

Rinsing away the threat: Antiviral mouthwashes and their efficacy (Review)

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Abstract. The oral cavity is a gateway through which respiratory viruses, such as SARS CoV-2 enter. Thus, mouthwashes are potential routes of controlling the viral spread. The present review discusses the effectiveness of formulations containing povidone-iodine, cetylpyridinium chloride, chlorhexidine, hydrogen peroxide and phthalocyanine derivatives. By disrupting viral structures, oxidizing proteins, inhibiting replication and modulating inflammation, these agents exert their antiviral effects. A systematic search on the PubMed and Google Scholar databases was conducted, including articles published between 2020 and 2025. The present review incorporates systematic reviews, as well as *in vitro*, *in vivo*, clinical and observational studies evaluating the virucidal activity, real-world efficacy and preventive potential of antiviral mouthwashes. From these studies, it is indicated that these mouthwashes markedly reduce salivary viral loads; however, this reduction is transient, formulation-dependent and requires repeated use. Other concerns are variability in effectiveness, potential for the disruption of the oral microbiome and improving user compliance. Future research is required to focus on the long-term safety of these products, determine prolonged antiviral activity and design optimized formulations. When used in combination with standard infection control practices, antiviral mouthwashes may be effective, low-cost adjuncts for reducing viral transmission, particularly in high-risk environments, such as healthcare and dental facilities. As further evidence becomes available, the integration of these mouthwashes into public health plans may enhance the preparedness for future viral outbreaks.

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1. Introduction

Viruses, particularly respiratory viruses, such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), pose immense challenges to public health as they easily transmit through aerosols and droplets, as well as through direct contact with contaminated surfaces. The oral cavity provides a prime location for viral replication, thus becoming a reservoir for viral particles; saliva also plays a vital role in this regard. Accordingly, reducing viral loads in oral fluids has come to occupy a place of prominence in efforts toward halting the spread of viruses, particularly in high-risk environments such as clinics and hospitals (1,2). Antiviral mouthwashes are easily applied, are inexpensive and are an accessible means of infection control. Traditionally used mouthwashes aid in the maintenance of oral hygiene as they are bactericidal or fungicidal agents; however, there is currently an increasing interest in the evaluation of their virucidal potentials. Studies have primarily focused on povidone-iodine (PVP-I), chlorhexidine gluconate (CHX), cetylpyridinium chloride (CPC), essential oils and newer compounds phthalocyanine derivatives. These agents function through the disruption of the viral envelopes or interference with replication processes, thus leading to a loss of viral infectivity and shedding (3). Schürmann *et al* (2) focused on CPC-based formulations as they could break viral lipid membranes, which prevented coronaviruses and other related pathogens from spreading. Rodríguez-Casanovas *et al* (3) and Carrouel *et al* (4) in their study demonstrated that few mouthwashes can effectively eliminate viruses.

Mouthwashes with essential oils have anti-inflammatory properties that have helped individuals deal with the systemic effects of viral infections and have also made antiviral treatment more flexible. The efficiency of such mouthwashes in decreasing viral shedding among patients having mild or asymptomatic COVID-19 has been proven through clinical studies performed by Takeda *et al* (5) and Vilhena *et al* (6).

