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Systematic Review

The effect of mouthrinses on severe acute respiratory syndrome coronavirus 2 viral load
A systematic review

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ABSTRACT

Background. Considering that the oral cavity is a major entryway and reservoir for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the aim of the authors was to perform a systematic review of in vivo and in vitro studies to assess the effectiveness of mouthrinses on SARS-CoV-2 viral load.

Types of Studies Reviewed. The authors searched PubMed, Web of Science, Scopus, MedRxiv, and bioRxiv databases, including in vitro and in vivo studies assessing the virucidal effect of mouthrinses on SARS-CoV-2 or surrogates. From a total of 1,622 articles retrieved, the authors included 39 in this systematic review.

Results. Povidone-iodine was the most studied mouthrinse (14 in vitro and 9 in vivo studies), frequently showing significant reductions in viral load in vitro assays. Similarly, cetylpyridinium chloride also showed good results, although it was evaluated in fewer studies. Chlorhexidine gluconate and hydrogen peroxide showed conflicting results on SARS-CoV-2 load reduction in both in vitro and in vivo studies.

Practical Implications. Povidone-iodine–based mouthrinses appear to be the best option as an oral prerinse in the dental context for SARS-CoV-2 viral load reduction. Although the results of primary studies are relevant, there is a need for more in vivo studies on mouthrinses, in particular, randomized controlled clinical trials, to better understand their effect on SARS-CoV-2 viral load and infection prevention.

Key Words. Saliva; COVID-19; decision making; microbiology; public health; infection control.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a betacoronavirus. Beyond the SARS-CoV-2 outbreak, betacoronaviruses have been associated with 2 other outbreaks, namely, severe acute respiratory syndrome and Middle East respiratory syndrome.1,2 Binding of SARS-CoV-2 to human cells mainly occurs via the angiotensin-converting enzyme 2 receptor,3,4 which is highly expressed in the oral cavity, mainly in the epithelium of the tongue but also in gingival tissue, particularly on the buccal surface of the sulcular epithelium. Considering that the oral cavity may represent a major entryway and a reservoir of SARS-CoV-2,5-7 the scientific community adjusted disinfection protocols and preprocedural protocols for dental practice. Widespread use of protective suits was advised, and use of goggles and shoe covers was reinforced, as well as stricter patient triage ahead of the appointment.8

Preprocedural gargling with a mouthrinse was hypothesized to act possibly as an additional protective measure, reducing the oral load of SARS-CoV-2.9 Even before the COVID-19 pandemic, preprocedural gargling was used in dentistry to reduce microbiol load before surgeries or routine procedures.9 There are published guidelines advising the use of some mouthrinses aiming to reduce SARS-CoV-2 salivary viral load before dental appointments, in particular, the use of hydrogen peroxide (H2O2) mouthrinses.10-14 However, supporting evidence on the effectiveness of mouthrinses on SARS-CoV-2 viral load is still scarce, with no systematic reviews analyzing the evidence from both
in vitro and in vivo studies on this question, to the best of our knowledge. Thus, our study aimed to assess the effectiveness of mouthrinses in reducing SARS-CoV-2 viral load.

**METHODS**

**Protocol and registration**

We conducted this review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist and registered it on the PROSPERO website (CRD42021237418).

**Eligibility criteria**

Inclusion criteria included in vitro and in vivo studies assessing the virucidal effect of mouthrinses on SARS-CoV-2 or surrogates. Exclusion criteria included reviews, letters to the editor, personal opinions, product news, book chapters, case reports, congress abstracts, protocol suggestions, editorials, correspondence articles, recommendations, trial designs, hypotheses, and studies with animals.

**Information sources and search strategy**

To develop this review, we performed searches in MEDLINE (via PubMed), Scopus, and Web of Science databases. We conducted searches on January 13, 2021, with an update on November 23, 2021. This search was complemented with a manual search on MedRxiv and bioRxiv preprint databases. Full query is described in Table 1. Given that the first scientific publications on SARS-CoV-2 concern the year 2020, we limited the search to articles published in 2020 and 2021.

**Study selection**

After removing duplicates, 2 reviewers (A.S.) and (M.A.) independently reviewed the titles and abstracts of retrieved publications. Studies not excluded in the screening phase were fully read, with full-text analysis also independently performed by the 2 investigators. Any divergence was solved via a discussion with a third reviewer.

**Data extraction**

The 2 reviewers independently extracted data using a purposely built online form. Any inconsistency in data collection was resolved through discussion with a third author (B.S.M.). The following variables were retrieved from each primary study: author, title, year, country, type of study, sample number and type, patient characterization, intervention and control group, virus strain, type of mouthrinse, concentration, number of mouthrinses per day, rinsing duration, treatment duration, and decrease in viral load. For in vitro studies, the cell lineage used and existence of interfering substances were also assessed.

**Risk of bias (RoB) in individual studies**

The 2 reviewers independently carried out assessment of the RoB of included randomized controlled trials (RCTs) according to the Cochrane Collaboration tool for assessing RoB. Disagreements between reviewers were resolved after discussion and analysis. No RoB assessment was performed on in vitro studies or observational before-and-after studies owing to a lack of consensually accepted tools for assessing RoB in those specific studies.

**Summary measures**

We considered all outcome measures directly evaluating SARS-CoV-2 viral load. Main outcome measures presented in our systematic review are viral load expressed in logarithmic (log) reduction value, copies per milliliter, and relative light units. When primary studies used a mouthrinse with known concentration and presented the viral load decrease in logarithmic scale, we interpreted such results following the European Norm EN-14476, which recognizes antiseptics’ virucidal capacity when achieving a reduction on viral load equal to or greater than 4 log10. Therefore, we classified the results of the primary in vitro studies when expressed in log scale according to 3 levels considering virucidal activity (viral load reduction): high efficacy (≥ 4 log10; +), moderate efficacy (≥ 3 log10 and < 4 log10; ±), and low efficacy (< 3 log10; −). To simplify the comparison between studies, we converted results expressed in molars to percentages (%; g/100 mL). We converted results presented as a percentage of inactivation or fold reduction to a logarithmic scale.

**ABBREVIATION KEY**

| CHX: Chlorhexidine gluconate. |
| CPC: Cetylpyridinium chloride. |
| Ct: Cycle threshold. |
| H2O2: Hydrogen peroxide. |
| NA: Not applicable. |
| PCR: Polymerase chain reaction. |
| PVP-I: Povidone-iodine. |
| RCT: Randomized controlled trial. |
| RoB: Risk of bias. |
| SARS: Severe acute respiratory syndrome. |
| CoV-2: Coronavirus 2. |
Synthesis of results
Owing to methodological diversity of included primary studies, it was not possible to carry out a meta-analysis.

RESULTS
Study selection
We retrieved a total of 1,560 articles from bibliographic databases (MEDLINE, Scopus, Web of Science) and 62 from preprint databases. The study selection process is described in the figure.

Study characteristics
Of the 39 included studies, 33 were published as peer-reviewed articles, and 6 were preprints (eTable 2, available online at the end of this article).20-58 Twenty-four of the published articles were performed in vitro, and 9 were in vivo, 5 of which were RCTs, whereas the remaining were uncontrolled before-and-after studies. Five of the included preprints were performed in vitro, and 1 was in vivo.

In vivo studies included COVID-19—positive hospitalized patients20-28 and home-isolated patients.23,29 All in vivo studies quantified SARS-CoV-2 viral load via polymerase chain reaction (PCR), targeting genes E2,20,23,25 RNA-dependent RNA polymerase,21,23,25 nucleocapsid,23-25,27,28 S, and R.24 Three in vivo studies used water as a control,22,25,28 and 1 used RNA from guanidinium thiocyanat-inactivated virus.27 One used a similar solution regarding aspect and content but without virucidal components.29 In vivo studies evaluated the reduction of SARS-CoV-2 in viral titers: 4 presented the results with cycle threshold (Ct) fold changes,22,24,25,28 3 in the form of a logarithmic reduction value,21,23,26 1 in the form of a logarithmic reduction percentage scale,29 1 in a percentage scale,27 and 1 in copies per mL.19
Regarding SARS-CoV-2 strains used across in vitro studies, several used well-characterized strains, the most used being USA-WA1/2020. Four studies used a SARS-CoV-2 strain directly obtained from an infected patient, whereas 1 study did not report the strain used. In vitro studies were performed under dirty, clean, or both conditions, with the terms dirty and clean referring to the existence of interfering substances. Two in vitro studies did not provide information about the existence of interfering substances.

In vivo and in vitro studies applied the intervention solution for a predetermined period—mouthrinse contact time, most commonly ranging from 15 through 120 seconds. Seven in vitro studies included periods of application of 5 minutes or more.

RoB within studies
Two RCTs were marked as high RoB studies, whereas the other 3 were marked as low RoB studies (eTable 3, available online at the end of this article). The other 5 in vivo studies were uncontrolled before-and-after studies that included a low number of participants and for which the assessment of RoB was not feasible.

Results of individual studies
Five in vivo studies showed the virucidal efficacy of povidone-iodine (PVP-I) solutions on SARS-CoV-2 (eTable 4, available online at the end of this article). Seneviratne and colleagues conducted an RCT and reported that a 30-second rinse with 0.5% PVP-I conducted on a group of 4

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Table 1. Povidone-iodine in vitro effect on severe acute respiratory syndrome coronavirus 2 oral viral load.

| CONCENTRATION, % | CONTACT TIME, S | BIDRA AND COLLEAGUES | PELLETIER AND COLLEAGUES | FRANK AND COLLEAGUES | HASSANDARVISH AND COLLEAGUES | ANDERSON AND COLLEAGUES | BIDRA AND COLLEAGUES |
|------------------|----------------|-----------------------|--------------------------|----------------------|----------------------------|------------------------|----------------------|
| 0.5              | 15             | +                     | NA                       | ±                    | +                          | NA                     | ±                    |
|                  | 30             | ±                     | NA                       | ±                    | +                          | NA                     | ±                    |
|                  | 60             | NA                    | NA                       | NA                   | NA                         | NA                     | ±                    |
| 0.75             | 15             | NA                    | NA                       | NA                   | NA                         | NA                     | ±                    |
|                  | 30             | NA                    | NA                       | NA                   | NA                         | ±                      |                      |
|                  | 60             | NA                    | NA                       | NA                   | NA                         | ±                      |                      |
| 1.0              | 15             | NA                    | NA                       | NA                   | +                          | NA                     | NA                   |
|                  | 30             | NA                    | NA                       | NA                   | +                          | NA                     | NA                   |
|                  | 60             | NA                    | NA                       | NA                   | NA                         | ±                      |                      |
| 1.25             | 15             | +                     | NA                       | ±                    | NA                         | NA                     | NA                   |
|                  | 30             | ±                     | NA                       | ±                    | NA                         | NA                     | NA                   |
|                  | 60             | NA                    | NA                       | NA                   | NA                         | NA                     | NA                   |
| 1.5              | 15             | +                     | NA                       | NA                   | NA                         | ±                      |                      |
|                  | 30             | ±                     | NA                       | ±                    | NA                         | NA                     | NA                   |
|                  | 60             | NA                    | NA                       | NA                   | NA                         | ±                      |                      |
| 2.5              | 15             | NA                    | NA                       | ±                    | NA                         | NA                     | NA                   |
|                  | 30             | NA                    | NA                       | ±                    | NA                         | NA                     | NA                   |
|                  | 60             | NA                    | NA                       | NA                   | NA                         | ±                      |                      |
| > 2.5            | 15             | NA                    | NA                       | NA                   | NA                         | NA                     | NA                   |
|                  | 30             | NA                    | NA                       | NA                   | +                          | NA                     | NA                   |
|                  | 60             | NA                    | NA                       | NA                   | NA                         | NA                     | NA                   |

* Results interpreted according to European Norm-14476, considering a reduction on viral load ≥ 4 log₁₀ as a high efficacy (+), a reduction ≥ 3 log₁₀ < 4 log₁₀ as a moderate efficacy (±), and a reduction < 3 log₁₀ as a low efficacy (−). † Preprint article. ‡ Ranging from 0.45%-0.58%. § NA: Not applicable. ¶ Concentrations up to 10%.
hospitalized patients resulted in a significant reduction of viral load 6 hours after rinsing compared with water. However, no significant differences were found 5 minutes and 3 hours after rinsing. After using the same concentration of PVP-I but by performing 2 consecutive 30-second rinses, Chaudhary and colleagues verified a 61% reduction on viral load after 15 minutes and a 97% reduction after 30 minutes. The RCT conducted by Elzein and colleagues found a significant mean Ct difference increase between the paired samples before and after a 30-second 1% PVP-I rinse. In an uncontrolled before-and-after clinical study, Lamas and colleagues reported that a 60-second 1% PVP-I rinse led to a significant drop ($\geq 5 \log_{10}$) in viral load in 1 of the 4 patients evaluated, sustained for at least 3 hours. Jayaraman and colleagues found that 1% PVP-I could reduce the mean (standard deviation) viral load in saliva up to 1.8 (1.1) log$_{10}$. Significant reductions were observed after 20 and 60 minutes.

