) explored the antiviral effect of persimmon extract (PE) on human NoV, NoV GII.4, and its surrogate MS2 bacteriophages, as well as the connection between the quantity of persimmon tannin (PT), a particular component of PE, to find the PE's active compound. They observed that using solutions with 0.11 mg/mL of PT reduced the infectivity of MS2 by more than 2.5 log PFU/mL (log plaque-forming unit/mL) and the noroviral genome density by more than 70%. The results showed that the main active element in PE was PT and promoted the use of PE as a non-toxic antiseptic. PT's antiviral action and astringent properties are probably connected to the decrease of the noroviral genome and the inactivation of the virus. Other researchers have also observed that the presence of PT is correlated with the antiviral activity of PE. For instance, Méndez et al. (2021) discovered that 5 mg/mL of PE significantly ($p < 0.05$) reduced MNV titers below detection limits. Interestingly, they also found that a higher polyphenol content might be associated with a stronger antiviral activity, as tannin concentrations greater than 0.11 mg/mL were observed to be required to lower the infectivity of MNV by more than 2.5 log PFU/mL. It has also been proposed that *Houttuynia cordata* polysaccharide (HP) extract may be a promising antiviral compound to treat NoV illnesses. In this case, Cheng et al. (2019) investigated how this substance affected MNV infectivity and discovered that when MNV was treated with 500 μg/mL HP, MNV infectivity dropped to an undetectable level. The distortion and ballooning of viral particles brought on by the chemical are thought to be the action mechanism that prevents virus entry into target cells.

Plant extracts are a known natural source with antimicrobial properties. Grape seed extract (GSE) is rich in proanthocyanidins (a class of phenolic compounds that take the form of oligomers or polymers of polyhydroxy flavan-2-in units, such as (+)-catechin and (-)-epicatechin)

that have benefits to human health like neuroprotective, cardioprotective, anti-ulcer and anticarcinogenic properties (Negi, 2012). Li, Baert, et al. (2012) proved that a 0.2 mg/mL GSE treatment caused a >3 log PFU/mL reduction of MNV. The effect of GSE in the NoV is due to the denaturation and damage of the viral capsid protein; for instance, 0.2 mg/mL of GSE causes the disappearance of the spherical structure of virus-like particles (VLPs) of human NoVs. This, consequently, leads to a reduction in the ability of the virus to bind to the capsid and in its infectivity. Moreover, it is important to notice that the capsid viral denaturation may also affect other proteins; therefore, when using GSE as a disinfectant for food or water contact surfaces in the food industry, potential interferences from other substances must be taken into account.

Hepatitis B virus (HBV), a member of the *Hepadnaviridae* family, causes hepatitis B as well as severe damage and even liver cancer in humans. The infection can be spread by body fluids or by exposure to blood that contains the vírus (Liang, 2009). Plants extracts and some polysaccharides have been used as antiviral agents against HBV. For example, curcumin, a well-known natural phenol derived from turmeric (*Curcuma longa* L.), has showed antiviral activity against HBV due to the inhibition of HBV gene expression and replication by down-regulation of PGC-1α, a protein co-activating HBV transcription (Rechtman et al., 2010). Another example of a natural compound with efficacy against HBV is isochlorogenic acid A from *Laggera alata*, which blocks the translation step of HBV replication (Hao et al., 2012). Also, *in vitro* tests have determined that dehydrocheilanthifoline (DHCH), an alkaloid isolated from *Corydalis saxicola*, may be a promising candidate in the therapy of HBV infection as it allows a reduction in extracellular and intracellular DNA levels, as well as a reduction of covalently closed circular DNA (cccDNA) of HBV (Zeng et al., 2013). Similarly, Xu et al. (2008) proved that epigallocatechin-3-gallate (EGCG), a constituent of green tea (*Camellia sinensis*), reduced the expression of HBV-specific antigens, extracellular DNA levels, intracellular replicative intermediates, and covalently closed circular DNA (cccDNA).

