Systematic review of the effect of endodontic irrigants over coronaviruses

Revisão sistemática do efeito dos irrigantes endodônticos sobre os coronavirus

Revisión sistemática del efecto de los irrigantes endodónticos sobre los coronavirus

Received: 04/26/2021 | Reviewed: 05/04/2021 | Accept: 05/12/2021 | Published: 05/29/2021

Amjad Abu Hasna
ORCID: https://orcid.org/0000-0002-1112-985X
São Paulo State University, Brazil
E-mail: d.d.s.amjad@gmail.com
Eduardo Bresciani
ORCID: https://orcid.org/0000-0001-9299-8792
São Paulo State University, Brazil
E-mail: eduardo.bresciani@unesp.br

Abstract
*Objective***:** This systematic review aimed to discuss a possible effect of sodium hypochlorite (NaOCl) over the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the new generation of corona virus, which was reported firstly in December 2019 in Wuhan, China. *Methods***:** Electronic search was performed for studies up to March 31, 2021 in the following databases: PubMed, LILACS, BBO, Scopus, web of science and Cochrane considering clinical trials and laboratory studies that evaluated the action of NaOCl over SARS-CoV-2. *Results***:** Numerous founded studies reported effectivity of NaOCl in different concentrations and exposure times over corona viruses including the SARS-CoV-2. However, none of the studies evaluated this action in the root canal system. No metanalysis was conducted due to variability of methods or lack of information of included articles. *Conclusion***:** NaOCl has a possible effectivity over SARS-CoV-2 as it dissolves the organic material of virus membrane, but this should be evaluated in the root canal systems.
Keywords: Coronavirus; Sodium hypochlorite; Covid-19; SARS-CoV-2.

Resumo
*Objetivo***:** Esta revisão teve como objetivo discutir um possível efeito do hipoclorito de sódio (NaOCl) sobre o novo Coronavírus da síndrome respiratória aguda grave 2 (SARS-CoV-2), a nova geração do coronavírus, que foi relatado pela primeira vez em dezembro de 2019 em Wuhan, China. *Métodos***:** Foi realizada busca eletrônica de estudos até 31 de março de 2021 nas seguintes bases de dados: PubMed, LILACS, BBO, Scopus, web of science e Cochrane considerando estudos clínicos e laboratoriais que avaliaram a ação do NaOCl sobre o SARS-CoV-2. *Resultados*: Vários estudos encontrados relataram a eficácia do NaOCl em diferentes concentrações e tempos de exposição sobre os tipos diferentes de coronavírus, incluindo o SARS-CoV-2. No entanto, nenhum dos estudos avaliou essa ação no sistema de canais radiculares. A metanálise não foi possível ser realizada pelara variabilidade de métodos empregados ou pela falta de dados importantes em alguns artigos. *Conclusão***:** O NaOCl tem uma possível eficácia sobre o SARS-CoV-2, pois dissolve o material orgânico da membrana do vírus, mas isso deve ser avaliado nos sistemas de canais radiculares.
Palavras-chave: Coronavírus; Hipoclorito de sódio; Covid-19; SARS-CoV-2.