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Martínez Lamas *et al* (7) in their study has confirmed the virucidal properties of PVP-I, suggesting its clinical use, particularly in dentistry. The antiseptic CHX, frequently used in dentistry, has also demonstrated short-term virucidal activity. Jain *et al* (8) found that a 0.2% CHX solution inactivated >99.9% of SARS-CoV-2 within 30 sec, demonstrating its rapid action compared to PVP-I. Evidence from the literature has indicated that CHX only reduces the viral load for a short period of time and is therefore less effective as a standalone treatment. Its combination with other agents, such as PVP-I needs to be evaluated in a clinical setting (9). CHX is a rapid, yet temporary addition to more long-lasting agents, such as PVP-I, and it can greatly reduce oral viral loads when used in conjunction with phthalocyanine derivatives and CPC (10). Perussolo *et al* (10) conducted a study where they tested three types of mouthwash randomly. They discovered that these mouthwashes were able to decrease the load of SARS-CoV-2 among hospitalized patients. This supports the concept that mouthwashes may limit the spread of the virus. Mouthwashes containing phthalocyanine derivatives have also shown promising efficacy in reducing hospitalization periods for patients with COVID-19, and CPC-containing mouthwashes have also shown promising *in vitro* activity against enveloped viruses (11,12). Both CPC and phthalocyanine derivatives possess notable antiviral activity. CPC functions by disrupting the lipid envelope of viruses, which leads to rapid virucidal effects (5), while phthalocyanine derivatives inhibit viral replication and reduce inflammation, which renders them very useful in high-risk and hospitalized patients (6).

The majority of the formulations integrate antimicrobial and anti-inflammatory properties, thereby enhancing their efficacy in reducing viral loads and improving clinical outcomes (13). Although various mouthrinses that act against viruses, as studied in previous literature (14-17), have been proven to be useful and affordable, their functional properties against these viruses need to be fully investigated.

The present review provides an overview of the effectiveness of antiviral mouthwashes, particularly based on scientific studies, in an aim to assess the role of these mouthwashes in reducing the spread of viruses. For this purpose, the PubMed and Google Scholar databases were searched to provide related data for the present review, which concentrated on systematic reviews, as well as *in vitro*, *in vivo*, clinical and observational studies evaluating the virucidal activity, real-world efficacy and preventive potential of antiviral mouthwashes that were published between 2020 and 2025. The present review discusses the mechanisms and relative efficacy, clinical effectiveness and preventive potential of several mouthwash formulations.

2. Antiviral mouthrinses

Types of antiviral mouthwashes. Antiviral mouthwashes are formulated to degrade the structures of viruses, inhibit multiplication and decrease infectivity in the oral environment. There is a plethora of types, each with its mode of action:

PVP-I. PVP-I is an iodine-based antiseptic solution. This disrupts the lipid envelope and then causes oxidation of the viral proteins. As a result, the viruses become inactivated.

This product has wide applicability over viruses, such as SARS-CoV-2 and is hence used quite commonly for preprocedural rinsing and infection control in health care settings (1,18).

CPC. This compound is a quaternary ammonium agent that functions at the lipid envelope level leading to membrane disintegration and the release of viral genetic material, ultimately resulting in viral inactivation. It also has some anti-inflammatory effects and can effectively kill viruses, such as influenza A and respiratory syncytial virus (RSV). It is very commonly used for everyday oral hygiene, although it can also be used in managing symptomatic viral infections (5,13). CPC is a broad-spectrum antiseptic agent often mixed with zinc or other additives to enhance its performance, according to Garcia-Sanchez *et al* (19).

Hydrogen peroxide (H₂O₂). H₂O₂ produces reactive oxygen species (ROS), which oxidizes viral proteins, rendering viruses, including SARS-CoV-2, vulnerable to oxidative stress. It is commonly applied in general disinfection as well as a mouthrinse; however, it is not effective compared to PVP (20). According to the systematic review performed by Ortega *et al* (16), there is no scientific evidence supporting the use of hydrogen peroxide mouthwash for reducing the viral load of SARS-CoV-2 in saliva.

Phthalocyanine-based mouthwashes. Phthalocyanine derivatives present in mouthwashes interfere with nucleic acid synthesis and thus inhibit viral replication. They are particularly effective for use in high-risk environments and for use preventively in immunocompromised individuals (21).

Alcohol-based mouthwashes. These mouthwashes contain 20-30% of ethanol, they interfere with the lipid envelope of enveloped viruses and can denature proteins, leading to viral inactivation. There are only a limited number of clinical studies evaluating the antiviral potential of mouthrinses (22). Although mouthwashes are used for routine oral hygiene maintenance, they have limited direct efficacy against SARS-CoV-2 since more ethanolic concentration is required for virucidal property. However, their broad-spectrum antiseptic properties render them a valuable component of infection control protocols (18,23). Listerine contains essential oils and alcohol, which are effective against enveloped viruses, such as herpes simplex virus and influenza A. However, its efficacy against SARS-CoV-2 is uncertain (24,25).

