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# ARCHIVOS DE LA SOCIEDAD ESPAÑOLA DE OFTALMOLOGÍA

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## Original article

# Hypochlorous acid as an antiseptic in the care of patients with suspected COVID-19 infection<sup>☆</sup>



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## ABSTRACT

**Purpose:** The SARS-CoV-2 virus, which causes COVID-19 disease, is transmitted by aerosols or by contact with infected surfaces. The route of entry to the body is through the nasal, oral or conjunctival mucosa. Health workers must use effective protection measures against the entry of the virus into mucous membranes, both physical and antiseptic filters. There is an antiseptic used in Ophthalmology that we believe could have virucidal action against the SARS-CoV-2 virus, formulated based on 0.01% hypochlorous acid.

**Methods:** An exhaustive search has been carried out in the databases of Pubmed and Web of Science to identify relevant articles on the virucidal activity of hypochlorous acid in different concentrations until October 4, 2020.

**Results:** There is evidence of the virucidal efficacy of 0.01% hypochlorous acid against SARS-CoV-2. According to the different scientific publications reviewed, hypochlorous acid has virucidal efficacy against different viruses, among them, SARS-CoV-2.

**Conclusions:** The 0.01% hypochlorous acid could act as an effective antiseptic against SARS-CoV-2, exerting a barrier on the mucosa to prevent COVID-19 infection. It can be used on the eyes, nose and mouth. We consider it necessary to assess its use in the protocol for patient health care in ophthalmology consultations, as well as to recommend its use to the general population to reduce viral load and/or prevent transmission of infection. Additional in vivo studies would be required to confirm its antiseptic action.

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## Ácido hipocloroso como antiséptico en la atención al paciente con sospecha de infección por COVID-19

### R E S U M E N

#### Palabras clave:

Ácido hipocloroso  
Antiséptico  
SARS-CoV-2  
COVID-19  
Conjuntivitis  
Virucida

**Propósito:** El virus SARS-CoV-2, causante de la enfermedad COVID-19, se transmite por aerosoles o por contacto con superficies infectadas. La ruta de entrada al cuerpo se produce a través de la mucosa nasal, oral o conjuntival. El personal sanitario debe usar medidas de protección efectivas a la entrada del virus en mucosas, tanto filtros físicos como antisépticos. Uno de los antisépticos usados en oftalmología, formulado a base de ácido hipocloroso al 0,01%, consideramos que podría tener acción virucida frente al virus SARS-CoV-2. El objetivo del estudio fue revisar la evidencia científica sobre la actividad virucida del ácido hipocloroso frente al SARS-CoV-2.

**Métodos:** Se realizó una búsqueda exhaustiva en las bases de datos de Pubmed y Web of Science para identificar artículos relevantes sobre la actividad virucida del ácido hipocloroso en diferentes concentraciones, publicados hasta el 4 de octubre de 2020.

**Resultados:** La búsqueda arrojó un total de 20 artículos. Los estudios analizados mostraron pruebas de la eficacia virucida del ácido hipocloroso, a una concentración del 0,01%, frente al SARS-CoV-2, así como frente a otros virus.

**Conclusiones:** El ácido hipocloroso al 0,01% podría actuar como antiséptico eficaz frente al SARS-CoV-2, creando una barrera protectora sobre las mucosas para evitar la entrada del virus y el desarrollo de la infección COVID-19. El producto puede ser aplicado en ojos, nariz y boca, sin efectos nocivos. Por ello, consideramos necesario valorar su uso en el protocolo de atención sanitaria al paciente en consultas de oftalmología, así como recomendar su uso a la población general para disminuir la carga viral y/o evitar transmisión de la infección. No obstante, se requerirían estudios adicionales *in vivo* para confirmar su acción virucida.

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## Introduction

The rapid spread and infectiousness of the SARS-CoV-2 virus forces us to be constantly on the lookout for protective measures. Transmission occurs by aerosols or by contact with infected surfaces<sup>1</sup>. The pathway of entry into the body is through the nasal, oral or conjunctival<sup>2</sup> mucosa. One of the routes of transmission of SARS-CoV-2 is through tears and can produce conjunctivitis<sup>3,4</sup> as a symptom. *In vitro* and *in vivo* studies have shown that the eye may serve a dual purpose for the establishment of infection. On the one hand, it would serve as a gateway and on the other hand, as a site of virus replication as has been seen to occur with respiratory viruses<sup>5</sup>.