Resumen
*Objetivo***:** Esta revisión tuvo como objetivo discutir un posible efecto del hipoclorito de sodio (NaOCl) en el nuevo coronavirus del síndrome respiratorio agudo severo 2 (SARS-CoV-2), la nueva generación de coronavirus, que se informó por primera vez en diciembre de 2019 en Wuhan, China. *Métodos***:** Se realizó una búsqueda electrónica de estudios hasta el 31 de marzo de 2021 en las siguientes bases de datos: PubMed, LILACS, BBO, Scopus, web of science y Cochrane considerando estudios clínicos y de laboratorio que evaluaron la acción de NaOCl sobre el SARS-CoV-2. *Resultados***:** Varios estudios encontrados han informado de la eficacia de NaOCl a diferentes concentraciones y tiempos de exposición en diferentes tipos de coronavirus, incluido el SARS-CoV-2. Sin embargo, ninguno de los estudios evaluó esta acción en el sistema de conductos radiculares. No se pudo realizar el metanálisis debido a la variabilidad de los métodos utilizados o la falta de datos importantes en algunos artículos. *Conclusión***:** El NaOCl tiene una posible efectividad sobre el SARS-CoV-2, ya que disuelve el material orgánico de la membrana del virus, pero esto debe evaluarse en los sistemas de conductos radiculares.
Palabras clave: Coronavirus; Hipoclorito de sodio; Covid-19; SARS-CoV-2.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 “SARS-CoV-2”, the new generation of coronavirus, was reported firstly in December 2019 in Wuhan, China. The novel virus was detected in patients saliva (To et al., 2020). As saliva can access the root canal through the periodontal ligament, dentinal tubules, open cavity, faulty restoration, apical foramen and accessory/secondary canals, (Narayanan & Vaishnavi, 2010) then the question is: Can SARS-CoV-2 access the root canal system as many viruses found in the root canal (Glick, Trope, Bagasra, & Pliskin, 1991; Slots, 2005)? Then, are the conventional endodontic irrigants effective over SARS-CoV-2?

The root canal treatment “RCT” success depends mainly on microorganisms disinfection (Abu Hasna, Ferrari, & Talge Carvalho, 2019; Abu Hasna, Khoury, et al., 2020; Abu Hasna, Ungaro, et al., 2019). More than 700 microorganism species exist in the root canal (Aas, Paster, Stokes, Olsen, & Dewhirst, 2005) those complicate the root canal disinfection because of the resistance of some microorganisms and the limited actions of some antimicrobial agents (Cavalli et al., 2017; Maekawa et al., 2013).

Sodium hypochlorite (NaOCl) was introduced into endodontics in the last half of the XIX century. (Sedgley, 2004) It is considered an effective irrigant over various bacteria like *Enterococcus faecalis, Escherichia coli* and *Streptococcus mutans*, as well, over fungi like *C.albicans.* (Abu Hasna, Pereira Da Silva, et al., 2020; Valera et al., 2009) It is also effective over microorganisms’ endotoxins like Lipopolysaccharides (LPS) and lipoteichoic acid (LTA) (Maekawa et al., 2011; Valera et al., 2014), and over the matrix metalloproteinases (MMP) (Carvalho et al., 2020). Beside, chlorhexidine (CHX), another well-known antimicrobial agent used in endodontics, which is effective over variety of microorganisms (Walia, Goswami, Mishra, Walia, & Sahay, 2019). However, its major disadvantage is the reduced pulp tissue dissolution capacity (Arslan, Guneser, Kustarci, Er, & Siso, 2015).

Therefore, this review aimed to understand a possible effect of the NaOCl and its behavior over SARS-CoV-2 as the presence of diverse microorganisms including bacteria, viruses and fungi in the root canal system complicates its disinfection.

2. Methodology

A systematic search using the PICO strategy was performed considering the endodontic infection and the influence of common irrigants over SARS-CoV-2. As the search resulted in no study, the authors reformulated the search to a broader aspect (considering the virus as the only component of the “P” within the PICO question). By changing the search strategy, the authors aim to compile all the information on the virus inactivation. Thus, the research question was as follows: Does NaOCl inactivate coronavirus?

The reformulated search follows: PICO strategy (Population – coronavirus; Intervention – use of NaOCl solution; Comparison – NaOCl and CHX; Outcome – reduction in virus load) considering clinical trials and laboratory studies that evaluated the action of NaOCl and CHX over SARS-CoV-2.

The inclusion and exclusion criteria were defined as the following:

Inclusion criteria

- In humans, in animals, in vitro and laboratorial studies.
- Quantification of coronaviruses and description of the test
- The use of NaOCl solution

Exclusion criteria

- Case report, review article, or opinion article
- Lack of evaluation of the coronaviruses’ levels

Research, Society and Development, v. 10, n. 6, e23810615457, 2021
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v10i6.15457

- The publication was based on a population from another study

Search strategy

Then, standard search keys were elaborated to look for studies in six data bases including (Pubmed, LILACS, BBO, Scopus, Web of Science and Cochrane) using the following key words. The initial search consisted in testing the Mesh and Entry terms, on the Medline base, with removal of terms resulting in no or duplicated studies. The initial search strategy was adapted for the other bases tested. The search strategies are presented in Table 1.