Among the polysaccharides, the ones obtained from the leaves of *Viscum coloratum* (Kom.) *Nakai* (VCP) exhibited antiviral efficacy against HBV by suppressing HBV antigen release and viral DNA replication in a dose-dependent manner (Chai et al., 2019). Polysaccharides extracted from *Radix Isatidis* (*Isatis indigotica* Fortune), a traditional Chinese herbal medicine, were also reported to effectively suppress HBV *in vitro* via activation of the JAK/STat upregulating and stimulation of the anti-HBV protein production, according to Wang et al. (2020). In a different study, also on the antiviral effectiveness of polysaccharides, Zhang et al. (2018) isolated a new water-soluble polysaccharide FVP1 from *Flammulina velutipes*, a species of agaric (gilled mushroom) that displayed antiviral activity by lowering the expression of hepatitis B surface antigen (HBsAg), hepatitis B e-antigen (HBeAg), and HBV DNA replication.

Like hepatitis B, hepatitis C is an inflammation of the liver, but in this case caused by the hepatitis C virus (HCV), a member of the *Flaviviridae* family. This virus can cause acute and chronic hepatitis, including liver cirrhosis and cancer, and is transmitted through exposure to infected blood. There is currently no effective vaccine against hepatitis C, so more research into natural antiviral compounds is needed (Serag, 2012). Over the past few decades, extensive studies have been conducted to identify anti-HCV agents from natural products and herbal medicines. As examples, chebulagic acid (CHLA) and punicalagin (PUG), polyphenolic secondary metabolites found in *Terminalia chebula* Retz., a medicinal plant, have been reported for their anti-HCV activities. These hydrolyzable tannins inhibit the entry of HCV and attachment into the host cell by targeting viral glycoproteins that interact with cell surface heparin sulfate (Lin et al., 2013). Other natural compounds, including EGCG, griffithsin (GRFT), curcumin, and tannic acid, have been shown to prevent HCV infection. EGCG inhibits the entry of HCV of all genotypes into hepatoma cell lines and primary human hepatocytes, preventing the virus from binding to target cells (Ciesek et al., 2011). In turn, GRFT is a protein isolated from a red alga *Griffithsia. In vitro* tests has shown to interfere with cell-to-cell HCV transmission and the interaction between viral capsid proteins and the viral receptor CD81, thus preventing infection (Meuleman et al., 2011). Likewise, curcumin was also found to be effective against HCV, with its mechanism of action inhibiting the entry of all HCV genotypes into hepatoma cells and primary human hepatocytes. This inhibition is justified by the effect of curcumin that alters the lipid bilayer properties of membranes that disrupt liposomes (Chen et al., 2013). Finally, tannic acid is a plant-derived polyphenol of gallic acid and glucose molecules that can inhibit HCV infection at low concentrations (<25 μM). Tannic acid belongs to a group of phenolic compounds called tannins that are present in food grains/cereals, fruits, herbs, vegetables, and beverages such as tea, red wine, and coffee. The ability of tannic acid to inhibit HCV is due to the interference of viral adsorption to the host cell membrane. This compound prevents the entry of the virus into the cells by forming macromolecular complexes on the cell surface (Bourvellec & Renard, 2012; Tsao, 2010) and inhibits cell-to-cell transmission but does not interfere with intracellular HCV replication. In addition, other studies have shown that tannic acid can still inhibit Influenza A and human papillomavirus at relatively low concentrations (Florin & Muller, 2014). Interestingly, tannic acid has a structure similar to EGCG, a green tea polyphenol tannin, which has previously been proven to also have antiviral activity against HVC by blocking virus entry and binding to cells (Ciesek et al., 2011; Hober et al., 2011).

Another virus of great concern is the human immunodeficiency virus (HIV) which is a member of the *Lentivirus* genus and part of the *Retroviridae* family. This virus targets and affects the human immune system, increasing the risk and impact of other diseases and infections. If not treated properly, it can progress to a more advanced state called AIDS (acquired immunodeficiency syndrome). HIV is transmitted from the body fluids of infected people as an encapsulated RNA virus that, upon entering the target cell, converts the RNA genome into a double-chain DNA (Sierra et al., 2005). Currently, there is no effective cure for HIV infection; however, several exhaustive studies have already published a list of potential natural compounds with antiviral capacity. Some researchers have shown that EGCG interferes at various levels of the HIV-1 life cycle, from the inhibition of replication in human peripheral blood mononuclear cells (*in vitro* tests) to the inhibition of reverse transcription (Nakane & Ono, 1989) to the destruction of virions by envelope binding (Fassina et al., 2012) and poor regulation of the CD4 receptor and interference with gp120 binding (Kawai et al., 2003). In this virus, curcumin also has an inhibitory effect confirmed by directly targeting and inhibiting viral proteins such as proteases (Vajragupta et al., 2005), integrases (Mazumder et al., 1995) and the *trans*-activator of transcription (Tat) protein, a viral transcription regulator (Ensoli et al., 1990). Furthermore, according to Li, Baert, et al. (2012), heparin acid sulfate groups, a polyanionic sulfated polysaccharide, or heparin-like substances are thought to reduce HIV infectivity by interacting with basic amino acid residues of Tat, a regulatory protein produced early after infection, and the primary mechanism of action of these substances is due to electrostatic interaction.