In vitro studies reported that PVP-I–containing mouthrinses have a virucidal effect on SARS-CoV-2 (eTable 5, available online at the end of this article). Table 1 summarizes the results found in different studies with application times up to 60 seconds and interpreted following EN-14476. Concentrations up to 0.75% showed moderate to high efficacy in reducing SARS-CoV-2 viral load. The 60-second application of PVP-I with concentrations from 0.5% through 0.58% had high efficacy results in the 4 studies evaluating this condition. Applying concentrations of PVP-I greater than 2.5% showed low (PVP-I at 7.5%), moderate (PVP-I at 5% and 7.5%), and high efficacy (PVP-I at 7.5% and 10%) within 15 through 30 seconds. The 60-second application also reached moderate to high efficacy results (PVP-I concentrations ranging from 5% to 10%).

| CONCENTRATION, % | MEISTER AND COLLEAGUES$^{46}$ | MEYERS AND COLLEAGUES$^{44}$ | STATKUTE AND COLLEAGUES$^{47,4}$ | DAVIES AND COLLEAGUES$^{49}$ | JAIN AND COLLEAGUES$^{40}$ | KARIWA AND COLLEAGUES$^{53}$ | SHET AND COLLEAGUES$^{54}$ |
|----------------|-----------------------------|-----------------------------|---------------------------------|------------------------------|-----------------------------|-----------------------------|-----------------------------|
| $= 0.5^{15}$   | NA                          | NA                          | NA                              | NA                           | NA                          | ±                           | +                           |
|                | NA                          | NA                          | NA                              | NA                           | NA                          | ±                           | +                           |
| $0.75$         | NA                          | NA                          | NA                              | NA                           | NA                          | NA                          | NA                          |
| $1.0$          | NA                          | NA                          | NA                              | NA                           | NA                          | NA                          | NA                          |
|                | –                           | NA                          | NA                              | –                            | NA                          | NA                          | NA                          |
| $1.25$         | NA                          | NA                          | NA                              | NA                           | NA                          | NA                          | NA                          |
| $1.5$          | NA                          | NA                          | NA                              | NA                           | NA                          | NA                          | NA                          |
| $2.5$          | NA                          | NA                          | NA                              | NA                           | NA                          | NA                          | NA                          |
| $> 2.5$        | NA                          | NA                          | NA                              | NA                           | NA                          | ±                           | +                           |
|                | ±                           | –                           | NA                              | NA                           | NA                          | ±                           | +                           |
|                | ±                           | NA                          | NA                              | NA                           | NA                          | ±                           | +                           |

Table 1 (Continued)
Regarding H$_2$O$_2$, Gottsauner and colleagues$^{20}$ conducted an in vivo study assessing virucidal efficacy of a 30-second H$_2$O$_2$ (1%) rinse. No significant difference was found between baseline and the viral load 30 minutes after rinsing. Chaudhary and colleagues$^{27}$ found that 2 consecutive 30-second H$_2$O$_2$ (1%) rinses led to a 90% reduction after 15 and 30 minutes. Jayaraman and colleagues$^{26}$ reported that a 30-second H$_2$O$_2$ (1.5%) rinse could decrease the mean (standard deviation) viral load up to 1.6 (1.5) log$_{10}$ after 60 minutes. A 60-second H$_2$O$_2$ (1.5%) rinse led to a significant reduction on viral load immediately after and 30 minutes after rinsing but not after 60 minutes.$^{28}$ In vitro studies on the virucidal effect of H$_2$O$_2$ showed very limited success (Table 2 and eTable 5, available online at the end of this article).

The virucidal efficacy of chlorhexidine gluconate (CHX) mouthrinses was evaluated with in vivo and in vitro studies (eTables 4 and 5, available online at the end of this article). In an RCT, Sen-enviratne and colleagues$^{22}$ studied the effect of CHX mouthrinses in a group of 6 patients and found no reduction of viral load. Another RCT by Elzein and colleagues$^{25}$ reported a mean Ct increase of 5.7 after a 30-second CHX (0.2%) rinse. Eduardo and colleagues$^{28}$ conducted an RCT to study the effect of a 30-second CHX (0.12%) rinse and found a significant reduction in viral load 60 minutes after rinsing. One other RCT, by Chaudhary and colleagues$^{27}$ reported that CHX (0.12%) achieved a 90% decrease in viral load 15 minutes after 2 consecutive 30-second rinses but only a 70% decrease after 30 minutes. Yoon and colleagues$^{21}$ performed an uncontrolled before-and-after clinical study on the effect of a 30-second CHX (0.12%) rinse in 2 hospitalized patients. The authors observed a transient decrease in viral load for 2 hours after rinsing. In 1 patient, 1 hour after rinsing, no decrease on viral load was observed. Jayaraman and colleagues$^{26}$ also reported a limited decrease in viral load in saliva after 90 minutes. Considering application times of up to 60 seconds (Table 2), in vitro application of CHX with concentrations lower than 0.16% showed low efficacy within 15, 30, and 60 seconds.$^{43}$ However, 1 study reported moderate efficacy within 30 seconds,$^{40}$ and another reported high efficacy after 30 and 60 seconds.$^{41}$ The use of 0.2% CHX also showed low efficacy after 30 seconds$^{46}$ and 60 seconds.$^{50}$ One preprint article reported that CHX (0.12%) achieved low, moderate, and high efficacy, depending on

| MOUTH'RINSE    | CONCENTRATION, % | CONTACT TIME, S | BIDRA AND COLLEAGUES$^{20}$ | MEYERS AND COLLEAGUES$^{44}$ | DAVIES AND COLLEAGUES$^{30}$ | MEISTER AND COLLEAGUES$^{26}$ | STEINHAUER AND COLLEAGUES$^{33}$ | STATKUTE AND COLLEAGUES$^{47},^{†}$ |
|----------------|------------------|-----------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| Hydrogen Peroxide | 1.5              | 15              | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    |
|                |                  | 30              | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    |
|                |                  | 60              | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    |
| Chlorhexidine Gluconate | ≤ 0.16$^{†}$ | 15              | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    |
|                |                  | 30              | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    |
|                |                  | 60              | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    |
|                | ≤ 0.3$^{†}$      | 20              | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    |
|                |                  | 30              | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    |
|                |                  | 60              | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    | NA$^{†}$                    |

* Results interpreted according to European Norm-14476, considering a reduction on viral load ≥ 4 log$_{10}$ as a high efficacy (+), a reduction ≥ 3 log$_{10}$ and < 4 log$_{10}$ as a moderate efficacy (±), and a reduction < 3 log$_{10}$ as a low efficacy (−). † Preprint article. ‡ NA: Not applicable. § Includes concentrations of 0.08%, 0.1%, 0.12%, and 0.16%. ¶ Includes concentrations of 0.04%, 0.05%, 0.07%, 0.075%, 0.1%, and 0.3%.
the viral strain used. Meister and colleagues reported low efficacy results after a 30-second rinse with a CHX mouthrinse with unknown concentration.

Cetylpyridinium chloride (CPC) in vivo virucidal activity was studied in an RCT by Seneviratne and colleagues on a group of 4 hospitalized patients (eTable 4, available online at the end of this article). CPC 0.075% mouthrinse significantly reduced viral load within 5 minutes of use. Compared with the control group, the viral load reduction with CPC was maintained for 3 and 6 hours. In vitro studies have found that CPC-containing mouthrinses have a virucidal effect on SARS-CoV-2 (eTable 5, available online at the end of this article). Considering application times between 30 and 60 seconds (Table 2), concentrations of up to 0.3% showed low to high efficacy.44,47,49,51,55,57 The 20-second application of CPC had moderate to high efficacy.55 Meyers and colleagues reported that a 120-second application of 0.07% CPC showed moderate to high efficacy. Muñoz-Basagoiti and colleagues reported moderate results with a 120-second application of CPC at a concentration of up to 10 mmol (0.3%).

Other mouthrinses, either more complex or with less frequently used active compounds, were studied in vivo and in vitro by several authors (eTables 4 and 5, available online at the end of this article). Carrouel and colleagues studied the effect of a 60-second rinse with a mouthrinse containing citrox and β-cyclodextrin. This study reported a significant decrease in viral load of approximately 13% when using the mouthrinse compared with a 7% decrease observed in the placebo group. Eduardo and colleagues conducted an RCT to study the effect of performing a 60-second H₂O₂ (1.5%) (Peroxyl; Colgate) rinse, combined with a 30-second CHX (0.12%) (Periogard; Colgate) rinse. This combined rinse only achieved minor in Ct values compared with the placebo group. However, when rinsing with a mouthrinse containing CPC (0.075%) and zinc lactate (0.28%), a significant decrease in salivary viral load was achieved for up to 60 minutes. In an uncontrolled before-and-after study, Schürmann and colleagues studied the effect of a 60-second Linola Sept (Dr. Wolff) rinse and reported a mean increase in Ct values of 3.1 (basal versus after rinsing).