Table.1 Search strategy according to each assessed database.

Pubmed: 51 articles (((((((((((Coronaviridae*[MeSH Terms]) OR Coronavirus Infections[MeSH Terms]) OR Coronavirus Infection*[Title/Abstract]) OR Middle East Respiratory Syndrome[Title/Abstract]) OR MERS[Title/Abstract]) OR COVID-19[Supplementary Concept]) OR COVID19[Title/Abstract]) OR 2019 novel coronavirus infection[Title/Abstract]) OR coronavirus disease 2019[Title/Abstract]) OR 2019-nCoV infection[Title/Abstract]) OR 2019 novel coronavirus disease[Title/Abstract])) AND ((Sodium Hypochlorite[MeSH Terms]) OR Sodium Hypochlorite[Title/Abstract])
LILACS and BBO: 0 articles (MH: Coronaviridae O “Infecciones por Coronavirus”) Y (“MH: Hipoclorito de Sodio”)
(MH: Coronaviridae OU “Infecções por Coronavirus”) E (“MH: Hipoclorito de Sódio”)
Scopus: 59 articles TITLE-ABS-KEY (coronaviridae OR "Coronavirus Infection" OR "Middle East Respiratory Syndrome" OR MERS OR covid-19 OR covid19 OR "2019 novel coronavirus infection" OR "coronavirus disease 2019" OR "2019-nCoV infection" OR "2019 novel coronavirus disease") AND TITLE-ABS-KEY ("Sodium Hypochlorite")
Web of science: 40 articles #1 TS=(coronaviridae OR "Coronavirus Infection" OR "Middle East Respiratory Syndrome" OR mers OR covid-19 OR covid19 OR "2019 novel coronavirus infection" OR "coronavirus disease 2019" OR "2019-nCoV infection" OR "2019 novel coronavirus disease") #2 TS=("Sodium hypochlorite”) #1 AND #2
Cochrane: 1 article #1 (Coronaviridae):kw OR (coronavirus infections):kw OR (coronavirus infections):ti,ab,kw OR (middle east respiratory syndrome):ti,ab,kw OR (MERS):ti,ab,kw (Word variations have been searched) #2 (covid-19):ti,ab,kw, #3 (covid19):ti,ab,kw, #4(2019 novel coronavirus infection):ti,ab,kw, #5 (coronavirus disease 2019):ti,ab,kw, #6 (2019 novel coronavirus disease):ti,ab,kw, #7 #1 or #2, #8 #7 or #3, #9 #8 or #4, #10 #9 or #5, #11 #10 or #6, #12 ("sodium hypochlorite"):kw, #13 #11 and #12

Source: Authors.

Study Selection and Data Collection Process

Eighty studies were obtained by these searches on different databases until 07/05/2021. The selected articles were alphabetically organized by title and duplicates could be identified and removed manually (one duplicated article was removed). Articles were further screened by title and abstract taking into account the eligibility criteria. Then, the full-text of selected articles was obtained and two reviewers (A.AH. and E.B.) classified those that met the inclusion criteria. In total ten articles were included. Relevant information about the study design, type of virus, interventions and exposure time, and outcomes were extracted using customized extraction forms by the authors independently.

3. Results and Discussion

The relevant extracted information is presented in (Table 2). The lack of quantitative data in five studies and the lack of standard deviation in the other studies hindered the authors to perform a metanalysis. Also, as the information should be of clinical importance right away, it was decided to not ask the authors of the selected studies for further data.

Table.2 Relevant information of the included studies. Treatments, exposure time and effectiveness (presented numbers are related to viral reduction found in the studies) are presented. References to the corresponding study is presented in the last column.