Herpes simplex type 1 (HSV-1) and type 2 (HSV-2) is a viral disease caused by the HSV virus belonging to the *Herpesviridae* family. This virus causes lesions at the level of mucous membranes in the human body (oral/perioral – HSV-1 – or genital – HSV-2) whose infection lasts for life, and there is currently no cure for this disease. Studies raise some natural compounds that could be used as potential anti-HSV infections (Morfin & Thouvenot, 2003). Experiments revealed that hydrolyzable CHLA tannins and PUG can inhibit HSV-1 entry by inactivating viral particles, preventing the binding, cell-to-cell spread, and further secondary infections. More specifically, CHLA and PUG prevent the interaction between cell surface glycosaminoglycans and HSV-1 glycoproteins (Lin et al., 2011).

Furthermore, similar to the effect of EGCG on HCV and HIV, this compound inhibits HSV by directly affecting virion inactivation and target cell incubation before infection, leading to the binding of the

compound to envelope proteins (Isaacs et al., 2008). Besides this, glucoevatromonoside, a cardenolide isolated from a Brazilian cultivar of *Digitalis lanata*, also demonstrated an antiviral activity against HSV. The inhibitory effect involves inhibiting viral protein synthesis, blocking the release of the virus and reducing the viral cell-to-cell spread. Studies also suggest that the compound alters the cellular electrochemical gradient, thus preventing the propagation of HSV-1 and HSV-2 (Bertol et al., 2011). Curcumin, another natural compound, was additionally proven to decrease the expression of HSV-1 viral immediate-early gene expression and, when applied as a pre-treatment in human genital epithelial cells, allows a reduction in HSV-2 release (Kutluay et al., 2008). Recently, it has been discovered that the pectin from *Cucumis melo* has shown potential as an alternative therapeutic agent for treating HSV-1 infection (Agostinho et al., 2021).

The many biological characteristics of polysaccharides obtained from natural sources with antiviral effects are being investigated to a greater extent. The work performed by Godoi et al. (2019) on the impact of pectin derived from the fruit tree *Inga* spp. against HSV-1 in HEp-2 cells (human laryngeal carcinoma cells) serves as an illustration of this. This work showed that pectin isolated from *Inga* spp. had a 94% suppression of HSV-1 virality at an inhibitory dose of 179 μg/mL. The theory behind the action is that replication was inhibited at the point of virus entrance or binding, most likely by blocking the virus or the conformational changes necessary to adhere to the cell surface. Moreover, the studies of Lopes et al. (2013), which assessed the impact of a sulfated polysaccharide isolated from *Caesalpinia ferrea* tree on HSV-1 replication, and the studies of Jin et al. (2015), which evaluated the activity of polysaccharides from *Euchema gelatinae* against HSV-1, support the greater viral inhibition observed at the early stages of replication in the first study. Additionally, Dong et al. (2011) were the first to describe the antiviral activity of polysaccharides derived from the climbing plant *Basella rubra* concerning HSV-2. Both pectin-like polysaccharides extracted from *B. rubra*, BRP-2 and BRP-4, showed potential anti-HSV2 properties *in vitro* by interfering with virus absorption into host cells. They also found that the pectin-like polysaccharide BRP-4 demonstrated a great therapeutic efficiency in mice infected with HSV-2, as determined by the degree of herpetic lesions, the survival rate of mice, and viral shedding.