In vitro studies included a diversity of complex mouthrinses. Listerine (Johnson & Johnson) mouthrinses were studied by several authors, although each formulation was assessed only in 1 study, apart from Listerine Cool Mint, which was assessed in 2 studies. Listerine mouthrinses showed variable efficacy (Table 3).44,46,47,50
### Table 3. Other mouthrinses in vitro effect on severe acute respiratory syndrome coronavirus 2 oral viral load.*

| MOUTHRINSE                                                                 | CONTACT TIME, S | MEYERS AND COLLEAGUES44 | MEISTER AND COLLEAGUES45 | STATKUTE AND COLLEAGUES47,† | DAVIES AND COLLEAGUES50 | STEINHAUER AND COLLEAGUES48 |
|---------------------------------------------------------------------------|----------------|--------------------------|--------------------------|-----------------------------|-------------------------|-----------------------------|
| Listerine Antiseptic (Johnson & Johnson)                                  | 30             | +                        | NA†                      | NA                          | NA                      | NA                          |
|                                                                             | 60             | +                        | NA                       | NA                          | NA                      | NA                          |
| Listerine Ultra (Johnson & Johnson)                                       | 30             | –                        | NA                       | NA                          | NA                      | NA                          |
|                                                                             | 60             | –                        | NA                       | NA                          | NA                      | NA                          |
| Listerine Cool Mint (Johnson & Johnson)                                   | 30             | NA                       | –                        | NA                          | NA                      | NA                          |
| Listerine Advanced Gum Treatment (Johnson & Johnson)                      | 30             | NA                       | NA                       | +                           | NA                      | NA                          |
| Listerine Advanced Defence Sensitive (Johnson & Johnson)                  | 60             | NA                       | NA                       | NA                          | ±                       | NA                          |
| Listerine Total Care (Johnson & Johnson)                                  | 60             | NA                       | NA                       | +                           | NA                      | NA                          |
| Equate                                                                    | 30             | –                        | NA                       | NA                          | NA                      | NA                          |
|                                                                             | 60             | –                        | NA                       | NA                          | NA                      | NA                          |
| Antiseptic Mouthrinse (CVS)                                               | 30             | –                        | NA                       | NA                          | NA                      | NA                          |
|                                                                             | 60             | –                        | NA                       | NA                          | NA                      | NA                          |
| Dequonal                                                                   | 30             | NA                       | –                        | NA                          | NA                      | NA                          |
| Octenident (Schülke & Mayr)                                               | 30             | NA                       | –                        | NA                          | NA                      | NA                          |
| ProntOral (B. Braum)                                                      | 30             | NA                       | –                        | NA                          | NA                      | NA                          |
| Corsodyl (GlaxoSmithKline)                                                | 30             | NA                       | NA                       | –                           | NA                      | NA                          |
| SCD Max                                                                   | 30             | NA                       | NA                       | –                           | NA                      | NA                          |
| Octenisept (Schülke & Mayr)                                               | 15             | NA                       | NA                       | NA                          | +                       | NA                          |
|                                                                             | 30             | NA                       | NA                       | NA                          | +                       | NA                          |
|                                                                             | 60             | NA                       | NA                       | NA                          | +                       | NA                          |
| OraWize+ (Aqualution Systems)                                             | 60             | NA                       | NA                       | –                           | +                       | NA                          |
| Mouthrinse Containing Ethanol (15.7%), Other Ingredients                  | 30             | NA                       | NA                       | NA                          | NA                      | NA                          |
|                                                                             | 60             | NA                       | NA                       | NA                          | NA                      | NA                          |
| Mouthrinse Containing Zinc Sulfate Heptahydrate, Other Ingredients         | 30             | NA                       | NA                       | NA                          | NA                      | NA                          |
|                                                                             | 60             | NA                       | NA                       | NA                          | NA                      | NA                          |
| Mouthrinse Containing a Mix of Amyloglucosidase, Other Ingredients         | 30             | NA                       | NA                       | NA                          | NA                      | NA                          |
|                                                                             | 60             | NA                       | NA                       | NA                          | NA                      | NA                          |
| Essential Iodine Solution                                                 | 60             | NA                       | NA                       | NA                          | NA                      | NA                          |
| ViruProx (Dr. Wittmann & Co)                                              | 30             | NA                       | NA                       | NA                          | NA                      | NA                          |
| BacterX Pro (EMS)                                                         | 30             | NA                       | NA                       | NA                          | NA                      | NA                          |
| Solution of CPC§ (0.05%) and CHX¶ (0.1%)                                  | 30             | NA                       | NA                       | NA                          | NA                      | NA                          |
| Dental Gel: Anionic Iron Tetracarboxyphthalocyanine (1%)                  | 30             | NA                       | NA                       | NA                          | NA                      | NA                          |
|                                                                             | 60             | NA                       | NA                       | NA                          | NA                      | NA                          |

* Results interpreted according to European Norm-14476, considering a reduction on viral load $\geq 4 \log_{10}$ as a high efficacy (+), a reduction $3 \log_{10}$ and $< 4 \log_{10}$ as a moderate efficacy (±), and a reduction $< 3 \log_{10}$ as a low efficacy (−). eTable 5, available online at the end of this article, can be consulted for assessment of the ingredients of test solutions. † Preprint article. ‡ NA: Not applicable. § CPC: Cetylpyridinium chloride. ¶ CHX: Chlorhexidine gluconate.
Table 3 (Continued)

| GREEN AND COLLEAGUES\(^{39,47}\) | ZOLTAN AND COLLEAGUES\(^{36}\) | KOCH-HEIER AND COLLEAGUES\(^{51}\) | SANTOS AND COLLEAGUES\(^{42}\) | KOMINE AND COLLEAGUES\(^{55}\) | SHEWALE AND COLLEAGUES\(^{39}\) | TIONG AND COLLEAGUES\(^{41}\) | MEISTER AND COLLEAGUES\(^{48}\) |
|----------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
| NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              | NA                              |
DISCUSSION

Summary of evidence

In this systematic review, we included primary studies assessing the virucidal effect of mouthrinses regarding SARS-CoV-2 that had a diverse set of methodologies and assessed a wide range of mouthrinses. PVP-I was the most frequently studied mouthrinse, with most in vitro studies showing some promising results. The results of in vivo studies also pointed to a positive effect of PVP-I on oral viral load reduction, although limitations were found in their methodologies. Similarly, CPC showed positive preliminary results. The use of H2O2 and CHX showed conflicting results on SARS-CoV-2 load reduction in both in vitro and in vivo studies.

To the best of our knowledge, our systematic review is the first to analyze information from both in vivo and in vitro studies. A previous systematic review had assessed in vitro studies, with results consistent with those reported in our study.15

Considering mouthrinses as antiseptics, they should follow regulating norms. The International Organization for Standardization defines in ISO-16408:2015 the chemical and physical properties of

Table 3. Other mouthrinses in vitro effect on severe acute respiratory syndrome coronavirus 2 oral viral load.4

| MOUTHRISE | CONTACT TIME, S | MEYERS AND COLLEAGUES44 | MEISTER AND COLLEAGUES46 | STATKUTE AND COLLEAGUES47,48 | DAVIES AND COLLEAGUES50 | STEINHAUER AND COLLEAGUES53 |
|-----------|----------------|-------------------------|--------------------------|----------------------------|--------------------------|-----------------------------|
| Mouthrinse: Anionic Iron Tetracarboxyphthalocyanine (0.1%) | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| GUM PAROEX (Sunstar Suisse), CHX (0.06%) and CPC (0.05%); GUM PAROEX, CHX (0.12%) and CPC (0.05%) | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| GUM PerioShield (Sunstar) | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| CloSYS Ultra Sensitive Rinse (Rowpar Pharmaceuticals), Sensitive Rinse, Oral Spray, Fluoride Toothpaste | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| Colgate Plax Fruity Fresh (Colgate-Palmolive) | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| Thymol | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| Bactidol (Johnson & Johnson [Philippines]) | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| Salt Water (2%) | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| Carragelose (1.2 mg/mL), Kappa-Carrageenan (0.4 mg/mL), Sodium Chlorite | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| Sodium Chlorite (0.9%), Panthenol | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| Xylometazolin Hydrochloride (1 mg/mL), Dextapanthenol (50 mg/mL); Sodium Hypochlorite (< 0.08%), Lithium Magnesium Sodium Silicate | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| Xylometazolin Hydrochloride (0.1%) | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| Hydroxypropyl Methyl Cellulose, Succinic Acid, Disodium Succinate | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| Galphimia, Luffa Oerculate, Sabadilla | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| Zincum Aceticum, Zincum Gluconium | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
| Anise Oil, Eucalyptus Oil, Levomenthol, Myrrh Extract, Clove Oil, Peppermint Oil Ratanhia Root Extract, Tormentil Root Extract | 30 | NA | NA | NA | NA | NA |
| | 60 | NA | NA | NA | NA | NA |
oral rinses, as well as their test methods, but guidelines for microbiological analysis are specific to mold, bacteria, and yeast, lacking virus instructions. There seems to be a lack of standardization on the evaluation of mouthrinses regarding virucidal properties. According to the EN-14476, an antiseptic is effective when it reduces viral load by 4 \( \log_{10} \) or more. Although EN-14476 is not specific toward oral rinses, owing to the lack of more appropriate regulation, we decided to compare our results in light of this European Norm for assessing mouthrinse virucidal properties.

Included primary studies had substantial diversity in their methodologies and results presentation, limiting our capacity to compare different mouthrinses. PVP-I—based mouthrinses appear to have potential for reducing SARS-CoV-2 in the oral cavity. Nonetheless, these results must be interpreted cautiously. The RCT conducted by Elzein and colleagues had a low RoB and reported a significant decrease in viral load after using mouthrinse. However, neither the RCT conducted by Seneviratne and colleagues, which had a high RoB and included just 16 patients, nor the RCT conducted by Chaudhary and colleagues revealed such a significant decrease. Jayaraman and colleagues did not find a significant decrease in an uncontrolled before-and-after study. It also

| GREEN AND COLLEAGUES | ZOLTAN AND COLLEAGUES | KOCH-HEIER AND COLLEAGUES | SANTOS AND COLLEAGUES | KOMINE AND COLLEAGUES | SHEWALE AND COLLEAGUES | TIONG AND COLLEAGUES | MEISTER AND COLLEAGUES |
|----------------------|-----------------------|---------------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| NA                   | NA                    | NA                        | –                     | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | –                     | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | +                     | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | NA                    | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | NA                    | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | NA                    | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | NA                    | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | NA                    | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | NA                    | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | NA                    | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | NA                    | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | NA                    | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | NA                    | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | NA                    | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | NA                    | NA                    | NA                    | NA                    | NA                    |
| NA                   | NA                    | NA                        | NA                    | NA                    | NA                    | NA                    | NA                    |

Table 3 (Continued)
seems that a dose-response relationship (that is, studies assessing the effect of higher PVP-I concentrations on SARS-CoV-2 viral load do not appear to obtain better results) or a time-response relationship does not exist.

The use of CPC mouthrinses for reducing the viral load also showed encouraging results. CPC has been shown to also be capable of inactivating influenza viruses both in vitro and in vivo but only after 10 minutes of contact time.\(^6^0\)

In the included primary studies, \(\text{H}_2\text{O}_2\) and CHX-based mouthrinses produced varied effects on SARS-CoV-2 viral load. As the effect of these mouthrinses was inconclusive, recommending their use may not be adequate. CHX and \(\text{H}_2\text{O}_2\) already are used in some oral health care products, with CHX displaying broad-spectrum antimicrobial activity,\(^6^1\) including against anaerobic oral bacteria.\(^6^2\) Worldwide government agencies and professional associations advise the use of preprocedural rinse with \(\text{H}_2\text{O}_2\) mouthrinses to reduce oral SARS-CoV-2 viral load,\(^1^0\)-\(^1^4\) so there may be a need to reconsider these directives.

Some complex mouthrinses like Listerine Total Care, Listerine Advanced, and Listerine Antiseptic showed promising results in reducing SARS-CoV-2 viral load in the oral cavity, although they were evaluated in only 1 or 2 studies each. Using these mouthrinses as a coadjuvant in oral health care is well established, contributing to the reduction of dental biofilm and gingivitis.\(^6^3\)

The included primary studies have the limitation of only evaluating the presence of viral particles and not their viability or infectious capacity, and, therefore, other techniques such as viability-PCR could be used to study the infectious potential of the virus. The US Environmental Protection Agency, the Centers for Disease Control and Prevention, and the Lawrence Livermore National Laboratory are developing a rapid viability-reverse transcription PCR to evaluate SARS-CoV-2 viability on surfaces and objects.\(^5^4\) Analyzing aerosols also could be a realistic way to study the impact of dental procedures on the dissemination of viral particles. Choi and colleagues\(^6^5\) performed a study on aerosol sampling in the emergency department of a university hospital, collecting a total of 44 samples, 12 of which were positive to known respiratory viruses—influenza A, influenza D, and adenovirus. Lędnicki and colleagues\(^6^6\) reported the generation of aerosols containing SARS-CoV-2 virions by patients with COVID-19 respiratory manifestations even in the absence of aerosol-generating procedures, which can lead to virus transmission. The authors also were able to quantify the generated viral particles detected from a distance of 2 m or more. These results highlight the importance of preventive measures such as prerinse antiseptic mouthrinse but also a rubber dam isolation, given that both strategies can reduce aerosol pathogen load significantly.\(^6^6,6^7\)

In addition to the wide diversity of methodologies and results presentations of the included studies, a major limitation of our systematic review is the small number of included RCTs, with only 5 meeting eligibility criteria.\(^2^2,2^5,2^7,2^9\) The validity of the conclusions is affected by the bias of the included primary studies, in this case, regarding the high RoB of 2 of the RCTs. Furthermore, the other 5 in vivo studies had important limitations in their designs, including the absence of randomization or even a control group and a relatively low number of included patients, which prompts a low level of evidence and hampers the precision of their estimates, respectively. Although in vitro studies are part of the tests proposed by EN-14476,\(^1^9\) their results cannot be transposed directly to in vivo application of these mouthrinses. In vivo studies should be RCTs that are conducted with a better study design, include a higher number of patients, include a control solution, and express their results as virus logarithmic reduction, allowing a better interpretation of results with a greater level of evidence.