CHX. CHX has been extensively studied for its broad-spectrum antimicrobial activity, even against viruses. It disrupts cell membranes and consequently does not allow viral replication, in addition to inactivating the viruses within the oral cavity. CHX has generated interest as it can significantly reduce the viral load of SARS-CoV-2. The study by Huang and Huang (26) revealed a marked decrease in the levels of SARS-CoV-2 RNA in oropharyngeal samples following treatment with CHX mouthwash, thus supporting its use in infection control protocols. CHX also plays a role in reducing the risk of viral transmission in healthcare settings, particularly when used preprocedurally. Other studies have suggested that CHX can be incorporated into regular oral hygiene to assist in lowering oral viral loads, even in patients with symptomatic viral infections (27,28).

Other solutions. Other active ingredients, such as zinc-based solutions and enzyme-protein mixtures are virucidal. Zinc-based solutions help to prevent viral multiplication in the

Table I. Comparison of mouthrinse formulations.

Mouthwash formulation	Mechanism of action	Virus efficacy	Types of studies	Concentration	Reduction %	Contact time (Refs.)
Povidone-iodine (PVP-I)	Lipid envelope disruption; protein oxidation	SARS-CoV-2	<i>In vitro</i>	1%	99.99%	15-30 sec (1)
Cetylpyridinium chloride (CPC)	Lipid envelope disruption; anti-inflammatory properties	SARS-CoV-2, influenza A, RSV	<i>In vitro</i> and clinical	0.005%	99.9%	30 sec (5)
Chlorhexidine (CHX)	Lipid envelope disruption; protein oxidation	SARS-CoV-2	Clinical (RCT)	0.12-0.2%	99.9%	30 sec (8)
Phthalocyanine-based mouthwash	Inhibition of viral replication; anti-inflammatory effects	SARS-CoV-2	<i>In vitro</i>	0.02-0.05%	90%	30 sec, 1 min and 5 min (21)

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; RSV, respiratory syncytial virus; ROS, reactive oxygen species; RCT, randomized controlled trial.

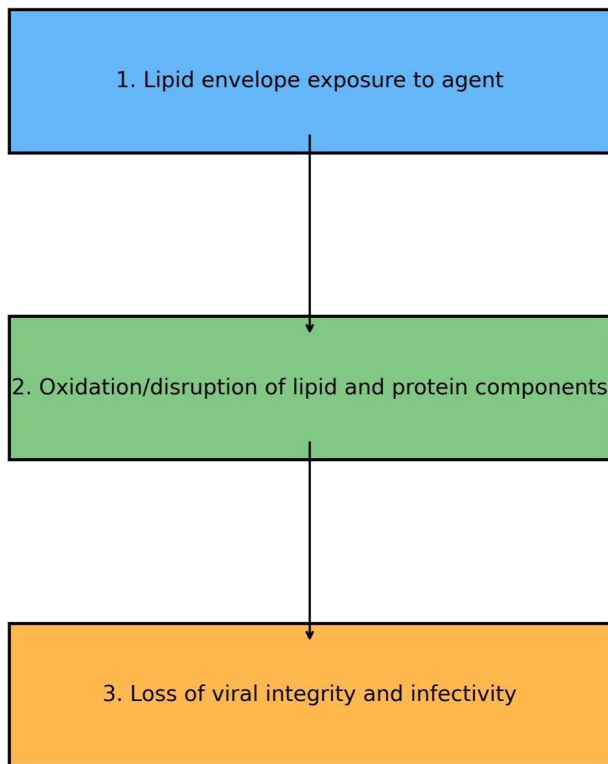


Figure 1. Diagram of the sequential steps of lipid envelope disruption and its cascading effects.

nasopharyngeal region (29). In addition, the enzyme-protein mixtures have been found to be capable of inhibiting surrogate viruses, such as feline coronavirus, thereby rendering them useful in extended antiviral applications (14).