Focusing on COVID-19 caused by SARS-CoV-2, the virus with the greatest current focus, several authors have tried to discover natural compounds effective against it from experiences with SARS-CoV and MERS, based on a series of criteria (absorption, distribution, metabolism, protein structure, etc.). Zhang et al. (2020) identified 13 natural compounds and their mechanisms of action. Of these compounds, sugiol (a constituent of the class of organic compounds known as diterpenoids), lignan (a polyphenol found in licorice), and betulinic acid (obtained from *Peucedani radix*, licorice, *Eriobotryae folium*, *Forsythiae Fructus*, *Hedysarum multijugum maxim.*, *Cortex mori* and *Tamaricis cacumen*) were able to inhibit the replication of the virus and the 3CLpro (the main viral protease). Other plants like *Fortunes bossfern rhizome* (producer of harmonil) and *Lepidii semen descurainiae semen* (producer of dihomo-γ-linolenic acid), for example, can also inhibit SARS-CoV-2 by preventing replication, 3CLpro and entry of the virus in the first case, and targeting 3CLpro in the second.

Some polyphenolic compounds have also shown an antiviral activity against SARS-CoV-2. The antioxidant activity of plants is due to the presence of polyphenolic chemicals in plants. For instance, Paraiso et al. (2020) studied the effects of the polyphenols resveratrol and emodin at various phases of the SARS-CoV-2 life cycle. They concluded that these substances could block the binding of the SARS-CoV-2 protease spike to the ACE-2 receptor, hence preventing viral entrance into host cells, which subsequently prevents the replication of viral proteins and RNA Another study showed that curcumin had antiviral properties, particularly during the initial stages of SARS-CoV-2 infection, by preventing the virus from entering host cells and inhibiting the virus' capacity to multiply in human cells (Chainani-wu, 2003). In a subsequent 2020 research, Kumar examined the antiviral effectiveness of rosmarinic, oleanolic, ursolic acids, and methyleugenol acid derived from *Ocimum sanctum* as well as the chemicals azadirachtin, nimbin, epoxyazadiradione, and gedunin from *Azadirachta indica*. The findings showed that via binding to the spike glycoprotein, RNA polymerase, and/or its protease, all-natural compounds under investigation were efficient in blocking attachment and replication of the SARS-CoV-2 virus (Kumar, 2020). Additionally, Llivisaca-Contreras et al. (2021) reported phenolic compounds from *Melia azedarach* L., *Camellia sinensis (L.) Kuntze*, and essential oil compounds from *Laurus nobilis* L., *Salvia officinalis* L., and *Thuja orientalis* L. displayed an antiviral action against SARS-CoV-2 replication owing to the inhibition of RNA polymerase or RNA-dependent proteases.

Other noteworthy substances were found by Ali et al. (2021). Glycyrrhizin, a saponin-like substance found in *Glycyrrhiza glabra* L. (licorice), prevents SARS-CoV virus replication in its beginning phases by interfering with the ACE-2 receptor. Comparable to this, other organo-sulfur compounds that interact with the ACE-2 receptor have been found in the essential oil of common garlic, *Allium sativum*. Diarylheptanoids, isolated from the alder *Alnus japonica*, prevents papain-like protease from acting as a required enzyme for the replication of SARS-CoV. Finally, the chameleon plant, *Houttuynia cordata*, has an extract that inhibits the SARS-CoV3C protease (3CLpro) and RNA-dependent RNA polymerase (RdRp). Additionally, several studies have documented lactoferrin's ability to suppress SARS-CoV-2. Furthermore, Carvalho et al. (2020) reported that bovine lactoferrin significantly reduced SARS-CoV-2 load in human adenocarcinoma basal alveolar epithelial cells and African green monkey kidney epithelial cells by about 84.6% and 68.6%, respectively, at a lactoferrin concentration of 1 mg/mL. Afterwards, Hu et al. (2021) demonstrated that, regardless of the cell type of lactoferrin, both bovine and human lactoferrin suppressed SARS-CoV-2 replication in a variety of cell lines by blocking the cell surface HSPG (heparan sulfate proteoglycans) receptors during the viral attachment process.

There is ample evidence that a diversity of food grade and natural compounds present antiviral activity. Although at an early research stage, the demonstrated potential and ongoing efforts to discover new active compounds establish the ground for applying natural antiviral compounds in food systems.

4. Antiviral edible films and coatings

The development of edible films with embedded antimicrobials can be an effective measure in controlling the appearance of pathogens in food to control food microbiota and enhance food safety and quality. There are already several publications on films with antibacterial properties; however, further research is needed to investigate the antiviral efficacy of films and coatings in foods.

