Dear Sirs,

In order to clarify the messages issued by some companies, DENTAID would like to state some points.

The current recommendations and treatments specified by the health authorities of different countries are based on current knowledge of the biology of the SARS-CoV-2 virus and the clinical consequences of its infection in humans. Under these circumstances, different expert committees have developed guidelines and suggestions that allow for us to try to reduce the likelihood of contagion or to decrease the spread of the virus in a simple way. Some of these are: social distancing, the use of a mask, hand washing and the use of hydroalcoholic gel, the use of mouthwash, etc.

The medical and dental associations that have made these recommendations resonate include:

Table 1.- Some dental associations and health authorities that recommend the use of mouthwash prior to dental care.

Country	**Health authorities**
United States	American Dental Association (ADA)
Portugal	Ordem médicos dentistas
France	Association dentaire française (ADF)
Italy	Associazione Nazionale Dentisti Italiani (ANDI)
Switzerland	Swiss Dental Association (SSO)
Belgium	Conseil de l'art dentaire de Belgique
Norway	Norwegian Institute of Public Health
Canada	Canadian Dental Association
Australia	Australian Dental Association
Spain	Consejo General de Dentistas de España

In the documents issued by said associations , apart from the recommendations regarding the organisation of the clinic, the reception of patients, the use of PPE, mobility in common spaces, etc., it is recommended that the patient rinse, prior to any dental activity, using povidone-iodine, hydrogen peroxide or cetylpyridinium chloride (CPC). Although experts support these measures, they also point out that they are based on indirect evidence and on the mechanism of action of these molecules and agree that well-designed clinical studies must be carried out to demonstrate their effectiveness (1, 2).

That being said, recommending a pre-rinse prior to dental care has a coherent basis that allows us to hypothesise that the use of a mouthwash, which carries an element with antiviral activity (anti SARSCov-2), could help to decrease the viral load in saliva; this way, the probability that a COVID^{+} individual might infect individuals in their immediate environment would diminish.

Different authors have shown that during the first week that COVID^{+} patients present with symptoms, the viral load in saliva is 10^{4}-10^{8} copies/mL. These results coincide with those obtained in the samples taken using swabs from the nasopharyngeal and oropharyngeal regions. These authors even propose the use of saliva as a diagnostic tool for COVID-19 due to the ease of sampling and because, in addition, it constitutes a low risk and less invasive procedure (3, 4, 5, 6). Likewise, it has been shown that saliva is a vehicle for the transmission of different pathogens such as: Epstein-Barr virus, Herpes simplex virus, cytomegalovirus, human papilloma virus, Zika virus (7, 8, 9). And, based on different publications, the World Healh Organization considers that one of the main sources of transmission of the SARS-CoV-2 virus is through the saliva and droplets that an infected person expels when speaking, singing, sneezing or coughing. Therefore, regardless of whether the nasal region may be the main route of infection, it is undeniable that the virus is "alive" and at a high load in saliva, and therefore, this constitutes an important source of contagion for the eyes, the mouth and the nasal region itself (https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions, 6, 10).

Regarding the scientific evidence that indicates that CPC could be a useful tool for reducing the spread of SARS-CoV-2. The study by Popkin et al, 2017 demonstrates the antiviral activity of this quaternary ammonium and determines that the EC50 (Effective virucidal concentration) for six different strains of influenza virus falls within the range of 5.0-12.5 µg/ml; these concentrations are between 50 and 100 times lower than the CPC concentrations that several of the mouthwashes on the market have. Also, they prove in an animal model, *in vivo*, that a spray with 0.1% CPC decreased the morbidity and mortality in mice infected with influenza virus. Furthermore, the authors demonstrate that the mechanism by which CPC inactivates the Influenza virus is through destabilisation and disruption of the viral envelope. This same spray was used in a randomised, double-blind, placebo-controlled pilot study that aimed to demonstrate that said formula could prevent upper respiratory infections caused by viruses (Influenza virus, respiratory syncytial virus, human metapneumovirus, rhinovirus and adenovirus).

Although, in this pilot study, no significant differences were found regarding the ability to prevent upper respiratory infections, between the group that used the placebo and the experimental group, significant differences were observed in relation to the severity and duration of cough and sore throat. Certainly, a spray is not the same as a mouthwash, as when using a spray, the dose volumes correspond to approximately 0.3-0.5 ml, and in the case of the mouthwash, 10 to 15 ml are used, which could even allow gargling. On the other hand, mouthwashes do not normally contain xanthan gum; however, many of them are formulated with glycerine.

Finally, in 2019, Shen et al published a study in the *Journal of Virology* that analysed the antiviral capacity of a wide range of compounds, on 4 different types of coronavirus. Within a subgroup of 36 molecules, CPC ranked ninth, showing powerful antiviral activity, with EC50 values of between 0.6 and 7.6 μM.

Although we are far from confirming that CPC could cure the disease caused by SARS-CoV-2, it can be stated that this molecule has outstanding antiviral activity, not only against Influenza virus and coronavirus but also against Hepatitis B virus and Herpes simplex virus (14, 15). The rapid progression of the COVID-19 pandemic has not allowed for the development of adequate clinical studies to prove the effectiveness of most of the medical recommendations and protocols currently in use, for example, the use of different antiviral molecules (remdesivir, lopinavir, ritonavir, oseltamivir, hydroxychloroquine), COVID-19 convalescent plasma therapy, hand washing, 4-hand work, avoiding the use of the air/water syringes, etc (16). Clinical studies aimed at demonstrating the true impact of the use of mouthwash as a tool to help prevent the spread of the SARS-CoV-2 virus are underway. And just as the use of povidone and peroxide is recommended, the evidence for the use of mouthwashes with CPC appears to be more consistent.

In conclusion, none of the assertions regarding the use of mouthrinse with CPC indicate that these could cure COVID-19 disease; $COVID^{+}$ patients have a high viral load in saliva, constituting a vehicle for the virus by which it could spread to other people. The use of mouthrinse with antiviral components could serve as a tool to help reduce the spread of the virus. For this reason, using mouthrinse with cetylpyridinium chloride, a molecule that has been used for over 30 years in oral healthcare, could be a simple and safe means of reducing viral load in the mouth.

Figure 1.-. Countries that have adopted the use of mouthwash prior to dental care.

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