Antiviral mouthwashes: Mechanisms and efficacy. The efficacy of antiviral mouthwashes depends on their active ingredients, concentration and mechanisms of action. A standardized comparison of these formulations, incorporating virus strain, test type, effectiveness and real-world applications

is provided in Table I. Various mechanisms of viral disruption include the following:

Lipid envelope disruption. The lipid envelope is essential for the infectivity of enveloped viruses, such as SARS-CoV-2. If this structure is disrupted, the virus is no longer infectious. Some of the common agents that function by lipid envelope disruption mechanism are as follows:

i) PVP-I. PVP-I is an oxidizing agent; it destroys the lipid and protein moieties of the viral envelope causing a structural collapse that leads to the inactivation of the virus. The recent study by Hassandarvish *et al* (1) indicated that concentrations of PVP-I from 0.23-1% provide >99.99% inactivation of SARS-CoV-2 in only 15 sec after contact. The study by Barrueco *et al* (28) also highlighted the efficacy of PVP-I in reducing viral infectivity in clinical and public health settings. Therefore, PVP-I has proven to be very useful in the preparation of pre-procedural oral rinses for use in the healthcare environment as it can markedly reduce viral loads in aerosols (Fig. 1).

ii) CPC. CPC disrupts the lipid envelope due to its capability to penetrate it and leak out the viral content. Rius-Salvador *et al* (30) reported a reduction in the viral titers of influenza A and RSV by >99.9% with an oral care concentration within 30 sec (30). Thus, CPC is very safe and effective for day-to-day oral hygiene and can be used effectively in non-clinical settings to regulate enveloped viruses.

iii) CHX. CHX disrupts the lipid envelope of SARS-CoV-2, similar to PVP-I and CPC. Its positive charge destabilizes and inactivates the viral membrane by binding to its negatively charged components. CHX rapidly inactivates viruses at 0.1-0.2%, rendering it a useful pre-procedural rinse in dentistry and healthcare (8).

Alcohol-based solutions. These ethanol solutions achieve the disruption of the lipid envelope bilayer around the virus; furthermore, ethanol can facilitate protein denaturation inside the virus. SARS-CoV-2 and various other enveloped viruses can become deactivated with solutions containing >60% alcohol for less than half a second or instant (18,23). Such

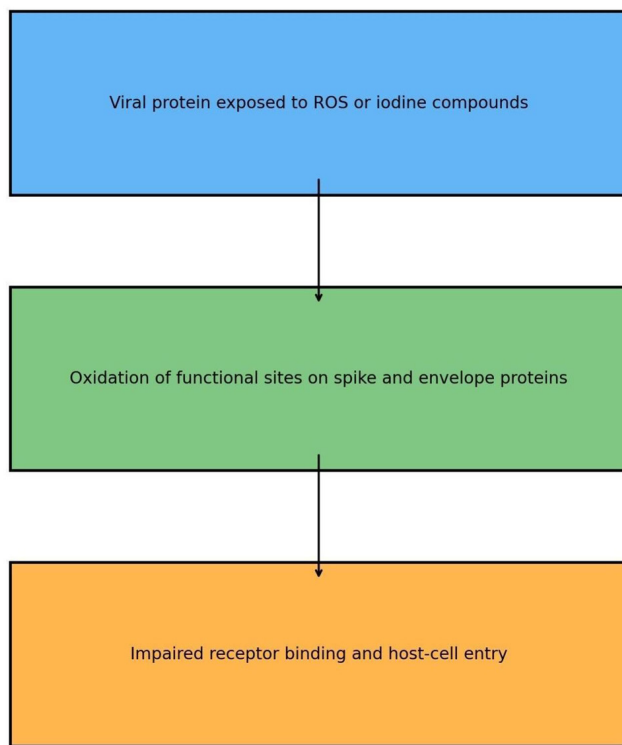


Figure 2. Diagram of the sequential steps of protein oxidation mechanism.

fluids are frequently implemented for hand sanitizer disinfections; these same solutions have a low utilization in mucous membranes.