Some *in vitro* studies showed the capacity of edible films to act as antiviral agents. Amankwaah et al. (2020) evaluated the efficacy of chitosan-based films enriched with green tea extract (GTE) against MNV. GTE is a derivative of the cultivated evergreen tea plant (*Camellia sinensis* L.), of the family *Theaceae,* with known inhibitory properties against a wide range of pathogens. Results showed that films of chitosan (2%, w/w) dissolved in a 1% acetic acid solution containing 5 and 10% (w/v) of GTE in glycerol after 24 h of incubation allowed a reduction ($p < 0.05$) of MNV of 1.6 and 4.5 log PFU/mL, respectively. Thus, it was concluded that this film formulation is effective against MNV, possibly due to phenolic compounds such as catechin and polyphenols present in GTE. In 2018, Fabra et al. reported the antiviral capacity of alginate films containing phenolic extracts such as GTE and GSE against MNV and HAV. The matrix of the alginate-based films consisted of 1 g of alginic acid sodium salt dissolved in 100 mL of water, to which GTE, GSE, 0.25 g of oleic acid, 0.25 g of soybean, 0.15 g of edible fatty acids, and 0.2 g of Tween 80 were added. Films containing GTE and GSE at 0.75 g extract/g alginate showed a reduction of MNV titers of 1.92 and

1.67 log $TCID_{50}$/mL (Median Tissue Culture Infectious Dose), respectively, and a reduction of 1.92 and 1.50 log $TCID_{50}$/mL for HAV titers, respectively. For films with GTE and GSE at a concentration of 0.5 g extract/g alginate, there was a reduction in MNV titers of 2 and 0.96 log $TCID_{50}$/mL, respectively, and a log reduction of HAV titers of 1.25 and 1.38 log $TCID_{50}$/mL, respectively. Results showed that edible alginate films containing phenolic extracts exhibited antioxidant and antiviral activity against MNV and HAV, in which the GTE tested showed better antiviral and antioxidant properties than GSE. More recently, Cerqueira et al. (2023) have shown that edible films based on sodium alginate and sucrose ester incorporated with different active compounds (gallic acid, geraniol and GTE) have *in vitro* anti-SARS-CoV-2 activity. Results demonstrated that geraniol and GTE present high antiviral activity at low concentrations (0.313%, w/v) and maintain their activity during four weeks of storage. The different *in vitro* studies have shown that green tea and grape seeds extracts can be effective against viruses at concentrations as low as 0.313%, but high amounts can be required for more effective antiviral capacity. It is important to highlight that the combination of the different film forming materials can have an impact in the results obtained, since materials such as surfactants (e.g., sucrose ester) or polysaccharides (e.g., sodium alginate) can present antiviral activity.

The use of edible coating on food surfaces also requires that the antiviral activity is evaluated directly on food surfaces. In that regard, some studies showed the antiviral activity of the edible coatings used on red fruit surfaces. For example, Falcó et al. (2018) studied the infectivity of MNV and HAV in strawberries and raspberries coated with alginate-oleic acid incorporated with GTE (0.7%, w/w). They found that pH affects the antiviral efficacy of GTE-containing films, with the inhibition of MNV and HAV at pH 7 being lower than that at pH 5.5, and activity being higher on MNV than HAV. Tests were performed at different incubation temperatures. At 37 °C significant reductions ($p < 0.05$) of MNV were observed, namely reductions of 3.42 log $TCID_{50}$/mL at pH 7 and 5.76 log $TCID_{50}$/mL at pH 5.5. Also, incubation at 37 °C caused a reduction in HAV titers of 1.37 log $TCID_{50}$/mL at pH 5.5. On the other hand, at pH 7 there was practically no effect against HAV and incubation at 10 °C did not affect both viruses since they resist low temperatures.