A recurrent inadequacy found in the selected studies was the inclusion of times of application not feasible in clinical practice. Some in vitro studies had application times of 30 minutes,\(^3^1\) and 1 preprint article also considered an application with a duration of 72 hours.\(^5^2\) We find these application times unrealistic and not adequate for clinical practice because patients normally are able to gargle only for a short period,\(^6^6\) usually up to 60 seconds.

**Suggestions for future studies**

There is a need for more in vivo and in vitro studies on different mouthrinses that consider adequate and realistic application times of up to 60 seconds. A well-designed RCT with a larger number of patients should be considered a priority when it comes to design of in vivo studies. On the basis of results from already published primary studies, future studies should focus mainly on mouthrinses based on PVP-I and CPC. Furthermore, the studies should present their results in the form of a
logarithmic reduction that can be compared according to EN-14476. Studying mouthrinse-induced cytotoxicity should be a concern when assessing virucidal properties of different mouthrinses with different concentrations. Studying viral viability after rinsing and viral presence in aerosols should be considered to better assess the real impact of virus dissemination in the dental setting. Overall, guidelines for the standardized evaluation of the effect of mouthrinses on viruses are needed.

CONCLUSIONS

Considering the current knowledge, using PVP-I—based solutions as a preprocedural rinse in the dental setting appears to be potentially effective in reducing SARS-CoV-2 oral load. There are no powerful arguments for considering the use of H2O2 and CHX to be effective regarding SARS-CoV-2 virus, and their use as preprocedural mouthrinses aiming to reduce SARS-CoV-2 oral load should be revised. More RCTs together with in vitro studies are needed to further evaluate mouthrinses based on PVP-I and CPC and test other commercially available mouthrinses showing potential results on SARS-CoV-2 load reduction.

SUPPLEMENTAL DATA

Supplemental data related to this article can be found at: https://doi.org/10.1016/j.adaj.2021.12.007.
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## Table 1. Database search strategy.

| DATABASE                        | QUERY                                                                 |
|---------------------------------|----------------------------------------------------------------------|
| MEDLINE (via PubMed)            | (mouthwash* OR "mouth rinse" OR "oral rinse" OR rinse OR gargl* OR "gargle lavage" OR "oral irrigation" OR "oral lavage") AND (COVID-19 OR COVID19 OR sars-cov-2 OR 2019-nCoV OR COVID OR coronavirus) |
| Scopus                          | (mouthwash* OR "mouth rinse" OR "oral rinse" OR rinse OR gargl* OR "gargle lavage" OR "oral irrigation" OR "oral lavage") AND (covid-19 OR covid19 OR sars-cov-2 OR 2019-ncov OR covid OR coronavirus) |
| Web of Science                  | TS=((mouthwash* OR "mouth rinse" OR "oral rinse" OR rinse OR gargl* OR "gargle lavage" OR "oral irrigation" OR "oral lavage") AND (COVID-19 OR COVID19 OR sars-cov-2 OR 2019-nCoV OR COVID OR coronavirus)) |
| MedRxiv and bioRxiv             | COVID-19 AND mouthwash                                              |
| STUDY                        | IN VITRO | IN VIVO | Randomized Controlled Trials | Uncontrolled Before-and-After Studies |
|-----------------------------|----------|---------|-------------------------------|----------------------------------------|
| **Peer-Reviewed**           |          |         |                               |                                        |
| Anderson and colleagues,    | Yes      | No      | No                            | No                                     |
| 45, 2020                    |          |         |                               |                                        |
| Bidra and colleagues,       | Yes      | No      | No                            | No                                     |
| 30, 2020                    |          |         |                               |                                        |
| Bidra and colleagues,       | Yes      | No      | No                            | No                                     |
| 34, 2020                    |          |         |                               |                                        |
| Frank and colleagues,       | Yes      | No      | No                            | No                                     |
| 33, 2020                    |          |         |                               |                                        |
| Gottsauner and colleagues,  | No       | No      | Yes                           |                                        |
| 20, 2020                    |          |         |                               |                                        |
| Hassandarvish and colleagues,| Yes      | No      | No                            | No                                     |
| 36, 2020                    |          |         |                               |                                        |
| Lamas and colleagues,       | No       | No      | Yes                           |                                        |
| 53, 2020                    |          |         |                               |                                        |
| Meister and colleagues,     | Yes      | No      | No                            | No                                     |
| 46, 2020                    |          |         |                               |                                        |
| Pelletier and colleagues,   | Yes      | No      | No                            | No                                     |
| 32, 2020                    |          |         |                               |                                        |
| Seneviratne and colleagues, | No       | Yes     | No                            | No                                     |
| 27, 2020                    |          |         |                               |                                        |
| Yoon and colleagues,        | No       | No      | Yes                           |                                        |
| 31, 2020                    |          |         |                               |                                        |
| Almanza-Reyes and colleagues,| Yes      | No      | No                            | No                                     |
| 54, 2021                    |          |         |                               |                                        |
| Carrouel and colleagues,    | No       | Yes     | No                            | No                                     |
| 29, 2021                    |          |         |                               |                                        |
| Chaudhary and colleagues,   | No       | Yes     | No                            | No                                     |
| 27, 2021                    |          |         |                               |                                        |
| Davies and colleagues,      | Yes      | No      | No                            | No                                     |
| 57, 2021                    |          |         |                               |                                        |
| Eduardo and colleagues,     | No       | Yes     | No                            | No                                     |
| 28, 2021                    |          |         |                               |                                        |
| Elzein and colleagues,      | No       | Yes     | No                            | No                                     |
| 39, 2021                    |          |         |                               |                                        |
| Jain and colleagues,        | Yes      | No      | No                            | No                                     |
| 40, 2021                    |          |         |                               |                                        |
| Kariwa and colleagues,      | Yes      | No      | No                            | No                                     |
| 53, 2021                    |          |         |                               |                                        |
| Koch-Heier and colleagues,  | Yes      | No      | No                            | No                                     |
| 51, 2021                    |          |         |                               |                                        |
| Komine and colleagues,      | Yes      | No      | No                            | No                                     |
| 55, 2021                    |          |         |                               |                                        |
| Meister and colleagues,     | Yes      | No      | No                            | No                                     |
| 48, 2021                    |          |         |                               |                                        |
| Meyers and colleagues,      | Yes      | No      | No                            | No                                     |
| 44, 2021                    |          |         |                               |                                        |
| Muñoz-Basagoit, and colleagues,| Yes | No | No | No |
| 57, 2021                    |          |         |                               |                                        |
| Santos and colleagues,      | Yes      | No      | No                            | No                                     |
| 52, 2021                    |          |         |                               |                                        |
| Santos and colleagues,      | Yes      | No      | No                            | No                                     |
| 38, 2021                    |          |         |                               |                                        |
| Schürmann and colleagues,   | No       | No      | Yes                           |                                        |
| 24, 2021                    |          |         |                               |                                        |
| Shewale and colleagues,     | Yes      | No      | No                            | No                                     |
| 38, 2021                    |          |         |                               |                                        |
| Shet and colleagues,        | Yes      | No      | No                            | No                                     |
| 54, 2021                    |          |         |                               |                                        |
| Steinhauser and colleagues, | Yes      | No      | No                            | No                                     |
| 43, 2021                    |          |         |                               |                                        |
| Tiong and colleagues,       | Yes      | No      | No                            | No                                     |
| 41, 2021                    |          |         |                               |                                        |
| Xu and colleagues,          | Yes      | No      | No                            | No                                     |
| 37, 2021                    |          |         |                               |                                        |
| Zoltán,                     | Yes      | No      | No                            | No                                     |
| 36, 2021                    |          |         |                               |                                        |
| **Preprint**                |          |         |                               |                                        |
| Green and colleagues,       | Yes      | No      | No                            | No                                     |
| 49, 2020                    |          |         |                               |                                        |
| Mantlo and colleagues,      | Yes      | No      | No                            | No                                     |
| 35, 2020                    |          |         |                               |                                        |
| Muñoz-Basagoiti and colleagues,| Yes | No | No | No |
| 39, 2020                    |          |         |                               |                                        |
| Statkute and colleagues,    | Yes      | No      | No                            | No                                     |
| 47, 2020                    |          |         |                               |                                        |
| Anderson and colleagues,    | Yes      | No      | No                            | No                                     |
| 37, 2021                    |          |         |                               |                                        |
| Jayaraman and colleagues,   | No       | No      | Yes                           |                                        |
| 26, 2021                    |          |         |                               |                                        |
## eTable 3. Risk of bias assessment.

| STUDY                          | RANDOM SEQUENCE GENERATION | ALLOCATION CONCEALMENT | SELECTIVE REPORTING | OTHER SOURCES OF BIAS | BLINDING (PARTICIPANTS AND PERSONNEL) | BLINDING (OUTCOME ASSESSMENT) | INCOMPLETE OUTCOME DATA |
|-------------------------------|-----------------------------|-------------------------|---------------------|-----------------------|----------------------------------------|-------------------------------|------------------------|
| Seneviratn, and Colleagues, 22 | +⁴                           | +                       | +                   | ?                     | +                                      | −                            | +                      |
| Carrouel and Colleagues, 2021 | +                            | +                       | +                   | +                     | +                                      | +                            | ?                      |
| Chaudhary and Colleagues, 2021 | ?                            | +                       | ?                   | ?                     | +                                      | +                            | ?                      |
| Eduardo and Colleagues, 2021  | +                            | +                       | +                   | +                     | −                                      | +                            | +                      |
| Elzein and Colleagues, 2021   | ?                            | +                       | +                   | ?                     | +                                      | +                            | +                      |

*⁺: Low risk of bias. †: Unclear risk of bias. ⁡: High risk of bias.
TABLE 4. In vivo efficacy of different mouthrinses on severe acute respiratory syndrome coronavirus 2 viral load.