Protein oxidation. Surface proteins, such as the SARS-CoV-2 spike protein mediate host-cell entry; the oxidation of these proteins is now known to block viral infection (Fig. 2).

PVP-I. PVP-I rapidly oxidizes viral surface proteins, thereby neutralizing them and preventing viral attachment to host cells. Hassandarvish *et al* (1) demonstrated that PVP-I reaches a 4-log reduction in infectivity within 15 sec of exposure. Thus, this speed renders PVP-I suitable for general oral hygiene use, particularly in risk settings where the speed of viral inactivation is necessary.

H₂O₂. H₂O₂ produces volatile ROS that oxidizes viral proteins, thus hindering virus penetration into host cells. In their systematic review, Ortega *et al* (16) suggested that 1.5-3% H₂O₂ reduces the infectivity of viruses by as much as 80% within a period of 30-60 sec.

CHX. By rupturing the viral envelope, CHX helps to inactivate viral proteins even though it does not directly oxidize them. The viral surface proteins, including the spike protein, are disrupted; thus, the virus cannot bind to host cells. This action accentuates its general antiviral action (9).

Membrane disruption. Of note, apart from protein oxidation, some agents such as PVP-I and CPC can affect the lipid envelope of viruses causing structural instability that enhances viral inactivation. Such disruption can supplement protein oxidation, leading to a greater extent of reduction in infectivity of the virus (31).

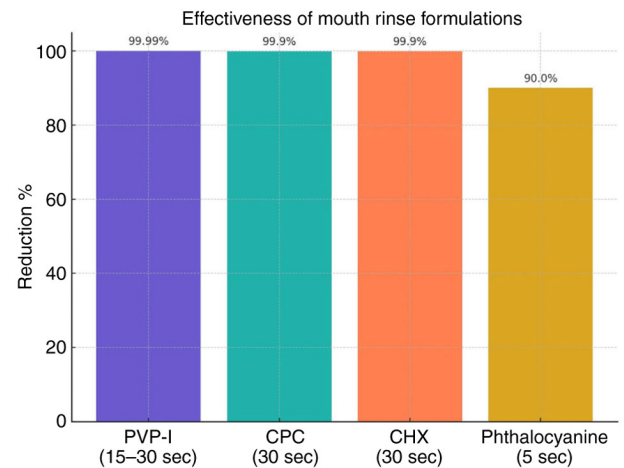


Figure 3. Viral load reduction percentages for different agents PVP-I, povidone-iodine; CHX, chlorhexidine gluconate; CPC, cetylpyridinium chloride plotted against the contact time of the mouthwash on the bar graph.

Viral load reduction. Antiviral mouthwashes are critical in reducing viral loads in the oral cavity, minimizing the risk of transmission, particularly in high-risk environments such as clinical and dental settings.

PVP-I and CPC. Both are effective in achieving rapid and significant reductions in viral loads. PVP-I, as a pre-procedural rinse can reduce the salivary viral loads by >99%; effects can be observed up to 30 min post-rinse (1,18). Similarly, CPC provides comparable effectiveness and confers anti-inflammatory benefits; thus, it can be considered as a good option for oral hygiene in clinical as well as nonclinical environments (31).

H₂O₂ and alcohol-based mouthwashes. H₂O₂ must remain in contact for 1-2 min in order to be able to reduce viral loads by 80%. Higher concentrations will achieve this in a more rapid manner; however, the residual activity would not last as long (16,22). Alcohol-based mouthwashes compromise viral lipid envelopes, but lack prolonged virucidal activity, requiring repeated use for sustained viral reduction (23).