Biocidal agent	Concentration	Virus	Exposure time	Effectivity	Reference
Sodium hypochlorite	Unknown	Porcine parvovirus (PPV)	Unknown	Effective	(Brown, 1981)
		Pseudorabies and transmissible gastroenteritis viruses	Unknown	Effective	(Brown, 1981)
Sodium hypochlorite	Unknown	Mouse hepatitis virus (MHV)	Unknown	Effective	(Saknimit et al., 1988)
		Canine coronavirus (CCV)	Unknown	Effective	(Saknimit et al., 1988)
Sodium hypochlorite	0.8% soda and sodium hypochlorite with 1-degree chlorometric	Coronavirus in animals	Unknown	Effective	(Maris, 1990)
Chlorine solution	more than 10 mg/L chlorine	SARS-CoV	30 minutes	Effective	(X.-W. Wang et al., 2005)
Chlorine dioxide	40 mg/L chlorine dioxide	SARS-CoV	30 minutes	Effective	(X.-W. Wang et al., 2005)
Sodium hypochlorite	50,000 ppm of active chlorine	SARS-CoV (GVU6109)	5 minutes	Effective >3 log10	(Lai et al., 2005)
Sodium hypochlorite	0.21%	MHV (MHV-2 and MHV-N)	30 seconds	Effective ≥4.40 log10	(Dellanno et al., 2009)
Sodium hypochlorite	1:100	MHV	1 minute	Ineffective 0.62 log10	(Hulkower et al., 2011)
		Transmissible gastroenteritis virus (TGEV)	1 minute	Ineffective 0.35 log10	(Hulkower et al., 2011)
Sodium hypochlorite	0.5%	human coronavirus 229E	10 minutes	Ineffective 3.00 $\log_{10}$	(Tyan et al., 2018)
Sodium hypochlorite with color additive	0.5%	human coronavirus 229E	10 minutes	Effective ≥4.50 $\log_{10}$	(Tyan et al., 2018)
Sodium hypochlorite	0.21	SARS-CoV-2	30 sec	Effective ≥ 4.0	(Akram, 2020)

Source: Authors.

Sodium hypochlorite irrigant over SARS-CoV-2

It is not the first time in this century to appear a new coronavirus. According to the study of Gorbalenya et al, (Gorbalenya et al., 2020) two times when a severe or even life-threatening disease was introduced into humans from a zoonotic reservoir: the severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS). Once again, a new coronavirus known at the moment as SARS-CoV-2 belongs to the sequence-based family classification and threatening the human being. (Zhou et al., 2019)

In endodontics, there are no studies in the literature evaluated the effect of NaOCl or any other irrigant over SARS-CoV-2. In the literature, all articles evaluated the effect of NaOCl or CHX over coronaviruses, but not the SARS-Cov-2 itself, in wastewater, stool, urine or stainless-steel surfaces, but not in the root canal (*in vitro* or *in vivo* studies). Thus, these results found in the literature may not be suitable for root canal treatment as the root canal infection involves diverse factors like micro-organisms, endotoxins, matrix metalloproteinases and growth factors, (Gomes & Herrera, 2018) in addition to dentin debris and smear layer that reduce irrigants effectivity. (Arias-Moliz et al., 2016; Morago et al., 2016)

NaOCl is a widely used endodontic irrigant was mentioned in the literature as an effective antimicrobial agent. (Siqueira, Rôças, Favieri, & Lima, 2000) Furthermore, it was mentioned as an effective antiviral agent over many viruses like porcine parvovirus (PPV), pseudorabies and transmissible gastroenteritis viruses after five minutes of incubation. Neither the adequate concentration of NaOCl, nor the exposure time, was mentioned in that study. (Brown, 1981)

As well, mouse hepatitis virus (MHV) and canine coronavirus (CCV) are two viruses belonging to the family of Coronaviruses and both can be disinfected by NaOCl in addition to other disinfectant agents, like sodium chloride (Saknimit, Inatsuki, Sugiyama, & Yagami, 1988). On the other hand, a more recent study related that 1:100 NaOCl was not effective in disinfecting two coronaviruses including MHV and transmissible gastroenteritis virus (TGEV) over a stainless steel surface. (Hulkower, Casanova, Rutala, Weber, & Sobsey, 2011)

The efficacy of NaOCl over these viruses may be explained by its capacity in dissolving the organic material present in the outer membrane (envelope and membrane proteins). This was mentioned in the literature in many studies that explain this greater capacity in dissolving organic material than other endodontic irrigants like CHX. (Gomes et al., 2013; Khademi, Usefian, & Feizianfard, 2007; Tartari et al., 2016; Tejada et al., 2019; Wright, Scott, Kahler, & Walsh, 2020) The same explanation was mentioned in the study of Maris et al. (Maris, 1990) that presented 0.8% soda and NaOCl with 1 degree chlorometric as the most active antiviral agent over coronavirus due to its dissolving capacity.