In 2020, The *Lancet* published the first systematic review and meta-analysis addressing the issue of ocular manifestations or complications due to SARS-CoV-2 infection and positivity by reverse transcription polymerase chain reaction (RT-PCR) of tear or conjunctival secretion samples<sup>6</sup>. The meta-analysis showed that in patients with COVID-19, 3.17% had ocular manifestation, but only 1.94% of them had positive RT-PCR of conjunctival smear. However, despite the presence of virus in the ocular fluid, only 33.3% of patients showed signs of conjunctivitis/conjunctival chemosis or red eyes. On the other hand, among patients with COVID-19-associated conjunctivitis/red eyes, only 28.65% showed evidence of the presence of the virus in the ocular fluid. That is, the absence of ocular symptoms does not mean that the virus is not present in

the ocular fluid or that the appearance of ocular symptoms is related to the presence of the virus<sup>6</sup>.

There are other international studies not included in the previous review, such as that of Xia et al.<sup>7</sup>, in which they prospectively analyzed the presence of SARS-CoV-2 in tears and conjunctival secretion of patients with COVID-19. In their analysis, they only isolated the virus in the tear of one patient with conjunctivitis. Patients without ocular symptoms had a negative RT-PCR. However, they indicated that the low abundance of virus in tear and conjunctival secretions does not eliminate the risk of transmission through conjunctival tissue.

In the light of these data, healthcare workers are advised to take appropriate precautions regardless of the presence or absence of ocular manifestations, as lack of eye protection has been associated with an increased risk of SARS-CoV-2 transmission<sup>8</sup>. Therefore, the American Academy of Ophthalmology recommends ophthalmologists to take special care with patients given the proximity of the patient's nose and mouth during ophthalmic examination and the risk of exposure to tears that may potentially contain virus<sup>9</sup>.

Currently, for the adequate protection of healthcare personnel, only physical filters such as goggles and masks are used. However, in addition to these physical barriers, antiseptic substances capable of eliminating the virus at the point of entry such as the conjunctival, oral and nasal mucosa should be sought in order to increase protection against SARS-CoV-2. An antiseptic substance is capable of destroying or inhibiting the reproduction of microorganisms on living tissue. A dis-

infant performs the same function, but on an inanimate surface<sup>11</sup>.

One of the disinfectants approved for the elimination of SARS-CoV-2 is hypochlorous acid<sup>12</sup>. Hypochlorous acid results from the union of acid chlorine oxide (Cl<sup>-</sup>) with water (H<sub>2</sub>O). Chemically it can be described as an undissociated oxygen-dependent, unstable and reactive chlorine ion. The effectiveness of hypochlorous acid lies in its highly oxidizing capacity. It is a reactive oxygen species, and is produced by macrophages and neutrophils, in what is known as a respiratory burst during the fight against pathogens<sup>13</sup>. It has a broad spectrum, fast action and a wide margin of safety, so it is used to keep in check and prevent a large number of skin and mucosal infections<sup>14</sup>. Hypochlorous acid 0.01% has been approved by the Australian Medicines Agency, the Australian Register of Therapeutics Goods (ARTG) as an effective disinfectant against COVID-19<sup>15</sup>.

The aim of this study was to review the scientific evidence on the virucidal activity of hypochlorous acid against SARS-CoV-2. As the entry point of SARS-CoV-2 virus is through the mucous membranes, the present study is relevant because it is an antiseptic substance for use in the nasal, oral and conjunctival mucous membranes.

## Methods

### Scientific literature search strategy

The main resources used for the medical literature search were the PubMed and Web of Science databases. An exhaustive search of studies published in English or with an abstract in English up to 1 October 2020 was conducted to identify relevant information on the virucidal activity of hypochlorous acid at different concentrations. The keywords used were: *hypochlorous acid*, *antiseptic*, *SARS-CoV-2*, *COVID-19*, *conjunctivitis* and *virucidal* which were used independently and in different combinations. Reference lists of the analysed articles were also considered as a potential source of information.

## Results

The literature search produced a total of 20 articles, from which the following information was extracted.