CHX. CHX has been shown to rapidly reduce viral load in the oral cavity. In a systematic review, Rahman *et al* suggested that 0.12% CHX solution decreased SARS-CoV-2 viral load by 99.9% within 30 sec (32). This renders CHX an excellent choice for pre-procedural rinses (Fig. 3), which help to reduce viral transmission in dental and healthcare settings (32).

Anti-inflammatory effects. Antiviral mouthwashes are indispensable in lowering viral loads within the oral cavity, thus markedly reducing the inflammatory mediators by indirectly decreasing the stimulus to the inflammatory cells (2).

CPC. CPC suppresses pro-inflammatory cytokines, such as IL-6 and TNF- α by reducing the viral load. This will thereby reduce both oral cavity site-specific inflammation, as well as the associated systemic inflammation. Onozuka *et al* (33) reported that the regular use of CPC enhances promotes the recovery of patients from mild and moderate COVID-19 symptoms (5,33).

Phthalocyanine derivatives. These derivatives scavenge ROS, thus averting morbidity through the inhibition of pro-inflammatory cytokines production. Vilhena *et al* (6) demonstrated its efficacy in reducing oral inflammation in

patients with COVID-19, pointing towards increasing their role in high-risk hospital setups. The key feature is its antiviral action that also has role in reducing the inflammatory burden, which provides great value to patients that have immunocompromised states (6).

CHX. CHX reduces oral inflammation. It can improve oral health in patients with symptomatic COVID-19 by reducing gingival inflammation and bacterial load. This helps patients with systemic diseases, such as diabetes, where inflammation can accelerate disease progression (9,10,26). The anti-inflammatory effects of CPC, CHX and phthalocyanine derivatives have effects beyond oral health due to reduction in viral load, contributing to the systemic benefits of reduced complications, such as cytokine storms and secondary infections in patients with viral infections, such as COVID-19.

Applications during the COVID-19 pandemic. Among the various mouthwashes, PVP-I at concentrations between 0.2 to 2.5% has been observed to significantly decrease up to 99.99% of SARS-CoV-2 particles with an incubation period of <15 sec following its application (1,18). Due to its potent virucidal effect, PVP-I is the preferred pre-procedural oral rinse for several types of healthcare settings, particularly in dental practices where aerosol-generating procedures are inevitable, resulting in a higher risk of airborne transmission of viruses (18). Furthermore, the study conducted by Choudhury *et al* (11) also established that PVP-I mouthwashes decrease nasopharyngeal viral loads and help decrease secondary transmission in patients, particularly those who are mild or asymptomatic carriers. Additionally, the adaptability of PVP-I, which also has wide-range effectiveness against other viruses including Enteroviruses and Coxsackieviruses, has been further justified as a management agent for the future viral pandemic outbreak (34). Other formulations, including CPC and chlorhexidine, were also found to be helpful during the pandemic and found a niche in medical and dental care, where CPC was shown to be particularly useful. CPC mouthwashes have been shown to decrease viral titers and also effective for aerosol-generating procedures (5). CHS is another antiviral agent that has been strongly indicated as effective in combating the pandemic. Jain *et al* (8) reported that CHX mouth rinse may significantly reduce the levels of SARS-CoV-2 RNA in the oral cavity. CHX mouthwashes were widely used in aerosol-generating procedures in dental and healthcare settings, primarily to decrease viral loads (8). In addition, the use of CHX as a topical antimicrobial agent, as reported by Huang and Huang (26), led to the reduction in inflammatory burden caused by viral infections, thus contributing to a more rapid recovery in patients with COVID-19 (26). The pandemic also witnessed the emergence of novel antiviral agents, including phthalocyanine-based mouthwashes, which have been demonstrated to significantly reduce viral loads and inflammation (6). These formulations, which are used in critical care settings, were incorporated into infection control plans with other antiviral treatments to maximize protection (6,20). Zinc-based and chlorhexidine solutions, which have broad-spectrum antimicrobial activity, were applied to further limit the spread of viruses, particularly in nasopharyngeal areas, by inhibiting viral replication (28,35).