All the coronaviruses are present in air droplets and respiratory liquids including saliva. (Henwood, 2020; Hulkower et al., 2011; Kampf, Todt, Pfaender, & Steinmann, 2020) The severe acute respiratory syndrome coronavirus (SARS-CoV) remains infectious in respiratory specimens for more than 7 days at room temperature. NaOCl (which contains 50,000 ppm of active chlorine) can reduce the virus load by >3 $\log_{10}$ within 5 min. (Lai, Cheng, & Lim, 2005) Similar results were found in another study stating that 0.21% of NaOCl can inactivate SARS-CoV over surfaces after a 30s contact time (Dellanno, Vega, & Boesenberg, 2009) and 0.5% NaOCl with color additive guarantee a complete viral inactivation of human coronavirus 229E. (Tyan, Kang, Jin, & Kyle, 2018) Lastly, SARS-CoV can survive for 3 days in stool, at least 17 days in the urine at 20 °C and for more than 17 days at 4 °C in both stool and urine. However, SARS-CoV could be disinfected by chlorine solution which is derived by dissolving NaOCl. (Wang et al., 2005)

In the literature, it was evaluated the effect of CHX over coronaviruses and related that 0.02% CHX was not effective over MHV, (Dellanno et al., 2009). A more recent study alerting health professionals that chlorhexidine digluconate is ineffective for inactivating some coronavirus subtypes, and thus it is also ineffective over the SARS-CoV-2. (Assis, Araújo, & Lopes, 2020)

It was impossible to find studies that evaluate the effect of endodontic irrigants over SARS-CoV-2 in the root canal due to its novel appearance. However, It is believed that SARS-CoV-2 may act like the other viruses in the same category of coronaviruses like SARS-CoV and MERS, (Henwood, 2020) more recently, NaOCl was recommended as effective disinfectant of SARS-CoV-2. (J. Wang et al., 2020) More recent studies stated that sodium hypochlorite concentration (0.1-0.5 %) is effective over the novel SARS-CoV-2. (Akram, 2020; Barbato et al., 2020)

4. Conclusion

It may be concluded that NaOCl has a possible effectivity over SARS-CoV-2 (Table.2) but this should be evaluated in the root canal systems.

Acknowledgments

The authors deny any conflict of interest.

References

Aas, J. A., Paster, B. J., Stokes, L. N., Olsen, I., & Dewhirst, F. E. (2005). Defining the normal bacterial flora of the oral cavity. *Journal of Clinical Microbiology*, *43*(11), 5721–5732. 10.1128/JCM.43.11.5721-5732.2005

Abu Hasna, A., Ferrari, C. H., & Talge Carvalho, C. A. (2019). Endodontic treatment of a large periapical cyst with the aid of antimicrobial photodynamic therapy - Case report. *Brazilian dental science*, *22*(4), 561–568. 10.14295/bds.2019.v22i4.1745

Abu Hasna, A., Khoury, R. D., Toia, C. C., Gonçalves, G. B., de Andrade, F. B., Claudio António Talge Carvalho, & Valera. (2020). In vitro Evaluation of the Antimicrobial Effect of N-acetylcysteine and Photodynamic Therapy on Root Canals Infected with Enterococcus faecalis. *Iranian Endodontic Journal*.