In another work, Falcó et al. (2019) proved the antiviral effect of pure carrageenans derived from its ability to neutralize the positive charges on the surface of cells with the negative charges of the sulfate groups, which interfere with the uptake of viruses into cells. They assessed the antiviral effect of carrageenans (κ−, ι− and λ−) and GTE incorporated (0.7%, w/w) in film-forming dispersions (FFD) in blueberries and raspberries, at room temperature (25 °C) and refrigerated temperature (10 °C), against MNV and HAV. The effect of carrageenans was investigated by dipping blueberries and raspberries, previously inoculated with the viruses, into carrageenan-based FFD with and without GTE, and stored at 10 °C (overnight – ON and 4 days) and 25 °C (ON). It was found that the antiviral activity was higher for carriers with higher viscosity (κ− carrageenan) due to a more cohesive matrix. This cohesive matrix results from the gelling ability of the carrageenan that prevents the sorbed water from diffusing easily through the biopolymer matrices. In blueberries, a coating treatment at 25 °C with ON incubation provided a reduction of MNV to levels below the detection limits for κ- and ι-carrageenan films containing GTE, and for λ-carrageenan coatings containing GTE was obtained a reduction of 3.54 log $TCID_{50}$/mL. Under the same conditions, κ- and ι-carrageenan film coatings without GTE allowed a 2.5 log reduction of MNV. On the other hand, at 25 °C, in raspberries, the reduction of MNV was smaller, only 2.25 and 2.79 log for ι- and λ-carrageenan films with GTE, respectively. Additionally, in blueberries, at 10 °C ON and 4 days of storage, it were obtained reductions of 2.38 and 3.13 log $TCID_{50}$/mL of MNV, while in raspberries coated with λ-carrageenan coatings containing GTE, for both storage periods, the infectivity limits were lower than the detection levels. Overall, MNV infectivity levels were higher in blueberries than in raspberries. This effect is due to the lower pH of the raspberries surface, which causes a synergistic effect of pH and GTE and leads to values below the detection limits. Regarding HAV, there was no significant reduction in coated berries. In blueberries coated with κ-, ι- and λ-carrageenan coatings containing GTE, after ON incubation at 25 °C, the reduction was 2.88, 2.92, and 1.83 log $TCID_{50}$/mL, respectively, and, under these same conditions, there was only a reduction of 1.37 log $TCID_{50}$/mL HAV titers in raspberries coated with λ-carrageenan containing GTE. At refrigerated temperatures of 10 °C, the reductions in HAV titers were higher in raspberries than blueberries, being of 1.79, 1.75, and 1.71 log $TCID_{50}$/mL after ON incubation for κ-, ι- and λ-carrageenan coatings containing GTE, respectively. Another interesting work conducted by Moreno et al. (2020) aimed to compare the antiviral potential of three different polysaccharide-based matrices (agar, alginate, and agar/alginate mixture) enriched with polyphenols extract from *Larrea nitida* (Ln). The matrices were composed of 1 g of agar, alginate, or a 1:1 mixture of the two dissolved in 100 mL of water, in which 50 mg of Ln extract was added after being dissolved in 0.3 g of glycerol. Tests were performed *in vitro* by inoculating fresh blueberries with MNV that were later stored at 10 °C and 25 °C. Blueberries coated only with agar (without incorporation of Ln extract) allowed a reduction in MNV titers of 2.54 log after ON and 2.88 log after 4 days of incubation at 10 °C, while at 25 °C the MNV infectivity reduced to levels below the limit of detection. It should be noted that these values are in line with those obtained by Falcó et al. (2019) for carrageenan. Furthermore, Moreno et al. (2020) found that the antiviral capacity of agar-based coatings incorporated with Ln extract did not improve at 25 °C ON, most likely due to the inherent antiviral properties of agar. On the contrary, the incorporation of Ln extract in agar/alginate mixture matrices allowed an increase in the antiviral capacity, with a reduction in MNV titers of 0.88 and 0.92 log PFU/mL after ON at 10 °C and 4 days at 10 °C treatments, respectively, and a reduction of 1.37 log PFU/mL after ON at 25 °C. Besides this, Ln extract proved to be non-toxic or genotoxic at 500 μg/mL and able to improve the water vapour barrier properties of edible films by reducing the water vapour permeability from 8.47 to 6.10, from 8.30 to 6.04, and from 7.83 to 6.06 g Pa^{-1} s^{-1} m^{-2} for agar, alginate and in agar/alginate-based films when incorporated with Ln extract, respectively. Thus, Ln can be considered a promising natural antiviral compound that can reduce and eliminate human enteric viruses (Moreno et al., 2020). Lastly, a study by Sharif et al. (2021) discussed allyl isothiocyanate (AITC), a volatile and aliphatic sulfur-containing compound with known antimicrobial activity, as a potential antiviral compound against MNV in blueberries. In this work, an edible film was developed based on Persian gum (PG), a polysaccharide that can attract and bind water, and on gelatin, in which AITC was added at different concentrations (0.1 and 0.5%). Blueberries were inoculated with MNV suspensions, then treated with aqueous suspensions of PG, gelatin, and AITC, and finally incubated. Greater MNV reductions were achieved at higher incubation temperatures (between 37, 25, and 10 °C) and after ON incubation at 37 °C there was a reduction of MNV titers by 3.25 log $TCID_{50}$/mL and 3.00 log $TCID_{50}$/mL for 0.1% and 0.5% AITC, respectively. At 25 °C there was only a significant reduction ($p < 0.05$) of MNV for the highest concentration of AITC, while at 10 °C the MNV titers were reduced by 1.58 and 2.79 log $TCID_{50}$/mL after ON incubation with 0.1 and 0.5% AITC, respectively. The fact that the antiviral activity was higher at 37 °C does not mean that this effect is dose-dependent at this temperature. Thus, it is possible to conclude that AITC can be considered a potential antiviral compound against MNV (Sharif et al., 2021). Results showed that edible coatings could be used as carriers of antiviral compounds, which inhibit viruses on food surfaces at concentrations below 1%. The coating materials and their amount on the food surface can have a huge impact on the final results, having the last to be normalized for a better understanding of the influence of the antiviral coating. In addition, it would be important to understand how the coating application by spray could influence the final antiviral properties since, until now, only the dipping method was

