# Should antiseptic mouthwash or gargle be used in the prevention of COVID-19?

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*This rapid review summarizes the available evidence on the antiseptic mouthrinses and gargles in the prevention of COVID-19. This may change as new evidence emerges.*

## KEY FINDINGS

There is limited evidence to support the use of antiseptic mouthwash or gargle in the prevention of COVID-19.

- Chlorhexidine, povidone iodine, hexetidine, essential oils, cetylpyridinium chloride, and chlorine dioxide are the common active agents in mouthrinses and gargles available in the Philippines.
- **Povidone-iodine** is the only agent used in mouthwashes and gargles that has been documented to have antiviral activity against SARS-CoV-2 in-vitro.
- There are no completed randomized controlled trials evaluating the prophylactic effect of antiseptic mouthwash or gargle in SARS-CoV-2.
- Two ongoing clinical trials are assessing the use of povidone iodine gargle in preventing COVID-19.
- The CDC, WHO, PSMID and IDSA did not recommend the use of mouthwash or gargle as prophylaxis for COVID-19.

# RESULTS

Our search yielded a total of 107 unique results (duplicates removed). These were in-vitro studies and studies on use of pharynx gargle samples that were not relevant in this review. There were no completed studies that evaluated the use of mouthwashes or gargles in the prevention of COVID-19.

## Ongoing trials

We found two ongoing clinical trials investigating the use of mouthwash and gargle as prophylaxis for COVID-19. These studies are being done in the United Kingdom and United States. The characteristics of these trials are in Appendix 1.

## Safety

The use of mouthwashes and gargles are deemed to be relatively safe, with only minor adverse effects with long-term use, such as teeth staining. This is particularly seen in rinses that have cetylperidinium chloride and chlorhexidine as active ingredients. Oral mucosa and dental-crown staining and stomatitis may also occur less frequently (20).

PVP-1 with concentrations as high as 2.5% can be used as a mouth rinse safely for up to 5 months (30). Long-term use of povidone-iodine gargle has been associated with thyroid dysregulation, hence monitoring is recommended. Otherwise, it is generally well-tolerated and there are only rare cases of contact dermatitis and anaphylaxis. There is no evidence that long-term use of these antiseptics promote bacterial overgrowth, antimicrobial resistance and opportunistic infections (16,20).

## Recommendations from Other Guidelines

The United States National Institutes of Health, Center for Disease Control, Philippine Society for Microbiology and Infectious Disease and the Infectious Diseases Society of America did not give any recommendations for the use of mouthwashes and gargles as prophylaxis for COVID-19. (31–34).

# CONCLUSION

Among the active agents used in commercially-available mouthrinses and gargles in the Philippines, only **povidone-iodine** has been shown to have antiviral activity in-vitro against SARS-CoV-2. There are two ongoing clinical trials that are investigating the effect of prophylactic povidone-iodine gargle on the incidence of COVID-19.