### Studies on the virucidal activity of hypochlorous acid

There is published data from the 1960s, where Speir reported possible antiviral activity of chloride or halide salt compounds<sup>16</sup>.

A study carried out by the Animal Health Research Centre (IRTA-CReSA), in cell models, showed that hypochlorous acid is able to inhibit the replication of SARS-CoV-2 after 30 s, with a higher virucidal capacity after 10 min.

Kim et al. tested the efficacy of hypochlorous acid at low doses on nasal mucosa, with antibacterial, antifungal and antiviral activity. They observed more than 99% bactericidal or fungicidal activity for all species except *Candida albicans* in tap water at pH 7.0 and 8.4. In addition, it achieved a 3.2 log<sub>10</sub> reduction in cells exposed to human influenza A virus<sup>17</sup>.

In the study by Ramalingman et al. different cells were infected with DNA and RNA viruses. These included a human coronavirus, HCoV-229E, in liver cells. They found that viral inhibition by hypochlorous acid was an intracellular process and not a direct effect of chloride on viral particles or viral uptake and that this process did not occur by cytotoxicity<sup>18</sup>.

Landa-Solis et al. observed complete inactivation of HIV-1 and reduction of 3-log<sub>10</sub> in adenovirus after 5 min of contact and complete inactivation when contact occurred for 10 min against 20 ppm hypochlorous acid (0.002%)<sup>19</sup>.

Taharaguchi et al. studied the effect of hypochlorous acid 60 ppm (0.006%) on mouse hepatitis virus, Sendai virus, lymphocytic choriomeningitis virus, *Bordetella bronchiseptica*, *Pasteurella pneumotropica*, *Corynebacterium kutscheri*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. At 5 min, the determination of virus was practically null<sup>20</sup>.

## Discussion

Hypochlorous acid can act as an effective antiseptic against different viruses, according to the different *in vitro* studies carried out. Therefore, it has been approved by the Australian Medicines Agency for use as a disinfectant against SARS-CoV-2, at a concentration of 0.01%<sup>15</sup>.

The results of an investigation into the use of 0.01% HOCl as an ocular surface antiseptic in intravitreal injection (IVI) prophylaxis showed that the application of 0.01% HOCl spray as a rinse after applying 5% Betadine<sup>®</sup> provided greater patient comfort<sup>10</sup>. In addition, the antiseptic coverage provided by the 0.01% HOCl spray was equal to or better than that of Betadine<sup>®</sup> as it affects most of the pathogens commonly implicated in endophthalmitis. In ophthalmology we have a 0.01% hypochlorous acid eye spray (concentration 100 ppm) marketed as Ocudox<sup>®</sup> (Ocudox, BrillPharma, Spain) for the treatment of blepharitis due to Meibomian gland dysfunction and for ocular asepsis. It is classified as a medical device and is indicated for the treatment of blepharitis by applying a cotton pad soaked in the product to the base of the eyelashes and upper eyelid. According to its technical data sheet, it does not irritate the eyes, nose or throat, and does not produce cell damage. Neither the duration of its effect nor the maximum dose to be instilled is described, but the product disappears quite quickly (its effect is immediate, in less than 1 min it has the antiseptic action) and the dosage would be similar to that of the hydroalcoholic gels applied for hand disinfection. Hypochlorous acid is also used in dental procedures, in otorhinolaryngology, in the peritoneal cavity, in dermatology and in breast implants, all of them with good tolerance.

Based on the scientific evidence found on the virucidal action of hypochlorous acid at a concentration of 0.01% and despite the fact that its indication as a product for skin disinfection against COVID-19 is not yet registered, the use of the eye spray (0.01%–100 ppm) could be recommended as an additional protection measure for healthcare personnel, for the prevention of infection by SARS-CoV-2, applied directly to the eyes, nose and mouth before putting on the mask and protective goggles, as well as its use after removing the physical protection measures or in the event of possible accidental exposure. Its recommendation could even be considered in

the general population to reduce the viral load and/or prevent transmission of the infection.

However, further *in vivo* clinical studies would be necessary to confirm its effectiveness and safety as a virucidal against SARS-CoV-2, as well as the maximum duration of continuous use.

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## Conflict of interest

There is no conflict of interest with the disclosure.

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