tested.

Antiviral compound have also been applied to coat surfaces such as stainless steel, glass and plastics, as well as disinfectants of fresh-cut vegetable surfaces. For example, in 2017, Randazzo et al. tested the inhibitory effect of GTE on MNV and HAV inactivation in surface disinfection. First, they determined the antiviral activity of 5 mg/mL GTE, after 2 h at 37 °C, which corresponded to 1.08 and 2.42 log $TCID_{50}$/mL reductions of HAV and MNV, respectively. Then stainless steel and glass discs were inoculated with both MNV and HAV, in clean and dirty conditions. On clean surfaces, it was found that there were significant reductions ($p < 0.05$) in MNV for stainless steel and glass. For both materials, the application of GTE at concentrations of 5 mg/mL and 10 mg/mL for 15 min, induced a reduction of less than 1 log of HAV titer, and when applying 10 mg/mL of GTE, for 30 min, it was obtained a complete inactivation of this virus. It was also concluded that GTE is more effective against HAV than MNV in dirty conditions, such as on unclean surfaces; a concentration of 10 mg/mL of GTE when applied for 30 min reduced 2.09 and 1.64 log of MNV titers on stainless steel and glass discs, respectively, while a 15 min contact time allowed a reduction of 0.42 and 0.33 log MNV titers (Randazzo et al., 2017). Moreover, this study also aimed to evaluate the antiviral efficacy of GTE on fresh-cut vegetable surfaces as a substitute for chlorinated solutions, considering that in some European countries, the use of chlorine was limited due to the formation of secondary chemicals. In this sense, lettuce and spinach were inoculated with 10 mg/mL of GTE for 30 min. With higher viral titer, this treatment showed a 2.59 log reduction of MNV in spinach, and a 0.79 and 1.37 log reduction of HAV in lettuce and spinach, respectively. Based on these results, GTE demonstrates potential as a natural, safe alternative to conventional disinfectants for mitigating enteric viral contamination on both foods and surfaces (Randazzo et al., 2017).