3. Challenges, limitations and future directions

Although antiviral mouthwashes have demonstrated their utility, they are not free of challenges as regards their widespread use. A major hindrance is that the formulations vary, and so do the designs of studies conducted, which makes it challenging to standardize procedures for testing their efficacy. For example, some compositions are deactivated by saliva or organic matter when applied in practice, which could lower their effectiveness during real-time application (3,36). Another limitation is the long-term safety profile of oral antiseptics. CPC-containing mouthwashes alter the oral microbiome, leading to a possible risk of dysbiosis and poor oral health (13). Likewise, CHX formulations may cause taste impairment and tooth discoloration. According to Jain *et al* (8), future formulations require a balance of efficacy and minimal oral disruption friendly to the microbiome. Long-term clinical trials are required to evaluate the systemic impact of these formulations (37). One other less commonly used mouthwash is Chlorine dioxide, that has been proven to be effective in reducing viral load (38). User compliance is also an issue. Taste, cost and accessibility are the factors that prevent regular use, particularly outside clinical settings. Educational programs emphasizing the role of mouthwashes in infection control, along with palatable formulations, will enhance adoption. Public education programs, particularly for preprocedural mouth rinsing in high-risk settings such as dental offices, will lead to further increased use (34). Mouthrinses have short-term advantages; however, their place in more comprehensive infection control practices will be better understood with further research. Researchers are investigating newer formulations as possible remedies for these issues; these formulations have improved efficacy, longer duration of action and fewer side-effects.

Enzyme-based mouthwashes. These mouthwashes use lysozyme and proteases to break down viral structures. The ability to neutralize feline coronaviruses, a model for SARS-CoV-2, was shown by Buonavoglia *et al* (14).

Nanoparticle-infused mouthwashes. Silver and zinc oxide nanoparticles, for example, are used in mouthwashes to provide broad-spectrum antiviral action. Zinc oxide may protect existing formulations by interfering with viral replication (14).

Biofilm-targeting mouthwashes. Overcoming a significant limitation of conventional mouthwashes, biofilm-targeting mouthwashes, such as solutions infused with lactoferrin, aid in preventing viral adhesion to oral tissues.

Smart pH-responsive formulations. These change their acidity when viruses are detected, helping them function for longer periods of time to kill viruses. The long-term virucidal activity is sustained by pH-responsive CPC and CHX solutions, according to Rius-Salvador *et al* (30). Future research is required to focus on maintaining antiviral potency in the presence of organic matter, possibly through zinc-based antivirals combined with phthalocyanine derivatives. Further optimization of efficacy while minimizing adverse effects could be achieved by pairing CHX with anti-inflammatory agents and optimizing CHX concentration (8). To assess

efficacy across various populations and healthcare environments, further varied clinical trials are required. As these advanced formulations develop, their integration into routine infection control policies will necessitate additional validation. Antiviral mouthwashes may reinforce masks, physical distance and ventilation. Their widespread implementation in preprocedural medical settings has the potential to significantly improve patient safety and contribute to the long-term prevention of infectious diseases.

4. Conclusion

Antiviral mouthwashes are an integral, yet developing tool for preventing infections, particularly in dental and medical settings. While existing formulations successfully reduce viral loads, issues such as temporary efficacy, microbiome impact and compliance barriers must be addressed. Improving the stability of the formulation and creating designs that are easy for patients to use are crucial steps towards making them really useful.

In the future, standard clinical testing and innovative formulation approaches will be integral to incorporating mouthwashes in routine infection control practices. Given the progress to date and potential for continued improvements, these could become an increasingly accepted preventive tool, both to augment existing prevention strategies in daily practice and prepare for future pandemics.

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Authors' contributions

OT wrote the original draft of the manuscript, and conducted the literature search. GK conceptualized the study. SB performed the literature review. PLR supervised the study and edited and revised the manuscript. All authors have read and approved the final version of the manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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