## Declaration of Conflict of Interest

No conflict of interest

## REFERENCES

1. DePaola L, Spolarich E. Safety and efficacy of antimicrobial mouthrinses in clinical practice. Access. 2007;81(5):13–25.
2. Eggers M, Koburger-Janssen T, Ward LS, Newby C, Müller S. Bactericidal and Virucidal Activity of Povidone-Iodine and Chlorhexidine Gluconate Cleansers in an In Vivo Hand Hygiene Clinical Simulation Study. Infect Dis Ther. 2018;7(2):235–47.
3. Lim KS, Kam PCA. Chlorhexidine - Pharmacology and clinical applications. Anaesth Intensive Care. 2008;36(4):502–12.
4. Ashley KC. The antimicrobial properties of two commonly used antiseptic mouthwashes—Corsodyl and Oraldene. J Appl Bacteriol. 1984;56(2):221–5.
5. MIMS Online. Betadine Gargle & Paint/Betadine Throat Spray Dosage & Drug Information | MIMS.com Philippines [Internet]. 2020 [cited 2020 May 18]. Available from: https://www.mims.com/philippines/drug/info/betadine gargle and paint-betadine throat spray/?type=brief
6. MIMS Online. Bactidol Dosage & Drug Information | MIMS.com Philippines [Internet]. 2020 [cited 2020 May 18]. Available from: https://www.mims.com/philippines/drug/info/bactidol/?type=brief
7. MIMS Online. Orahex-AF Dosage & Drug Information | MIMS.com Philippines [Internet]. 2020 [cited 2020 May 18]. Available from: https://www.mims.com/philippines/drug/info/orahex-af/
8. MIMS Online. Oracare Dosage & Drug Information | MIMS.com Philippines [Internet]. 2020 [cited 2020 May 18]. Available from: https://www.mims.com/philippines/drug/info/oracare/?type=brief
9. U.S. National Library of Medicine. DailyMed - LISTERINE COOL MINT ANTISEPTIC - eucalyptol, menthol, methyl salicylate, and thymol [Internet]. 2019 [cited 2020 May 18]. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9d10eb10-568f-4863-9948-4ed990fbb474
10. U.S. National Library of Medicine. DailyMed - COLGATE TOTAL ADVANCED GUM HEALTH MOUTHWASH- cetylpyridinium chloride rinse [Internet]. 2016 [cited 2020 May 18]. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=330dda24-9b4b-2dca-e054-00144ff8d46c
11. Pelletier J, Tessema B, Westover J, Frank S, Brown S, Capriotti J. In Vitro Efficacy of Povidone-Iodine Nasal And Oral Antiseptic Preparations Against Severe Acute Respiratory Syndrome-Coronavirus 2 (SARS-CoV-2). Medrxiv [Internet]. 2020;2:1–7. Available from: http://medrxiv.org/cgi/content/short/2020.05.25.20110239
12. Bidra AS, Pelletier JS, Westover JB, Frank S, Brown SM, Tessema B. Rapid In-Vitro Inactivation of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Using Povidone-Iodine Oral Antiseptic Rinse. J Prosthodont. 2020;2:1–14.
13. Nagatake T, Ahmed K, Oishi K. Prevention of respiratory infections by povidone-iodine gargle. Dermatology. 2002;204(SUPPL. 1):32–6.
14. Shiraishi T, Nakagawa Y. Evaluation of the bactericidal activity of povidone-iodine and commercially available gargle preparations. Dermatology. 2002;204(SUPPL. 1):37–41.
15. Mukherjee PK, Esper F, Buchheit K, Arters K, Adkins I, Ghannoum MA, et al. Randomized, double-blind, placebo-controlled clinical trial to assess the safety and effectiveness of a novel dual-action oral topical formulation against upper respiratory infections. BMC Infect Dis [Internet]. 2017;17(1):1–8. Available from: http://dx.doi.org/10.1186/s12879-016-2177-8
16. Eggers M. Infectious Disease Management and Control with Povidone Iodine. Infect Dis Ther [Internet]. 2019;8(4):581–93. Available from: https://doi.org/10.1007/s40121-019-00260-x
17. Kawana R, Kitamura T, Nakagomi O, Matsumoto I, Arita M, Yoshihara N, et al. Inactivation of human viruses by povidone-iodine in comparison with other antiseptics. Dermatology. 1997;195(suppl 2):29–35.
18. Eggers M, Koburger-Janssen T, Eickmann M, Zorn J. In Vitro Bactericidal and Virucidal Efficacy of Povidone-Iodine Gargle/Mouthwash Against Respiratory and Oral Tract Pathogens. Infect Dis Ther [Internet]. 2018;7(2):249–59. Available from: https://doi.org/10.1007/s40121-018-0200-7
19. Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. J Hosp Infect. 2020;104(3):246–51.
20. DePaola L, Spolarich E. Safety and efficacy of antimicrobial mouthrinses in clinical practice. Access. 2007;81(5):13–25.
21. Lim KS, Kam PCA. Chlorhexidine - Pharmacology and clinical applications. Anaesth Intensive

