

Can Mouthwash Douse the Spread of COVID-19?

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Can oral rinses help stop the spread of COVID-19? After reviewing evidence from more than 100 articles, researchers have concluded that some oral rinses may help curb the spread of SARS-CoV-2, but more research is "desperately" needed.

Although investigators recognize the role that such products might play in curtailing the pandemic, they are calling for more research to help shed some much-needed light on the subject.

It is possible that dampening down the levels of shed virus, even transiently, may have an impact on transmission of disease to vulnerable people or to healthcare professionals who routine work in the upper airway, such as ear, nose, and throat surgeons, anesthesiologists, and dentists, coinvestigator Albert Bosch, PhD, University of Barcelona, Spain, told *Medscape Medical News*.

"This idea needs testing in clinical trials where the impact of oral rinsing on the number of infectious virions is tested before and after rinsing, and if there is an effect, how long the effect persists would then need to be determined," Bosch added.

The review was [published online](#) May 14 in *Function*.

Virucidal Strategy

The SARS-CoV-2 virus is surrounded by a lipid envelope. Inserted into this biomembrane are the spike glycoproteins required for infection, the researchers note.

Robust though the virus may be, the lipid biomembrane may be its Achilles heel, said coinvestigator Syed A. Sattar, PhD, University of Ottawa, Canada. "We expect, based on studies on other similar viruses, that the membrane will be amenable to disruption," he said.

To interfere with the lipid envelope is a well-known virucidal strategy against many coronaviruses, and [previous research](#) has demonstrated the impact of many agents in this regard, the current investigators write.

[Such studies](#) have led to a consensus view that enveloped viruses, including SARS-CoV-2, are highly sensitive to 60% to 70% [ethanol](#), which causes almost immediate inactivation. These views have been echoed in recommendations by the World Health Organization (WHO) and the US Environmental Protection Agency.

However, current guidance from WHO regarding clinical management of SARS-CoV-2 in the home does not mention oral hygiene. This is likely due to the dearth of research into the possibility of oral antiviral strategies in the fight against the virus.

[Previous research](#) suggests that the salivary glands and throat are major sources of coronavirus replication. Furthermore, a high viral load in the mouth may contribute to the spread of disease in early stages of infection.

"It is known that the throat is a source of shed virus, especially in early-stage disease, and also in asymptomatic individuals who are also likely to be infectious," Bosch said.

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"There is increasing evidence that many people don't have symptoms, yet they are positive for SARS-CoV-2 through detection of virus in throat and nasal swabs," he added.

The Evidence to Date

Increased levels of viral shedding in the throat or lungs might also be associated with an increase in the propensity to infect others, the researchers add. As such, strategies aimed at reducing the number of infective virus particles in mucous membranes may help reduce the risk for transmission. One such strategy is to use oral rinses that target the lipid envelope around SARS-CoV-2.

But could these strategies actually work?

To help answer this question, the investigators conducted a literature review that examined several common ingredients in oral rinses, including ethanol, chlorhexidine, cetylpyridinium chloride, [hydrogen peroxide](#), and povidone-iodine. The researchers assessed the potential of each of these to disrupt the lipid envelope of the SARS-CoV-2 virus and potentially reduce viral spread.

With respect to ethanol, most studies have investigated the utility of higher concentrations of the compound. Few have examined the lower concentrations commonly found in commercially available mouthwashes.

The small amount of research that has been conducted with lower ethanol concentrations has been promising. Two such trials, both conducted in vitro, yielded positive outcomes in relation to virus denaturation.

In 2007, a study [concluded](#) that 20% ethanol completely inactivated three enveloped viruses – sindbis, [herpes simplex–1](#), and vaccinia. Another study [published](#) 10 years later showed that a 30-second exposure to a dilution containing 34% ethanol completely prevented coronavirus replication.

There is "an urgent need" to perform similar studies under biologically relevant conditions, such as in the mucosa and mouth, the current investigators note.

Some researchers have followed this path, examining the ability of commercially available mouthwashes to disrupt viral lipid envelopes with either ethanol or other active agents.

In 1995, [researchers tested](#) 26.9% ethanol plus essential oils against herpes, [influenza](#), [rotavirus](#), and adenovirus in vitro. Both herpes and influenza (which are enveloped) were significantly affected, whereas adenovirus and rotavirus (which are not enveloped) were not. This led the investigators to speculate that the oral rinse may alter the viral lipid envelope.

A 2010 unpublished follow-up study by the same group showed that a 30-second in vitro exposure to 21.6% ethanol with essential oils led to a more than 99.99% reduction of infectivity of [H1N1](#) influenza.

These studies "provide proof-of-concept that mouthwashes containing essential oils with 21-27% ethanol can inactivate enveloped viruses, both in the lab and in humans, with the likely mechanism being damage to the lipid envelope," the review authors write.

Nevertheless, more ethanol research needs to be performed, they add.

Different Formulations

"In our review, we summarize the small number of studies, mostly in Japan, that have been undertaken," said lead author Valerie O'Donnell, PhD, Cardiff University, Wales, United Kingdom.

Although the studies showed that oral rinsing had a positive effect, the studies "were small, not blinded, self-reported, or didn't define which respiratory pathogen was involved, so they all have limitations. This is why large-scale clinical trials are desperately needed," she added.