Given the potential for SARS-CoV-2 transmission through surfaces, active packaging materials for food may present a way to prevent it from spreading. In this regard, Mizielińska et al. (2021), developed an outer coating based on zinc oxide (ZnO) nanoparticles, carvacrol, and geraniol to determine whether it could be effective against viruses such as SARS-CoV-2. Initially, a solution of 0.082 g of ZnO nanoparticles solution was prepared in 100 mL of water, followed by the preparation of antiviral solutions ZG1 (99.9875 g of methyl-hydroxy-propyl-cellulose (MHPC) mixed with 0.0125 g of geraniol as an inner coating) and ZC1 (99.9875 g of MHPC mixed with 0.0125 g of carvacrol) to which 50 mL of the previously prepared nanoparticle solution was added. Polyethylene (PE) samples were then covered with these coatings. Researchers found that ZC1 and ZG1 coatings have a modest action against phage phi 6, which was used as a stand-surrogate for the coronavirus phage, as incubation of the phages with these coatings resulted in a reduction in bacteriophage titer (1 log) without eliminating any active phage particles. Furthermore, the study showed that ZG1 and ZC1 coatings, particularly geraniol and carvacrol, could be effective against SARS-CoV-2 transmitted by respiratory droplets. They were also considered good packaging materials to improve the quality and freshness of food products and to be used as external coatings to produce single-use food packaging and plastic bags for transporting food products. Also, these coatings would be effective due to ZnO nanoparticles' inherent protective qualities (Mizielińska et al., 2021). Also, regarding the antiviral activity of coatings towards SARS-CoV-2, Ordon et al. (2021) developed inner coatings based on supercritical CO_2 extracts of raspberry seed, pomegranate seed, and rosemary that proved to be more effective against phi6 bacteriophage particles (surrogate airborne viruses) than the previously described coatings. In this study, PE films were covered with the MHPC coating (12 g dissolved in 288 mL distilled water) containing: I) 2 g CO_2 raspberry seed extract; II) 2 g CO_2 pomegranate seed extract; III) 2 g CO_2 rosemary extract; IV) 1 g CO_2 raspberry seed extract and 1g CO_2 pomegranate seed extract; V) 1g CO_2 raspberry seed and 1g CO_2 rosemary extract; VI) 1 g CO_2 pomegranate seed and 1 g CO_2 rosemary extract; and VII) CO_2 extracts of raspberry seed, pomegranate seed, and rosemary – to which 1 g decyl glucoside, 1 g caprylyl/capryl glucoside and 36 g 4% MHPC were introduced into each mixture. Since the phi6 bacteriophages inactivated the bacteriophage particles during incubation, each of the seven coatings displayed considerable antiviral activity. After being incubated with each film coated with the active coating, the amount of phi6 particles was found to be zero, indicating that the phages had no effect on the number of host cells. In conclusion, it can be assumed that all the coatings tested demonstrated high antiviral activity against surrogate airborne viruses, allowing them to be applied as outer layers to food products to increase their shelf life, protect consumers, and prevent the spread of SARS-CoV-2, a major concern for people during the current pandemic (Ordon et al., 2021). However, the maintenance of these coatings in packaging surfaces during storage should be guaranteed, since these materials can leak from the surface when exposed to high amounts of water or mechanical stress.

5. Conclusion and future perspectives

The purpose of this review was to present an overview and better comprehend the current state of knowledge, research direction, and practices in the field of antiviral compounds and edible films and coatings regarding foodborne viral diseases as a strategy to ensure food safety. It was possible to understand that several traditional medicinal plants and herbs, plant-derived compounds, and their derived-products, like essential oils and extracts, show excellent antiviral properties. Thus, active edible films and coatings in food can be an effective strategy to contain infectious outbreaks. Several reports proved that antiviral edible films and coatings exhibited great potential against enteric viruses that cause foodborne illness, more specifically NoV and HAV; however, some antiviral agents are also very effective against other pathogenic viruses of great importance, such as HBV and HCV, HIV, HSV or even SARS-CoV-2. Their mechanisms of action are distinct, and although there is little information about the presence of these latter viruses in food, this possibility cannot be ruled out since they are responsible for large outbreaks worldwide, particularly in fresh foods. Also, the globalization of production lines has increased the likelihood of bad handling and poor hygienic conditions, contributing to viral dissemination.

Although natural products may be very effective in controlling the spread of these viruses in food, one of the main challenges is the stability of the natural antiviral compounds in film and coating matrixes. Therefore new strategies are needed to boost their functionality. Micro and nanoencapsulation systems may enhance antiviral action and should be considered when designing future experimental work related to edible films and coatings. The encapsulation system can shield these active compounds from degradation, enhance their solubility, and manage their release. There is a dearth of systematic studies since most of them are only developed in laboratories. Nevertheless, although the research found advantages in using antiviral compounds and subsequently in their incorporation in films and coatings, more extensive trials are needed to clear proof their effectiveness and safety, according to the current legislation.

Data availability

No data was used for the research described in the article.

Acknowledgements

This work received funding from EIT Food (Grant agreement ID: 20400), the innovation community on Food of the European Institute of Innovation and Technology (EIT), a body of the EU, under Horizon 2020, the EU Framework Programme for Research and Innovation.

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