Abu Hasna, A., Pereira Da Silva, L., Pelegrini, F. C., Ferreira, C. L. R., de Oliveira, L. D., & Carvalho, C. A. T. (2020). Effect of sodium hypochlorite solution and gel with/without passive ultrasonic irrigation on Enterococcus faecalis, Escherichia coli and their endotoxins. *F1000Research*, *9*, 642. 10.12688/f1000research.24721.1

Abu Hasna, A., Ungaro, D. M. de T., de Melo, A. A. P., Yui, K. C. K., da Silva, E. G., Martinho, F. C., & Gomes, A. P. M. (2019). Nonsurgical endodontic management of dens invaginatus: a report of two cases. [version 1; peer review: 2 approved]. *F1000Research*, *8*, 2039. 10.12688/f1000research.21188.1

Akram, M. Z. (2020). Inanimate surfaces as potential source of 2019-nCoV spread and their disinfection with biocidal agents. *Virusdisease*, *31*(2), 94–96. 10.1007/s13337-020-00603-0

Arias-Moliz, M. T., Morago, A., Ordinola-Zapata, R., Ferrer-Luque, C. M., Ruiz-Linares, M., & Baca, P. (2016). Effects of Dentin Debris on the Antimicrobial Properties of Sodium Hypochlorite and Etidronic Acid. *Journal of Endodontics*, *42*(5), 771–775. 10.1016/j.joen.2016.01.021

Arslan, D., Guneser, M. B., Kustarci, A., Er, K., & Siso, S. H. (2015). Pulp tissue dissolution capacity of QMix 2in1 irrigation solution. *European journal of dentistry*, *9*(3), 423–427. 10.4103/1305-7456.163229

Assis, M. S. de, Araújo, R. A. de A. M., & Lopes, A. M. M. (2020). Safety alert for hospital environments and health professional: chlorhexidine is ineffective for coronavirus. *Revista da Associacao Medica Brasileira*, *66Suppl 2*(Suppl 2), 124–129. 10.1590/1806-9282.66.S2.124

Barbato, L., Bernardelli, F., Braga, G., Clementini, M., Di Gioia, C., Littarru, C., & Cairo, F. (2020). Surface disinfection and protective masks for SARS-CoV-2 and other respiratory viruses: A review by SIdP COVID-19 task force. *Oral Diseases*. 10.1111/odi.13646

Brown, T. T. (1981). Laboratory evaluation of selected disinfectants as virucidal agents against porcine parvovirus, pseudorabies virus, and transmissible gastroenteritis virus. *American Journal of Veterinary Research*, *42*(6), 1033–1036.

Carvalho, C. A. T., Abu Hasna, A., Carvalho, A. S., Vilela, P. das G. F., Ramos, L. de P., Valera, M. C., & Oliveira, L. D. de. (2020). Clinical Study of Sodium Hypochlorite, Polymyxin B And Limewater Effect on MMP-3,-8,-9 In Apical Periodontitis. *Brazilian dental journal*, *31*(2), 116–121. 10.1590/0103-6440202003081

Cavalli, D., Toia, C. C., Flores Orozco, E. I., Khoury, R. D., Cardoso, F. G. da R., Alves, M. C., & Valera, M. C. (2017). Effectiveness in the removal of endotoxins and microbiological profile in primary endodontic infections using 3 different instrumentation systems: A randomized clinical study. *Journal of Endodontics*, *43*(8), 1237–1245. 10.1016/j.joen.2017.03.032

Dellanno, C., Vega, Q., & Boesenberg, D. (2009). The antiviral action of common household disinfectants and antiseptics against murine hepatitis virus, a potential surrogate for SARS coronavirus. *American Journal of Infection Control*, *37*(8), 649–652. 10.1016/j.ajic.2009.03.012

Glick, M., Trope, M., Bagasra, O., & Pliskin, M. E. (1991). Human immunodeficiency virus infection of fibroblasts of dental pulp in seropositive patients. *Oral surgery, oral medicine, and oral pathology*, *71*(6), 733–736. 10.1016/0030-4220(91)90284-j

Gomes, B. P. F. A., Vianna, M. E., Zaia, A. A., Almeida, J. F. A., Souza-Filho, F. J., & Ferraz, C. C. R. (2013). Chlorhexidine in endodontics. *Brazilian dental journal*, *24*(2), 89–102. 10.1590/0103-6440201302188