| STUDY                      | STUDY DESIGN  | SETTING                                                                 | INCLUDED PARTICIPANTS, NO. | ASSESSMENT OF VIRAL LOAD | PRODUCT, DURATION OF RINSE, S | COMPARISON | RESULTSTS |
|----------------------------|---------------|-------------------------------------------------------------------------|----------------------------|---------------------------|--------------------------------|-------------|-----------|
| Gottsauner and Colleagues, 2020 | Uncontrolled before-and-after study | Hospitalized patients with a positive test for SARS-CoV-2 within the past 72 h with a median age of 55 y. Single rinse performed in a single day. | 10 | Oropharyngeal swab, via RT-PCR† | H2O2 (1%), 30 | NA§ | Viral load decrease of $0.3 \times 10^3$ copies per mL. No significant differences were observed between the baseline viral load and viral load 30 min after the 1% H2O2 mouthrinse ($P = .96$). |
| Lamas and Colleagues, 2020  | Uncontrolled before-and-after study | Hospitalized and home-isolated patients with positive RT-PCR for SARS-CoV-2 in nasopharyngeal exudate with a median age of 63.5 y. Single rinse performed in a single day. | 4 | Nasopharyngeal swab and saliva (method not explained), via RT-PCR | PVP-I (1%), 60 | NA | In 2 of 4 patients, PVP-I resulted in a significant drop ($= 5 \log_{10}$ and $= 2 \log_{10}$ reductions in salivary viral load in each patient), which remained for at least 3 h. |
| Seneviratne and Colleagues, 2020 | RCT# | Hospitalized patients with a nasal swab and saliva RT-PCR positive for SARS-CoV-2. Mean (SD**) age per group: PVP-I (n = 4), 40.7 (11.5) y; CHX†† (n = 6), 43.6 (8.6) y; CPC‡‡ (n = 4), 35.7 (8.5) y; water (n = 2), 36 (14.1) y. Single rinse performed in a single day. | 16 | Saliva (passive drool), via RT-PCR | PVP-I (0.5%), 30 CHX (0.2%), 30 CPC (0.075%), 30 Water | Ct§§ values detected in all 16 patients were within the range of 15.6-34.5, with a mean (SD) value of 27.7 (4.8); results are presented in form of fold change calculated as a ratio between Ct value at different time points and Ct value at baseline. PVP-I: significant increase in fold change was obtained only at 6 h (ratio = 1) post rinsing with PVP-I in comparison with water ($P < .01$). In comparison with the water group, the PVP-I group patients had higher fold increases in Ct value after 5 min (ratio = 1.1) and 3 h (ratio = 1.2) of postrinsing, but no significance was achieved. CHX: patients showed a varied effect among saliva Ct values after 5 min rinsing, and hence further studies with a larger sample size are required to determine its significance. CPC: significant increase in fold change of Ct value at 5 min (ratio = 1) and 6 h (ratio = 0.9) was observed postrinsing with CPC mouthrinse compared with the water group patients ($P < .05$). Although the fold changes in Ct values were higher at 3 h (ratio = 0.9) in the CPC group, no significance was achieved ($P = .20$). |
| Yoon and Colleagues, 2020  | Uncontrolled before-and-after study | Hospitalized patients with a diagnosis of COVID-19 with a median age of 55.5 y. One rinse per day on 2 nonconsecutive days (days 3 and 6 of the study). | 2 | Saliva (method not specified), via RT-PCR | CHX (0.12%), 30 | NA | The viral load in the saliva decreased transiently for 2 h after using the CHX mouthrinse, but it increased again at 2-4 h postrinsing. On day 3, viral load was not detected at 1 h and 2 h postrinsing, on both patients. One of the patients showed a baseline viral load of 6.9 log_{10} and the other of 4.9 log_{10}. On day 6, 1 h after using the mouthrinse, there was no reduction in viral load in 1 patient. |

* SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2. † RT-PCR: Reverse transcription polymerase chain reaction. ‡ H2O2: Hydrogen peroxide. § NA: Not applicable. ¶ PVP-I: Povidone-iodine. # RCT: Randomized clinical trial. ** SD: Standard deviation. †† CHX: Chlorhexidine gluconate. ‡‡ CPC: Cetylpyridinium chloride. §§ Ct: Cycle threshold. ¶¶ CDCM: Mouthrinse containing β-cyclodextrin and citrox. ## RT-PCR: Reverse transcription polymerase chain reaction.
| STUDY                  | STUDY DESIGN | SETTING                                      | INCLUDED PARTICIPANTS, NO. | ASSESSMENT OF VIRAL LOAD | PRODUCT, DURATION OF RINSE, S | COMPARISON                      | RESULTS |
|-----------------------|--------------|----------------------------------------------|---------------------------|--------------------------|-------------------------------|--------------------------------|---------|
| Carrouel and Colleagues, 2021 | RCT          | Home-isolated patients with a diagnosis of COVID-19. Mean (SD) age per group: placebo (n = 88), 44.08 (16.16) y; CDCM (n = 88), 42.06 (14.97) y; 3 rinses per day, for 7 days | 176 | Saliva (method not specified), via (rt)RT-PCR | CDCM: β-cyclodextrin (0.1%) and citrox (0.1%), 60 s | Similar appearance and content solution without antiviral components | Day 1: A significant difference was observed in viral load reduction in the before-and-after comparison of the same patients receiving CDCM versus no difference for the placebo group from T1 (first sample other than basal on day 1) to T2 (second sample other than basal on day 1) (P = .036). The percentage median decrease (log10 copies/mL) was −12.6% (−29.6% to −0.2%) (CDCM) versus −6.7% (−21.2% to 10.4%) (placebo). At T3 (third sample other than basal on day 1), the salivary viral load decreases were significant for both groups compared with T1 (CDCM: P < .001; placebo: P = .002) but with no significant difference between the 2 groups. 7 days: continuous decrease for the CDCM group and the placebo group was observed for 7 days. On day 7, no significant difference between patients receiving CDCM and those receiving placebo (P = .388). In both groups, the viral load was significantly lower on day 7 than on day 1 T1 (P < .001) |
| Chaudhary and Colleagues, 2021 | RCT          | Hospitalized symptomatic adults (aged 21-80 y) with a diagnosis of COVID-19 via PCR. Median (range) age, 64 (25-82) y. Each mouthrinse group consisted of 10 participants. 2 consecutive rinses on a single day. | 40 | Saliva (passive drool), via PCR | PVP-I (0.5%), 30 s and 30 s H₂O₂ (1%), 30 s and 30 s CHX (0.12%), 30 s and 30 s Normal saline, 30 s and 30 s | RNA from trizol-inactivated virus as positive control | After 15 min, CHX (0.12%), H₂O₂ (1%), and normal saline reduced viral load by 90%. However, PVP-I (0.5%) only reduced the viral load by approximately 61% 15 min after the rinse. After 30 min, H₂O₂ (1%) and normal saline reduced the viral load by approximately 90%, whereas CHX (0.12%) led to an approximately 70% reduction. However, PVP-I (0.5%) led to a 97% reduction on viral load 30 min after the rinse. |
| STUDY           | DESIGN  | SETTING                                    | INCLUDED PARTICIPANTS, NO. | ASSESSMENT OF VIRAL LOAD | PRODUCT, DURATION OF RINSE, S | COMPARISON | RESULTS                                                                 |
|-----------------|---------|--------------------------------------------|----------------------------|--------------------------|-----------------------------|------------|-------------------------------------------------------------------------|
| Eduardo and Colleagues, 2021 | RCT     | Hospitalized (for up to 3 d) adults (aged 18-80 y), previously received a diagnosis of COVID-19 via nasal swab qualitative RT-PCR with mild to moderate symptoms. | 43                         | 0.075% CPC (0.075%) + zinc lactate (0.28%) | Distilled water | Significant difference in the mean (SD) Ct value was observed for CPC and zinc lactate (20.4 [3.7]-fold reduction), H2O2 (15.8 [0.08]-fold reduction), and H2O2 and CHX (2.1 [0.5]-fold reduction) immediately after the rinse (T1), when compared with baseline. 30 min after rinsing (T2), H2O2 had a significant mean (SD) reduction in viral load (6.5 [3.4]-fold reduction). CPC and zinc lactate had a significant reduction in mean (SD) Ct values up to 60 min (T3) after the rinsing (6.5 [3.4]-fold reduction), which was not observed after rinsing with H2O2 (0.3 [1.3]-fold reduction). CHX achieved a greater than 2-fold mean (SD) reduction (T1, 2.1 [1.5]-fold; T2, 6.2 [3.8]-fold; T3, 4.2 [2.4]-fold reductions). H2O2 and CHX and the placebo presented minor changes in mean (SD) Ct values across all time points assessed (T1, 2.1 [0.5]-fold reduction; T2, 1.6 [0.2]-fold reduction; T3, 3.9 [0.3]-fold reduction). CPC and zinc lactate mouthrinse and CHX led to a significant reduction in the SARS-CoV-2 viral load in saliva up to 60 min, whereas H2O2 provided a significant reduction up to 30 min after rinsing. |
| Elzein and Colleagues, 2021 | RCT     | Hospitalized patients with a diagnosis of COVID-19. Mean (SD) age per group: PVP-I group (n = 27), 39.9 (14.2) y; CHX group (n = 25), 47 (15.4) y; distilled water group (control) (n = 9), 57.2 (22.5) y. Single rinse performed in a single day. | 61                         | PVP-I (1%), 30 s CHX (0.2%), 30 s | Water          | Baseline: mean (SD) Ct value of human ribonuclease P in saliva samples before mouthrinse was 25.4 (2.5) (range, 18.4-32.2); 5 min after for CHX and PVP-I: mean (SD) Ct value of human ribonuclease P in saliva samples after mouthrinse was 26 (2.7) (range, 19.4-32.5). No significant difference was found between the mean Ct values of human ribonuclease P in the 2 groups (P = .332). PVP-I: significant mean (SD) difference between the paired samples before (29.9 [6.2]; median, 30.8) and after mouthrinse (34.4 [6.3]; median, 34.2) with 1% PVP-I (P < .0001). CHX: higher significant difference of means was found in paired samples using CHX 0.2% (P < .0001). The mean Ct increased 5.7 after mouthrinse. The mean (SD) Ct of pre- and postmouthrinse was 27.7 (7.2) (median, 27.1) and 33.9 (7.1) (median, 33.1), respectively. |
| STUDY             | STUDY DESIGN       | SETTING                                      | INCLUDED PARTICIPANTS, NO. | ASSESSMENT OF VIRAL LOAD | PRODUCT, DURATION OF RINSE, S | COMPARISON | RESULTS |
|------------------|---------------------|----------------------------------------------|---------------------------|--------------------------|-------------------------------|-------------|---------|
| Jayaraman and Colleagues, 2021 | Uncontrolled before-and-after study | Hospitalized patients with a diagnosis of COVID-19. Single rinse performed in a single day. | 36 | Saliva (passive drool) and exhaled respiratory droplets, via RT-PCR | PVP-I (1%); H2O2 (1.5%); CHX (0.2%) | NA | The mean (SD) reduction was significantly higher in respiratory droplets (92%) than in whole saliva samples (50%; \( P = .008 \)). PVP-I:  
- salvia 20 min: 1.8 (1.1) log10 reduction 60 min: 1.3 (0.9) log10 reduction - respiratory droplets 20 min: 2.5 (0.4) log10 reduction 60 min: 1.6 (1.9) log10 reduction  
- H2O2:  
- salvia 20 min: 1.2 (0.3) log10 reduction 60 min: 1.6 (1.6) log10 reduction 90 min: 1.5 (1.5) log10 reduction 180 min: 0.9 (0.8) log10 reduction -respiratory droplets 20 min: 3.5 (3.7) log10 reduction 60 min: 2.5 (2.8) log10 reduction 90 min: 1.9 (1.6) log10 reduction 180 min: 3.0 (0.03) log10 reduction  
- CHX:  
- salvia 90 min: 1.6 (1.2) log10 reduction 180 min: 0.4 (1.5) log10 reduction -respiratory droplets 90 min: 1.2 (0.8) log10 reduction 180 min: 0.6 (1.7) log10 reduction | |
| Schürmann and Colleagues, 2021 | Uncontrolled before-and-after study | Hospitalized patients with a diagnosis of COVID-19. Single rinse performed in a single day. | 34 | Pharyngeal swab, via RT-qPCR | Linola Sept (Dr. Wolff) (analogous composition to Biorepair Zahnmilch: aqua, sorbitol, xylitol, zinc hydroxyapatite, cellulose gum, zinc pyrrolidine carboxylic acid, aroma, peg-40, hydrogenated castor oil, sodium lauryl sulfate, sodium myristoyl saroninate, sodium methyl, cocoyl taurate, lactoferrin, sodium hyaluronate, sodium saccharin, sodium benzoate, phenoxyethanol, benzyl alcohol), 60 s | NA | The mean (SD) of Ct values before rinsing was 26.0 (5.8). The overall mean (SD) of Ct values after rinsing was 29.1 (6.1). Mean (SD) values showed an increase of the Ct values of 3.1 (0.6), which translated into a significant reduction of the viral load in the pharynx of about 90%. Most patients exhibited a 10-fold reduction of viral load, independently of the initial viral load. The viral load required approximately 6 h to recover to the initial viral load. Moreover, highly infectious patients were able to restore their initial viral load during this time, whereas less infectious patients were not able to restore their initial infectivity 6 h after gargling. | |
| STUDY | SARS-COV-2* STRAIN, CELLULAR LINE | TEST MOUTHRINSES, CONCENTRATION (%) | COMPARISON | INTERFERING SUBSTANCES | CONTACT TIME | RESULTS |
|-------|---------------------------------|-------------------------------------|------------|------------------------|--------------|---------|
| PVP-I† |                                 |                                     |            |                        |              |         |
| Anderson and colleagues,45 2020 | hCoV-19/Singapore/2/2020; Vero E6 | Antiseptic solution: PVP-I (10); antiseptic skin cleanser: PVP-I (7.5); gargle and mouthrinse: PVP-I (1.0), 1:2 dilution; throat spray: PVP-I (0.45) | PBS‡ | Dirty (0.3 g/L BSA§) | 30 s | ≥ 4 log₁₀ reduction of SARS-CoV-2 titers, for all the products |
| Bidra and colleagues,30 2020 | USA-WA1/2020; Vero 76 | PVP-I (0.5, 1.25, 1.5) | Water; ethanol (70%) | Clean | 15 s 30 s | 15 s: > 4.3 log₁₀ reduction of the infectious virus for all concentrations 30 s: > 3.6 log₁₀ reduction of the infectious virus for all concentrations |
| Bidra and colleagues,34 2020 | USA-WA1/2020; Vero 76 | PVP-I (0.5, 0.75, 1.5) | Water; ethanol (70%) | Clean | 15 s 30 s | 15 s: the solutions reduced > 3 log₁₀ of the viral load 30 s: the tested solutions reduced > 3.3 log₁₀ of the viral load |
| Frank and colleagues,33 2020 | USA-WA1/2020; Vero 76 | PVP-I (0.5, 1.25, 2.5) | Water; ethanol (70%) | Clean | 15 s 30 s | 15 s: the solutions tested were effective at reducing the viral load > 3 log₁₀ for all concentrations 30 s: the solutions were effective at reducing the viral load > 3.3 log₁₀ for all concentrations |
| Hassandarvish and colleagues,56 2020 | SARS-COV-2/MY/UM/6-3, TIDREC; Vero E6 | PVP-I (0.5, 1) | Water | Clean; dirty (3.0 g/L BSA and 3 mL/L human erythrocytes) | 15 s 30 s 60 s | 15 s: 1% PVP-I reduced > 5 log₁₀ viral titers. 0.5% PVP-I reduced > 4 log₁₀ viral load 30 s: 0.5% and 1% PVP-I reduced > 5 log₁₀ viral titers 60 s: 0.5% and 1% PVP-I reduced > 5 log₁₀ viral titers |
| Meister and colleagues,46 2020 | BetaCoV/Germany/Ulm01/2020, BetaCoV/Germany/Ulm02/2020, UKEssen; Vero E6 | Iso-Betadine mouthrinse 1.0%; PVP-I (1) | Cell culture medium | Dirty (100 µL mucin type I-S, 25 µL BSA Fraction V, and 35 µL yeast extract) | 30 s | Iso-Betadine mouthrinse reduced viral infectivity to up to 3 log₁₀ |
| Pelletier and colleagues,32 2020 | USA-WA1/2020; Vero 76 | Oral rinse PVP-I antiseptic (0.5, 0.75, 1.5)† | Water; ethanol (70%) | Clean | 60 s | After incubation with each nasal/oral antiseptic, viral load decrease of > 4 log₁₀ infectious viruses for all concentrations |
| Statkute and colleagues,47 2021 | England 2; Vero E6 | Videne: PVP-I (7.5) | NA** | Dirty (100 µL mucin type I-S, 25 µL BSA Fraction V, and 35 µL yeast extract) | 30 s | Videne had an effect of ≈ 3 log₁₀ reduction |
| Davies and colleagues,50 2021 | England 2; Vero E6 | Povident: PVP-I (0.58) | PBS | Clean | 60 s | ≥ 4.1 log₁₀ reduction or†† > 5.2 log₁₀ reduction |
| Jain and colleagues,40 2021 | SARS-CoV-2 strain used was isolated from a patient; Vero E6 | PVP-I (1) | NA | Clean | 30 s 60 s | 30 s: 99.8% inactivation 60 s: > 99.9% inactivation |

* SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2. † PVP-I: Povidone-iodine. ‡ PBS: Phosphate buffered saline. § BSA: Bovine serum albumin. ¶ A nasal PVP-I antiseptic (0.5%, 1.25%, 2.5%) was studied as a complement to the oral antiseptic. # Preprint article. ** NA: Not applicable. †† Depending on initial viral concentration (higher, lower). †‡ RLU: Relative light units. §§ H₂O₂: Hydrogen peroxide. ‖ CHX: Chlorhexidine gluconate. ## CPC: Cetylpyridinium chloride. *** pfu/mL: Plaque forming units per milliliter. ‡‡‡ TCID₅₀/mL: Median tissue culture infectious dose per milliliter. §§§ ppm: Parts per million. ††† APD: Anionic.
**Table 5. Continued**

| STUDY | SARS-COV-2* STRAIN, CELLULAR LINE | TEST MOUTHRINSES, CONCENTRATION (%) | COMPARISON | INTERFERING SUBSTANCES | CONTACT TIME | RESULTS |
|-------|-----------------------------------|-------------------------------------|------------|-----------------------|-------------|---------|
| Kariwa and colleagues, WK-521; Vero E6, 2021 | Isodine Gargle (ethical product) at 2 different concentrations: PVP-I (0.23) and PVP-I (0.47) | NA | Clean | 30 s Isodine Gargle (ethical product) PVP-I (0.23%); 30 s: > 3.1 log_{10} 60 s: > 3.6 log_{10} | 60 s: > 3.6 log_{10} Isodine Gargle (ethical product) PVP-I (0.47%); 30 s: > 3.2 log_{10} 60 s: > 4.0 log_{10} Isodine Gargle (consumer product) PVP-I (0.23%); 30 s: > 3.1 log_{10} 60 s: > 3.6 log_{10} Isodine Gargle C (consumer product) PVP-I (0.35%); 30 s: > 3.2 log_{10} 60 s: > 3.6 log_{10} Isodine Nodo Fresh (consumer product) PVP-I (0.45%); 30 s: > 3.8 log_{10} 60 s: > 3.8 log_{10} |
| Meyers and colleagues, HCoV 229e; HUH7, 2021 | Betadine 5%: PVP-I (5) | NA | Dirty (200 μL of 5% BSA) | 30 s: Decrease in viral load between > 3 log_{10} and < 4 log_{10} 60 s: Decrease in viral load between > 3 log_{10} and < 4 log_{10} 120 s: > 4 log_{10} reduction in viral load | 60 s: > 4 log_{10} 120 s: > 4 log_{10} reduction in viral load |