Other studies have investigated the potential of other oral rinse formulations on lipid-enveloped viruses. Chlorhexidine has [been shown](#) in vitro to reduce the viral concentration of enveloped viruses.

Given that chlorhexidine formulations can retain their oral antimicrobial activity [for up to 12 hours](#), the researchers note that combining them with ethanol may prove useful for reducing viral load over longer periods.

Povidone-iodine has also been the subject of a few [human studies](#), which have shown that repeated gargling can reduce incidence of both bacterial and viral infection. Nevertheless, povidone-iodine is currently available only in a few Asian countries. In addition, rare allergic reactions have [been reported](#) with its use.

Rinsing with chlorinated water or hypertonic saline is another option and has borne fruit in a pilot study from Japan. However, this study was nonblinded and self-reported "and so cannot be considered definitive," the current investigators write.

Another potential oral rinse is hydrogen peroxide, which causes oxygen free radical-induced disruption of lipid membranes. [Previous studies](#) have shown that coronavirus 229E and other enveloped viruses are inactivated at hydrogen peroxide concentrations of approximately 0.5%.

Although hydrogen peroxide concentrations greater than 5% can damage soft and hard tissues, little damage [has been reported](#) in the 1% to 3% concentration range commonly used in mouthwashes for teeth whitening.

Quaternary ammonium compounds are widely used microbicidal agents that interfere with protein or lipid components on the cell surface. One such compound is cetylpyridinium chloride, which has recently been shown to be active in vitro and in vivo

against influenza through direct attack on the viral envelope.

Key Questions Remain

For all the potential these oral rinses have, further research is needed to clarify what, if any, effect they may have on SARS-CoV-2 transmission, the review authors write.

They note that such research should answer several questions, including the following:

- Can viral load in the oropharynx be reduced through oral rinsing?
- If yes, which oral rinse might be clinically effective?
- Would a combination of agents in lower amounts be better tolerated, reduce adverse effects, and remain effective?
- What combinations, contact times, and frequency of use might induce antiviral activity and reduce infectivity of SARS-CoV-2?

To help answer these queries, the investigators suggest several research approaches. Epidemiologic studies may help establish on a population level whether oral rinses are associated with reduced rates of throat and [respiratory infections](#), including those caused by SARS-CoV-2.

More research into the SARS-CoV-2 virus is also needed, including research to determine the composition of its lipidome, the impact of ethanol or other agents on the infectivity of the spike protein, and the impact of temperature and soil load.

Further clinical studies could include population-based interventions. The investigators note that high-risk persons emerging from self-isolation may be one viable study population, as well as healthcare workers at high risk for infection.

Any study of the potential viability of oral rinses in this context also needs to examine the tolerability of these treatments.

"Theoretically, [oral rinses] could cause inflammation of the throat; but in a clinical study, this can be monitored and determined. And we suspect that in short-term use, there will be minimal risks if mouthwash is used correctly," coinvestigator David Thomas, BDS, PhD, of Cardiff University, said.

Despite many unknowns, the investigators are hopeful that research efforts will definitively answer ongoing questions. Whether the necessary research can be completed in time to address the COVID-19 pandemic is another question, they note.

"We are aware of some studies already being undertaken in other centers," O'Donnell said. Although thankful that the number of patients with COVID-19 has gone down recently, this has made "research in patients harder," she added.

Not surprisingly, O'Donnell and colleagues were reluctant to suggest the use of oral rinses as a potential option in the fight against SARS-CoV-2.

"Without the evidence, we cannot make any formal recommendations for the public. Research needs to be conducted to determine if oral rinses have any impact first," Thomas said.

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"However, the importance of maintaining good oral health is an increasingly recognized part of maintaining bodily health in general," he added.

"Just Get On With It"

Commenting for *Medscape Medical News*, Stephen J. Challacombe, PhD, King's College London, United Kingdom, was more definitive in his assessment of certain oral rinses and their role in curbing the spread of COVID-19.

In a review [published](#) earlier this year, Challacombe and colleagues assessed current evidence and concluded that povidone-iodine stands the best chance of reducing cross-infection.

"Although we haven't the evidence to absolutely prove that, the risk to healthcare workers is so high that there's every justification for going ahead and using it," Challacombe told *Medscape Medical News*.

He also recommends 1.5% hydrogen peroxide — even though it is not known whether it is inactivated in the presence of other organic matter. "Furthermore, it hasn't been tried in vivo against a coronavirus," he noted.

Chlorhexidine has been subject to less research, though its virucidal properties make it an attractive possibility in this context.

"It was tried against a coronavirus some years ago, and it wasn't terribly effective against them. But that doesn't mean it wouldn't be effective if you couldn't get hold of anything else. It's just that you've got far less of an evidence base than with povidone-iodine or hydrogen peroxide," Challacombe said.

Research notwithstanding, he sees little downside to using oral rinses in the fight against the spread of COVID-19.

"We have a problem and we don't have complete answers. But despite a lack of evidence, I see no reason for waiting if you've got a cheap, safe, and potentially effective option available in povidone-iodine," he said.

The bottom line is, you've got nothing to lose and potentially a lot to gain. So just get on with it. Dr Stephen Challacombe

"The bottom line is, you've got nothing to lose and potentially a lot to gain," Challacombe added. "So just get on with it."

The study authors and Challacombe have disclosed no relevant financial relationships.

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