Gomes, B. P. F. de A., & Herrera, D. R. (2018). Etiologic role of root canal infection in apical periodontitis and its relationship with clinical symptomatology. *Brazilian oral research*, *32*(suppl 1), e69. 10.1590/1807-3107bor-2018.vol32.0069

Gorbalenya, A. E., Baker, S. C., Baric, R. S., de Groot, R. J., Drosten, C., Gulyaeva, A. A., & Ziebuhr, J. (2020). *Severe acute respiratory syndrome-related coronavirus* : The species and its viruses – a statement of the Coronavirus Study Group. *BioRxiv*. 10.1101/2020.02.07.937862

Henwood, A. F. (2020). Coronavirus disinfection in histopathology. *Journal of histotechnology*, 1–3. 10.1080/01478885.2020.1734718

Hulkower, R. L., Casanova, L. M., Rutala, W. A., Weber, D. J., & Sobsey, M. D. (2011). Inactivation of surrogate coronaviruses on hard surfaces by health care germicides. *American Journal of Infection Control*, *39*(5), 401–407. 10.1016/j.ajic.2010.08.011

Kampf, G., Todt, D., Pfaender, S., & Steinmann, E. (2020). Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. *The Journal of Hospital Infection*, *104*(3), 246–251. 10.1016/j.jhin.2020.01.022

Khademi, A., Usefian, E., & Feizianfard, M. (2007). Tissue dissolving ability of several endodontic irrigants on bovine pulp tissue. *Iranian endodontic journal*, *2*(2), 65–68.

Lai, M. Y. Y., Cheng, P. K. C., & Lim, W. W. L. (2005). Survival of severe acute respiratory syndrome coronavirus. *Clinical Infectious Diseases*, *41*(7), e67–71. 10.1086/433186

Maekawa, L. E., Valera, M. C., Oliveira, L. D. de, Carvalho, C. A. T., Camargo, C. H. R., & Jorge, A. O. C. (2013). Effect of Zingiber officinale and propolis on microorganisms and endotoxins in root canals. *Journal of applied oral science : revista FOB*, *21*(1), 25–31.

Maekawa, L. E., Valera, M. C., Oliveira, L. D. de, Carvalho, C. A. T., Koga-Ito, C. Y., Jorge, A. O. C., & São Paulo State University, Brazil. (2011). In vitro evaluation of the action of irrigating solutions associated with intracanal medications on Escherichia coli and its endotoxin in root canals. *Journal of Applied Oral Science*, *19*(2), 106–112. 10.1590/S1678-77572011000200005

Maris, P. (1990). [Virucidal efficacy of eight disinfectants against pneumovirus, coronavirus and parvovirus]. *Annales de recherches veterinaires. Annals of veterinary research*, *21*(4), 275–279.

Morago, A., Ordinola-Zapata, R., Ferrer-Luque, C. M., Baca, P., Ruiz-Linares, M., & Arias-Moliz, M. T. (2016). Influence of smear layer on the antimicrobial activity of a sodium hypochlorite/etidronic acid irrigating solution in infected dentin. *Journal of Endodontics*, *42*(11), 1647–1650. 10.1016/j.joen.2016.07.023

Narayanan, L. L., & Vaishnavi, C. (2010). Endodontic microbiology. *Journal of conservative dentistry : JCD*, *13*(4), 233–239. 10.4103/0972-0707.73386

Saknimit, M., Inatsuki, I., Sugiyama, Y., & Yagami, K. (1988). Virucidal efficacy of physico-chemical treatments against coronaviruses and parvoviruses of laboratory animals. *Jikken dobutsu. Experimental animals*, *37*(3), 341–345. 10.1538/expanim1978.37.3_341

Sedgley, C. (2004). Root canal irrigation--a historical perspective. *Journal of the history of dentistry*, *52*(2), 61–65.