*Note: HCoV 229e is a coronavirus strain commonly used for testing viral inhibition.*
| Study | SARS-CoV-2 Strain, Cellular Line | Test Mouthrines, Concentration (%) | Comparision | Interfering Substances | Contact Time | Results |
|-------|---------------------------------|---------------------------------|-------------|------------------------|-------------|---------|
| Shet and colleagues, 2021 | Coronavirus strain OC43, coronavirus strain NL63, and coronavirus strain 229E; MRC-5, Vero CCL-81, and HCT-8 cells | PVP-I solution (0.5, 10) | Clean | PVP-I (0.5)% solution: | < 15 s | OC43 strain: 4 log₁₀ reduction (< 15 s); ≥ 5.75 log₁₀ reduction (15 s, 30 s, 60 s, and 5 min); NL63 strain: 4.75 log₁₀ reduction (< 15 s); ≥ 5.25 log₁₀ reduction (15 s, 30 s, 60 s, and 5 min); 229E strain: 3.75 log₁₀ reduction (< 15 s); 4.25 log₁₀ reduction (15 s); ≥ 5.25 log₁₀ reduction for contact times of 15 s, 30 s, 60 s, and 5 min | |
| Xu and colleagues, 2021 | USA-WA1/2020; HEK293T, HeLa | PVP-I (10) at different final dilutions (5, 0.5, and 0.05) | NA | No information available | 30 min | Only the 5% dilution of PVP-I was effective in inactivating the viruses (0 RLU) |
| H₂O₂ | USA-WA1/2020; Vero 76 | H₂O₂ (1.5, 3) | Water; ethanol (70%) | Clean | 15 s | 15 s: H₂O₂ (1.5%) reduced 1.3 log₁₀ infectious virus. H₂O₂ (3%) reduced 1.0 log₁₀ infectious virus 30 s: H₂O₂ (1.5%) reduced 1.0 log₁₀ infectious virus H₂O₂ (3%) reduced 1.8 log₁₀ infectious virus |
| STUDY | SARS-COV-2* STRAIN, CELLULAR LINE | TEST MOUTHRINSES, CONCENTRATION (%) | COMPARISON | INTERFERING SUBSTANCES | CONTACT TIME | RESULTS |
|-------|----------------------------------|-----------------------------------|------------|-----------------------|--------------|---------|
| Koch-Heier and colleagues, 2020 | SARS-CoV-2 Isolate "FI-100"; Vero E6 | H$_2$O$_2$ (1.5) | Nonvirucidal medium control of SARS-CoV-2 with infection medium; no-virus control containing infection medium and test solution | Clean | 30 s | H$_2$O$_2$ (1.5%) showed no effective reduction of the virus titer |
| Meister and colleagues, 2020 | BetaCoV/Germany/Ulm01/2020, BetaCoV/Germany/ Ulm02/2020, UKEssen; Vero E6 | Cavex oral rinse: H$_2$O$_2$ (concentration unknown) | Cell culture medium | Dirty (100 μL mucin type I-S, 25 μL BSA Fraction V, and 35 μL yeast extract) | 30 s | Viral load decrease between 0.3 log$_{10}$ and 1.8 log$_{10}$ |
| Davies and colleagues, 2021 | England 2; Vero E6 | Peroxyl: H$_2$O$_2$ (1.5) | PBS | Clean | 60 s | Reduction of the virus titer by 0.2 log$_{10}$ |
| Meyers and colleagues, 2021 | HCoV 229e; HUH7 | Peroxide Sore Mouth Cleanser: H$_2$O$_2$ (1.5%); H$_2$O$_2$ solution diluted to 1.5% in PBS: H$_2$O$_2$ (1.5%); Orajel Antiseptic Rinse: H$_2$O$_2$ (1.5%); menthol (0.1) | NA | Dirty (200 μL of 5% BSA) | 30 s | Virus load reduction between <1 log$_{10}$ and 2 log$_{10}$ for all concentrations and contact times |
| Xu and colleagues, 2021 | USA-WA1/2020, HEK293T, HeLa | Colgate Peroxyl: H$_2$O$_2$ (1.5) at different dilutions (0.75, 0.075, and 0.0075) | NA | No information available | 30 min | Colgate Peroxyl (0.75% and 0.075%) was effective in inactivating the viruses (0 RLU) |
| Koch-Heier and colleagues, 2020 | SARS-CoV-2 Isolate "FI-100"; Vero E6 | CHX (0.1) | Nonvirucidal medium control of SARS-CoV-2 with infection medium; no-virus control containing infection medium and test solution | Clean | 30 s | CHX (0.1%) showed no effective reduction of the virus titer |
| Meister and colleagues, 2020 | BetaCoV/Germany/Ulm01/2020, BetaCoV/Germany/ Ulm02/2020, UKEssen; Vero E6 | Chlorhexamed Forte: CHX (concentration unknown); Dynexidin Forte 0.2%: CHX (0.2%) | Cell culture medium | Dirty (100 μL mucin type I-S, 25 μL BSA Fraction V, and 35 μL yeast extract) | 30 s | Viral load decrease between 0.3 log$_{10}$ and 1.8 log$_{10}$ |
| Anderson and colleagues, 2021 | USA-WA1/2020, Alpha isolate: hCoV-19/England/ 204820464/2020, Beta isolate: hCoV-19/South Africa/KRISP-EC-K005321, and Gamma isolate: hCoV-19/Japan/Y7-503/2021; Vero E6 | CHX (0.2) with flavor | Ethanol (70%) | Clean; dirty (human saliva) | 30 s | USA-WA1/2020: CHX (0.2%) led to a 1.26 log$_{10}$ reduction; alpha isolate: 3.11 log$_{10}$ reduction; beta isolate: 4.11 log$_{10}$ reduction; gamma isolate: 3.36 log$_{10}$ reduction |
| Davies and colleagues, 2020 | England 2; Vero E6 | CHX antiseptic mouthrinse: CHX (0.2); Corsodyl (alcohol-free mint flavor): CHX (0.2) | PBS | Clean | 60 s | CHX antiseptic mouthrinse: 0.5 log$_{10}$ reduction; Corsodyl: 0.4 log$_{10}$ reduction |
| Jain and colleagues, 2021 | SARS-CoV-2 strain used was isolated from a patient; Vero E6 | CHX (0.12) and CHX (0.2) | NA | Clean | 30 s | For 30 s and 60 s: CHX (0.12%) led to a 99.9% inactivation. CHX (0.2%) led to a > 99.9% inactivation |
| Komine and colleagues, 2021 | JPN/TY/WK-521 strain; VeroE6/TMPRSS2 | GUM PAROEX: CHX (0.12) | PBS, ethanol (70%) | Clean | 30 s | GUM PAROEX (0.12%) led to a 0.2 log$_{10}$ reduction |
| Steinhauer and colleagues, 2021 | No available information | CHX (0.1 and 0.2) used in different dilutions (0.08 and 0.16) | Formaldehyde | Clean | 15 s | Both formulations had > 1 log$_{10}$ reduction of the viral load after 60 s and 5 min (CHX 0.2%) and after 10 min (CHX 0.1%) |
| STUDY | SARS-COV-2 STRAIN, CELLULAR LINE | TEST MOUTHRINSES, CONCENTRATION (%) | COMPARISON | INTERFERING SUBSTANCES | CONTACT TIME | RESULTS |
|-------|----------------------------------|--------------------------------------|------------|------------------------|--------------|---------|
| Tiong and colleagues, 2021 | SARS-CoV-2 strain was used isolated from a patient, SARS-CoV-2/MyUM/6-3 TIDREC (virus stock); Vero E6 | | | Clean; dirty (0.3 g/L BSA a 3 mL/L human erythrocytes) | | Reduction of 4 log<sub>10</sub> for all test times and conditions |
| Xu and colleagues, 2021 | USA-WA1/2020; HEK293T, HeLa | CHX (0.12) used in different final dilutions (0.06, 0.006, and 0.0006) | | No information available | | CHX (0.06%) was effective in inactivating the viruses (0 RU). CHX (0.006%) had a moderate anti-viral effect (> 2 x 10<sup>6</sup> RU) |
| CPC## | HCoV-SARS 229E; MRC-5 | Mouthrinse containing CPC (0.07), sodium fluoride, and flavor oil | | | | Viral load decrease of 3.1 log<sub>10</sub> for all contact times |
| Koch-Heier and colleagues, 2020 | SARS-CoV-2 Isolate "FI-100"; Vero E6 | CPC (0.05) | Nonvirucidal medium control of SARS-CoV-2 with infection medium; no-virus control containing infection medium and test solution | | | CPC (0.05%) reduced virus titer by 5.6 x 10<sup>4</sup> pfu/mL*** (0.7 log<sub>10</sub>) |
| Muñoz-Basagoiti and colleagues, 2020 | SARS-CoV-2 isolated from a nasopharyngeal swab; Vero E6 | Vitis CPC Protec: 2.063 mM of CPC; CPC: 10 mM of CPC diluted in distilled water | | | | Viral load decreased by 3 log<sub>10</sub> for all test solutions |
| Statkute and colleagues, 2020 | England 2; Vero E6 | Dentyflu Dual Action: CPC (0.05-0.1). Other active ingredients: isopropyl myristate, mentha arvensis extract. Dentyflu Fresh Protect: CPC (0.05-0.1). Other active ingredients: xylitol | | Dirty (100 µL mucin type I-S, 25 µL BSA Fraction V, and 35 µL yeast extract) | 30 s | Dentyflu mouthrinses completely eliminated the virus (> 5 log<sub>10</sub> reductions) |
| Anderson and colleagues, 2021 | USA-WA1/2020, Alpha isolate: hCoV-19/England/204820464/2020, Beta isolate: hCoV-19/South Africa/KRISP-EC-K005321, and Gamma isolate: hCoV-19/Japan/TY7-503/2021; Vero E6 | CPC (0.07), with flavor and mix of herbal extracts; CPC (0.07), with flavor | | Clean; dirty (human saliva) | 30 s | USA-WA1/2020; both CPC mouthrinses led to a ≥ 4 log<sub>10</sub> reduction; Alpha isolate: both mouthrinses led to a 3.11 log<sub>10</sub> reduction; Beta isolate: both mouthrinses led to a 4.11 log<sub>10</sub> reduction; Gamma isolate: both mouthrinses led to a 3.36 log<sub>10</sub> reduction |
| Komine and colleagues, 2021 | JPN/TY/WK-521 strain; VeroE6/TMPRSS2 | GUM WELL PLUS Dental paste: CPC (0.0125); GUM MOUTHWASH HERB 2020: CPC (0.04); GUM WELL PLUS dental rinse (alcoholic type): CPC (0.05); GUM WELL PLUS dental rinse (nonalcoholic type): CPC (0.05); GUM Oral Rinse: CPC (0.075); GUM disinfection spray for mouth/throat: CPC (0.3) | PBS, ethanol (70%) | | 20 s | 20 s: GUM MOUTHWASH HERB 2020 (0.04%) led to > 4.4 log<sub>10</sub> reduction; dental rinse (alcoholic type) (0.05%) led to a 4.2 log<sub>10</sub> reduction, and GUM WELL PLUS dental rinse (nonalcoholic type) (0.05%) led to a 4.1 log<sub>10</sub> reduction. GUM disinfection spray for mouth/throat (0.3%) achieved a > 3.4 log<sub>10</sub> reduction 30 s: GUM Oral Rinse (0.075%) led to a > 4.3 log<sub>10</sub> reduction 3 min: GUM WELL PLUS dental paste (0.0125%) led to a 3.3 log<sub>10</sub> reduction |
| Meyers and colleagues, 2021 | HCoV 229e; HUH7 | Crest Pro-Health: CPC (0.07) | | Dirty (200 µL of 5% BSA) | | Crest Pro-Health decreased viral load by at least 3 log<sub>10</sub> to > 4 log<sub>10</sub> for all contact times |
Table 5. Continued

| STUDY                          | SARS-COV-2* STRAIN, CELLULAR LINE | TEST MOUTHRINSES, CONCENTRATION (%) | COMPARISON                                                                 | INTERFERING SUBSTANCES | CONTACT TIME | RESULTS                                                                 |
|-------------------------------|-----------------------------------|--------------------------------------|---------------------------------------------------------------------------|------------------------|--------------|-------------------------------------------------------------------------|
| Muñoz-Basagoiti and colleagues, 2021 | SARS-CoV-2 D614G (isolated from a nasopharyngeal swab) and SARS-CoV-2 B.1.1.7; Vero E6 | Vitis Encias: with 1.47 mM of CPC (or 0.05); Vitis CPC Protect with 2.063 mM of CPC (or 0.07); CPC, 10 mM | Vehicles containing the same formulation but without CPC; virus mixed with 1 mL of media as positive control | Clean; dirty (saliva) | 30 s 60 s 120 s | 30 s: Vitis CPC decreased 10-fold (1 log10) the TCID50/mL††† of the B.1.1.7 SARS-CoV-2 variant (compared with untreated virus) 60 s: There was a reduction of infectivity above 1,000 (>3 log10) times regardless of the variant used or the duration of exposure to Vitis CPC 120 s: High doses of CPC (10 mM) effectively suppressed viral infection. CPC-containing mouthrinses decreased approximately 1,000 times the TCID50/mL of SARS-CoV-2, whereas vehicles had no impact on SARS-CoV-2 infectivity when compared with untreated virus |
| Other Mouthrinses