Care. 2008;36(4):502–12.
22. Deryabin PG, Galegov GA, Andronova VA, Botikov AG. Analysis of Antiviral Properties of Hexoral In Vitro against Some Viruses that Cause Acute Respiratory Infections and Herpes. Bull Exp Biol Med. 2016;160(3):353–6.
23. Meiller TF, Silva A, Ferreira SM, Jabra-Rizk MA, Kelley JI, DePaola LG. Efficacy of Listerine® Antiseptic in reducing viral contamination of saliva. J Clin Periodontol. 2005;32(4):341–6.
24. Dennison DK, Meredith GM, Shillitoe EJ, Caffesse RG. The antiviral spectrum of Listerine antiseptic. Oral Surgery, Oral Med Oral Pathol Oral Radiol. 1995;79(4):442–8.
25. Popkin DL, Zilka S, Dimaano M, Fujioka H, Rackley C, Salata R, et al. Cetylpyridinium Chloride (CPC) Exhibits Potent, Rapid Activity Against Influenza Viruses in vitro and in vivo. Pathog Immun. 2017;2(2):252.
26. Seo HW, Seo JP, Cho Y, Ko E, Kim YJ, Jung G. Cetylpyridinium chloride interaction with the hepatitis B virus core protein inhibits capsid assembly. Virus Res [Internet]. 2019;263(November 2018):102–11. Available from: https://doi.org/10.1016/j.virusres.2019.01.004
27. Li JW, Xin ZT, Wang XW, Zheng JL, Chao FH. Mechanisms of inactivation of hepatitis a virus in water by chlorine dioxide. Water Res. 2004;38(6):1514–9.
28. Sanekata T, Fukuda T, Miura T, Morino H, Lee C, Maeda K, et al. Evaluation of the antiviral activity of chlorine dioxide and sodium hypochlorite against feline calicivirus, human influenza virus, measles virus, canine distemper virus, human herpesvirus, human adenovirus, canine adenovirus and canine parvovirus. Vol. 15, Biocontrol Science. 2010. p. 45–9.
29. Ogata N, Shibata T. Protective effect of low-concentration chlorine dioxide gas against influenza A virus infection. J Gen Virol. 2008;89(1):60–7.
30. Frank S, Capriotti J, Brown SM, Tessema B. Povidone-Iodine Use in Sinonasal and Oral Cavities: A Review of Safety in the COVID-19 Era. Ear, Nose Throat J. 2020;
31. NIH Guidelines. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. 2020;2019.
32. Centers for Disease Control and Prevention. Dental Settings | CDC [Internet]. Interim Infection Prevention and Control Guidance for Dental Settings During the COVID-19 Response. 2020 [cited 2020 May 18]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/dental-settings.html
33. Cheng VC, Edwards KM, Gandhi R, Muller WJ. Infectious Diseases Society of America Guidelines on Infection Prevention for Health Care Personnel Caring for Patients with Suspected or Known COVID-19. 2020;
34. Philippine Society for Microbiology and Infectious Disease. INTERIM GUIDELINES ON THE CLINICAL MANAGEMENT OF ADULT PATIENTS. Philipp Soc Microbiol Infect Dis. 2020;31(March).
35. EU Clinical Trials Register. Amsterdam, The Netherlands: European Medicines Agency [Internet]. Identifier 2020-001721-31, Can a sinus rinse and mouth wash reduce viral load in COVID-19 positive individuals? 2020 [cited 2020 May 18]. Available from: https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001721-31/GB
36. ClinicalTrials.gov. Bethesda (MD): National Library of Medicine (US) [Internet]. Identifier NCT04364802, COVID-19: Povidone-Iodine Intranasal Prophylaxis in Front-line Healthcare Personnel and Inpatients. [cited 2020 May 18]. Available from: https://clinicaltrials.gov/ct2/show/NCT04364802

## Appendix 1. Characteristics of clinical trials

| No. | Clinical Trial ID / Title | Status | Start and estimated primary completion date | Study design | Country | Population | Intervention Group(s) | Comparison Group(s) | Outcomes |
|---|---|---|---|---|---|---|---|---|---|
| 1 | EudraCT 2020-001721-31<br><br>**Can a sinus rinse and mouth wash reduce viral load in COVID-19 positive individuals?** (35) | Ongoing | Start: May 1, 2020 | Randomized clinical trial (Phase II) | United Kingdom | 40 Adults<br>- Staff who have tested positive for COVID-19 and in home isolation<br>- Patients who have been tested positive for COVID-19 on general wards or about to be discharged who are well enough to administer nasal washes<br>- Household member of affected staff member and household members of affected patients on general ward once discharged to self-isolation | Iodonated povidone oralmucosal solution | Nasal wash | Primary outcome:<br>- Reduction of the amount of virus in the nose and throat – measured by Day 0, 2, 4, 7 and 14 RT-PCR from oral and nasopharyngeal specimens<br><br>Secondary outcomes:<br>- Reduction of transmission of the virus to co-residents – measured by percentage of household with positivity of COVID-19<br>- Reduction of symptom severity in positive individuals as reported by a self-reported questionnaire |
| 2 | NCT04364802<br><br>**COVID-19: Povidone-Iodine Intranasal Prophylaxis in Front-line Healthcare Personnel and Inpatients (PIIPPI)** (36) | Ongoing (recruiting) | April 29, 2020 to May 2021 | Non-randomized, open-label clinical trial | United States | 250 participants<br>- Frontline healthcare workers who are negative for COVID-19<br>- Inpatients with more than 7 days of hospitalization or who will undergo a significant surgical procedure | Povidone iodine nasal spray and gargle (10% diluted 1:30)<br><br>To use at the beginning, middle and end of shift | No intervention | Primary outcome:<br>- Percent of healthcare workers that will test positive for COVID-19 after 3 weeks and during the study<br>- Percent of patients that will test positive for COVID 19 after 2 weeks and during the study |

| No. | Clinical Trial ID / Title | Status | Start and estimated primary completion date | Study design | Country | Population | Intervention Group(s) | Comparison Group(s) | Outcomes |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | Secondary outcomes:<br>- Ease of use of PVP<br>- Comfort of PVP<br><br>Other outcomes:<br>- Adherence to treatment protocol for 3 weeks |