Siqueira, J. F., Rôças, I. N., Favieri, A., & Lima, K. C. (2000). Chemomechanical reduction of the bacterial population in the root canal after instrumentation and irrigation with 1%, 2.5%, and 5.25% sodium hypochlorite. *Journal of Endodontics*, *26*(6), 331–334. 10.1097/00004770-200006000-00006

Slots, J. (2005). Herpesviruses in periodontal diseases. *Periodontology 2000*, *38*, 33–62. 10.1111/j.1600-0757.2005.00109.x

Tartari, T., Bachmann, L., Maliza, A. G. A., Andrade, F. B., Duarte, M. A. H., & Bramante, C. M. (2016). Tissue dissolution and modifications in dentin composition by different sodium hypochlorite concentrations. *Journal of applied oral science revista*. *FOB*, *24*(3), 291–298. 10.1590/1678-775720150524

Tejada, S., Baca, P., Ferrer-Luque, C. M., Ruiz-Linares, M., Valderrama, M. J., & Arias-Moliz, M. T. (2019). Influence of dentine debris and organic tissue on the properties of sodium hypochlorite solutions. *International endodontic journal*, *52*(1), 114–122. 10.1111/iej.12986

To, K. K.-W., Tsang, O. T.-Y., Chik-Yan Yip, C., Chan, K.-H., Wu, T.-C., Chan, J. M. C., & Yuen, K.-Y. (2020). Consistent detection of 2019 novel coronavirus in saliva. *Clinical Infectious Diseases*. 10.1093/cid/ciaa149

Tyan, K., Kang, J., Jin, K., & Kyle, A. M. (2018). Evaluation of the antimicrobial efficacy and skin safety of a novel color additive in combination with chlorine disinfectants. *American Journal of Infection Control*, *46*(11), 1254–1261. 10.1016/j.ajic.2018.04.223

Valera, M. C., Maekawa, L. E., Chung, A., Cardoso, F. G. R., Oliveira, L. D. de, Oliveira, C. L. de, & Carvalho, C. A. T. (2014). The effect of sodium hypochlorite and ginger extract on microorganisms and endotoxins in endodontic treatment of infected root canals. *General dentistry*, *62*(3), 25–29.

Valera, M. C., Silva, K. C. G. da, Maekawa, L. E., Carvalho, C. A. T., Koga-Ito, C. Y., Camargo, C. H. R., & Lima, R. S. e. (2009). Antimicrobial activity of sodium hypochlorite associated with intracanal medication for Candida albicans and Enterococcus faecalis inoculated in root canals. *Journal of applied oral science : revista FOB*, *17*(6), 555–559.

Walia, V., Goswami, M., Mishra, S., Walia, N., & Sahay, D. (2019). Comparative Evaluation of the Efficacy of Chlorhexidine, Sodium Hypochlorite, the Diode Laser and Saline in Reducing the Microbial Count in Primary Teeth Root Canals - An In Vivo Study. *Journal of lasers in medical sciences*, *10*(4), 268–274. 10.15171/jlms.2019.44

Wang, J., Shen, J., Ye, D., Yan, X., Zhang, Y., Yang, W., & Pan, L. (2020). Disinfection technology of hospital wastes and wastewater: Suggestions for disinfection strategy during coronavirus Disease 2019 (COVID-19) pandemic in China. *Environmental Pollution*, *262*, 114665. 10.1016/j.envpol.2020.114665

Wang, X.-W., Li, J.-S., Jin, M., Zhen, B., Kong, Q.-X., Song, N., & Li, J.-W. (2005). Study on the resistance of severe acute respiratory syndrome-associated coronavirus. *Journal of Virological Methods*, *126*(1-2), 171–177. 10.1016/j.jviromet.2005.02.005

Wright, P. P., Scott, S., Kahler, B., & Walsh, L. J. (2020). Organic Tissue Dissolution in Clodronate and Etidronate Mixtures with Sodium Hypochlorite. *Journal of Endodontics*, *46*(2), 289–294. 10.1016/j.joen.2019.10.020

Zhou, J., Fang, L., Yang, Z., Xu, S., Lv, M., Sun, Z., & Xiao, S. (2019). Identification of novel proteolytically inactive mutations in coronavirus 3C-like protease using a combined approach. *The FASEB Journal*, *33*(12), 14575–14587. 10.1096/fj.201901624RR