|Green and colleagues, 2020 | HCoV-SARS 229E; MRC-5 | Mouthrinse containing ethanol (15.7), sodium fluoride, and flavor oil | NA | Clean | 30 s 60 s | Contact with ethanol, zinc, and enzyme and protein mouthrinses did not provide a substantial reduction in viral counts. Zinc: after 30 s, mean (SD) reduction of 1.2 (0.4) log10; after 60 s, mean (SD) reduction of 1.8 (0.1) log10; enzymes and proteins: after 30 s, mean (SD) reduction of 0.3 (0.3) log10; after 60 s, mean (SD) reduction of 0.2 (0.3) log10; ethanol: after 30 s, mean (SD) reduction of 0.2 (0.3) log10; after 60 s, mean (SD) reduction of 0.3 (0.3) log10 |
|Mantlo and colleagues, 2020 | USA-WA1/2020, Vero Cells | CupriDyne: iodine and cuprous iodide (250 ppm,** 25 ppm, 2.5 ppm) | Water (boiling and at room temperature) | Clean | 10 min 30 min 60 min | CupriDyne (25 ppm or 2.5 ppm) was not found to cause a significant difference in SARS-CoV-2 titers; CupriDyne (250 ppm) was shown to effectively inactivate the virus to a significant extent after 10, 30, and 60 min. After incubation with undiluted (250 ppm) CupriDyne for 10 min, viral titers dropped by 1 log10. Viral titers dropped 2 log10 after incubation with undiluted CupriDyne for 30 min. Further incubation with undiluted CupriDyne for 60 min reduced viral titers below the limit of detection. |
|Meister and colleagues, 2020 | BetaCoV/Germany/Ulm01/2020, BetaCoV/Germany/Ulm02/2020, UKEssen; Vero E6 | Dequonal: dequalinium chloride, benzalkonium chloride; Listerine Cool Mint: ethanol, essential oils; Otcenident mouthrinse: octenidine dihydrochloride; ProntOral mouthrinse: polyaminopropyl biguanide (polyhexanide) | Cell culture medium Dirty (100 μL mucin type I-S, 25 μL BSA Fraction V, and 35 μL yeast extract) | Dirty | 30 s | Dequonal and Listerine Cool Mint significantly reduced viral infectivity to up to 3 log10. Otcenident virucidal activities could be observed with reduction factors ranging between 0.3 log10 and 1.8 log10. With ProntOral, 1 strain was only moderately reduced, and the other 2 strains were inactivated. |
|Muñoz-Basagoiti and colleagues, 2020 | SARS-CoV-2 isolated from a nasopharyngeal swab; Vero E6 | Perio Aid Intensive Care: 1.47 Culture cell media mM of CPC and 1.33 mM of CHX | Clean | 120 s | No impact on SARS-CoV-2 infectivity, when compared with untreated virus |
| STUDY                                      | SARS-COV-2+ STRAIN, CELLULAR LINE | TEST MOUTHRINSES, CONCENTRATION (%) | COMPARISON | INTERFERING SUBSTANCES | CONTACT TIME | RESULTS |
|-------------------------------------------|-----------------------------------|-------------------------------------|------------|------------------------|--------------|---------|
| Statkute and colleagues, 2020             | England 2; Vero E6               | Corsodyl: ethanol (7), CHX (0.2); other active ingredient, peppermint oil Listerine Cool Mint: ethanol (21); other active ingredients: thymol (0.064), eucalyptol (0.092), methyl salicylate (0.060), and menthol (0.042) Listerine Advanced Gum Treatment: ethanol (23); other active ingredient: ethyl lauroyl arginate hydrochloride (0.147) SCD Max: CPC (0.07-0.1), sodium citric acid (0.05); other active ingredient: sodium monofluorophosphate | NA         | Dirty (100 μL mucin type I-S, 25 μL BSA Fraction V, and 35 μL yeast extract) | 30 s         | Listerine Advanced Gum Treatment eliminated the virus (> 5 log_{10} reduction). SCD Max and Listerine Cool Mint had a moderate effect (= 3 log_{10} reduction). Corsodyl was relatively ineffective (< 2 log_{10} reduction). |
| Almanza-Reyes and colleagues, 2021        | SARS-CoV-2 NL/2020 (BetaCoV/Netherlands/01); Vero E6 | Argovit silver nanoparticles (0.0004-0.5) | Culture cell media | Clean | 72 h | Argovit (0.3%) led to an 80% viral inactivation |
| Davies and colleagues, 2021               | England 2; Vero E6               | Listerine Advanced Defence Sensitive: dipotassium oxalate (1.4) Listerine Total Care: eucalyptol, thymol, menthol, sodium fluoride, zinc fluoride OraWize+ Aquafusion Systems: stabilized hypochlorous acid (0.01-0.02) | PBS        | Clean | 60 s | Listerine Advanced Defence Sensitive: ≥ 3.5 log_{10} or †† ≥ 4.2 log_{10} Listerine Total Care: ≥ 4.1 log_{10} reduction or †† ≥ 5.2 log_{10} OraWize+: ≥ 5.5 log_{10} or †† 0.4 log_{10} |
| Koch-Heier and colleagues, 2021           | SARS-CoV-2 Isolate “FI-100”; Vero E6 | ViruProX: CPC (0.05) and H_{2}O_{2} (1.5) BacterX pro: CHX (0.1), CPC (0.05), and fluoride anion (0.005) Solution of CPC (0.05) and CHX (0.1) | Nonvirucidal medium control of SARS-CoV-2 with infection medium; no-virus control containing infection medium and test solution | Clean | 30 s | Incubation with ViruProX reduced the virus titer by ≥ 6.8 × 10^6 pfu/mL (> 1.9 log_{10}) versus the medium control, whereas BacterX pro reduced by ≥ 8.4 × 10^6 pfu/mL (> 2.0 log_{10}) CHX (0.1%) and CPC (0.05%) reduced the virus titer by 6.7 × 10^6 pfu/mL (1.2 log_{10}) |
| Komine and colleagues, 2021               | JPN/DYWK/521 strain; VeroE6/TMPRSS2 | CPC + CHX mouthrinse: 2 formulations: GUM PAROEX, CHX (0.06) + CPC (0.05); GUM PAROEX, CHX (0.12) + CPC(0.05) GUM PerioShield: delmopinol hydrochloride (0.2) mouthrinse | PBS, ethanol (70%) | Clean | 30 s | Both CPC and CHX mouthrinse formulations led to a > 4.3 log_{10} reduction. The delmopinol hydrochloride mouthrinse (0.2%) led to a > 5.3 log_{10} reduction. |
| STUDY | SARS-COV-2 STRAIN, CELLULAR LINE | TEST MOUTHRINSES, CONCENTRATION (%) | COMPARISON | INTERFERING SUBSTANCES | CONTACT TIME | RESULTS |
|-------|----------------------------------|-------------------------------------|------------|------------------------|-------------|---------|
| Meister and colleagues,48 2021 | SARS-CoV-2 hCoV-19/ Germany/By-Bochum-1/2020; Vero E6 | Oral sprays: (A) Carragelose (1.2 mg/mL), kappacarrageenan (0.4 mg/mL), sodium chlorite; (B) Sodium chlorite (0.9), panthenol; (C) Xylometazolin hydrochloride (1 mg/mL), dexpanthenol (50 mg/mL); (D) Sodium hypochlorite (< 0.08), lithium-magnesium-sodium-silicate; (E) Xylometazolin hydrochloride (0.1%); (F) Hydroxypropyl methylcellulose, succinic acid, disodium succinate; (G) Galphimia, Luffa operculata, sabadilla | Cell culture medium | Dirty (substance mimicking nasal secretion) | 30 s | In general, oral sprays led to a > 1 log10 reduction: (A) 0.53 log10 reduction; (B) 0.13 log10 reduction; (C) 0.09 log10 reduction; (E) 0.20 log10 reduction; (F) 0.18 log10 reduction. Oral spray (G) led to no reduction, whereas oral spray (D) led to a 2.21 log10 reduction. Nasal spray (H) led to no reduction on viral load. Nasal spray (I) led to a ≥ 3.03 log10 or ≥ 4.69 log10 reduction (large volume plating, to reduce cell toxicity) |
| Meyers and colleagues,44 2021 | HCoV 229e; HUH7 | Listerine Antiseptic: eucalyptol (0.092), menthol (0.042), methyl salicylate (0.06), thymol (0.064) | NA | Dirty (200 µL of 5% BSA) | 30 s | Listerine Antiseptic decreased viral load by > 4 log10. After incubation times of 60 s and 120 s, no remaining infectious virus was detected. Listerine Ultra, Equate, and antiseptic mouthrinse showed lower efficacy (particularly after 30 s). However, these latter mouthrinses decreased infectious virus titers by > 2 log10. |
| Muñoz-Basagoiti and colleagues,57 2021 | SARS-CoV-2 D614G (isolated from a nasopharyngeal swab) and SARS-CoV-2 B.1.1.7; Vero E6 | Perio Aid Intensive Care (1.47 mM of CPC and 1.33 mM of chlorhexidine) | Vehicles containing the same formulation but without CPC; virus mixed with 1 mL of media as the positive control | Clean; dirty (saliva) | 30 s | 120 s: High doses of CPC (10 mM) effectively suppressed viral infection. CPC-containing mouthrinses decreased approximately 1,000 times the TCID50/mL of SARS-CoV-2, whereas vehicles had no impact on SARS-CoV-2 infectivity when compared with untreated virus |
| Santos and colleagues,42 2021 | SARS-CoV-2 strain used was isolated from a patient; Vero ATCC CCL-81 | Dental gel: APD** (1) Mouthrinse: APD (0.1) | Viral solution = cellular system as positive control. Cellular system only as the negative control | Clean | 30 s | Dental gel APD (1%): 99.99% (4 log10) reduction for all contact times Mouthrinse APD (0.1%): 90% (1 log10) reduction for all contact times |
| Santos and colleagues,58 2021 | SARS-CoV2/ SP02.2020 HSHE Br; Vero CCL-81 | APD derivative: 1 mg/mL (1-2), 0.5 mg/mL (1-4), 0.25 mg/mL (1-8), 0.125 mg/mL (1-16), 0.0625 mg/mL (1-32), 0.03125 mg/mL (1-64), 0.01562 mg/mL (1-128) | NA | No information available | 30 min | Significant reduction in viral load when compared with the positive control at the 1:2 (99.96%, < 4 log10), 1:4 (99.88%, < 3 log10), 1:8 (99.84%, < 3 log10), and 1:16 (92.65%, < 2 log10) titers. Minor viral neutralization was observed at the 1:32 (77.42%) and 1:64 (11.06%) titers. No virus neutralization was observed below the 1:128 titer. |
| STUDY | SARS-COV-2 STRAIN, CELLULAR LINE | TEST MOUTHRINSES, CONCENTRATION (%) | COMPARISON | INTERFERING SUBSTANCES | CONTACT TIME | RESULTS |
|-------|---------------------------------|-------------------------------------|------------|------------------------|--------------|---------|
| Shewale and colleagues, 2021 | USA-WA1/2020; Vero E6 | ClO SYS Ultra sensitive rinse, Sensitive rinse, Oral Spray: stabilized chlorine dioxide (0.1) ClO SYS fluoride toothpaste: stabilized chlorine dioxide (0.04) | PBS | Clean | 30 s 60 s 120 s | 30s: Ultra sensitive rinse led to a 1.96 log\(_{10}\) reduction; Sensitive rinse led to a 1.81 log\(_{10}\) reduction; Oral Spray led to a 2.98 log\(_{10}\) reduction. 60s: Ultra sensitive rinse led to a 1.39 log\(_{10}\) reduction; Sensitive rinse led to a 1.71 log\(_{10}\) reduction; Oral Spray led to a 2.67 log\(_{10}\) reduction. Sensitive fluoride toothpaste achieved a 2.26 log\(_{10}\) reduction with application times of 30 s, 60 s, and 120 s. |
| Steinbauer and colleagues, 2021 | No available information | octenisept: octenidine dihydrochloride (0.1) and phenoxyethanol (20), used in 20% (volume/volume) and 80% (v/v) concentrations | Formaldehyde | Clean | 15 s 30 s 60 s | Reduction of titers by $\geq 4.4 \text{ log}_{10}$ was observed for both concentrations and all contact times |
| Tiong and colleagues, 2021 | SARS-CoV-2 strain used was isolated from a patient, SARS-CoV-2/MY/UM/6-3 TIDREC (virus stock); Vero E6 | Colgate Plax Fruity Fresh: CPC (0.075), 0.05% sodium fluoride (0.05) XepaThymol: thymol (0.05) Bactidol: hexetidine (0.1),ethanol (9) Salt water: 2% (0.34 M), sodium chloride | Culture cell medium | Clean; dirty (0.3 g/L BSA and 3 mL/L human erythrocytes) | 30 s 60 s | Colgate Plax Fruity Fresh: 5 log\(_{10}\) reduction for all test times and conditions. Xepa Thymol: 0.75 log\(_{10}\) reduction after 60 s (clean conditions), 0.5 log\(_{10}\) reduction after 30 s (clean conditions), and after 30 s and 60 s (dirty conditions). Bactidol: 5 log\(_{10}\) reduction for all test times and conditions. Salt water: no effect on SARS-CoV-2 viral load. |
| Xu and colleagues, 2021 | USA-WA1/2020; HEK293T, HeLa | PVP-I (10) at different final dilutions (5, 0.5, and 0.05) | NA | No information available | 30 min | Only the 5% dilution of PVP-I was effective in inactivating the viruses (0 RLU) |
| Zoltán, 2021 | USA-WA1/2020; Vero 76 | 200 μg elemental iodine/mL at 3 dilutions (1:1; 2:1, and 3:1) | Water; ethanol (70%) | Clean | 60 s 90 s | 60 s: 3:1 dilution reduced viral titer by 2 log\(_{10}\), and 2:1 dilution reduced viral titers by 1.7 log\(_{10}\). 90 s: 1:1 dilution reduced viral titer by 2 log\(_{10}\) |