

A Potential Benefit of Hypochlorous Acid - Facial Sanitisation

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ABSTRACT

Sanitisation of the hands and surfaces has become part of everyday life. Due to the lack of an acceptable sanitising agent for the face, masks have been mandated. The face with its multitude of micro-organisms remains a reservoir for upper respiratory tract infections, with constant deposition of microbes. By reducing microbial load, the risk of both infection and severity are reduced. Hypochlorous acid (HOCl) has proven antimicrobial and anti-inflammatory activity, including efficacy against SARS-CoV-2. A facial sanitiser, alongside vaccination, hand and surface sanitisers, and masks, improves protection against SARS-CoV-2. The advantages of regular sanitising of the face and mask include reduced level of microbial contamination, risk of biofilm formation, and respiratory tract and skin infections. HOCl was reviewed as a face and mask sanitiser, concluding that it was a suitable compound.

1.0. Purpose

The purpose of this article is to introduce a novel concept of HOCl as a facial sanitising agent, with the aim of preventing viral and bacterial infection.

2.0. Introduction

The face, including the oral and nasal mucosa and the conjunctiva, is a major point of entry and point of infection for many pathogens involved in human diseases and it also serves as a reservoir for the growth of microorganisms. This is particularly true for SARS-CoV-2, and other infections (e.g., *S. pyogenes*, *S. aureus*, *rhinovirus*) of the respiratory tract. The face is contaminated by airborne pathogens and surface borne pathogens, and via unsanitised hands. On average, individuals who are well-educated on infection control involuntarily touch their faces 23 times per hour, where 44% of the face touches involved mucosal areas, and 56% non-mucosal surfaces^[1]. During the Covid-19 pandemic, regular hand and surface sanitisation

and regular hand washing has been emphasised in order to reduce cross contamination and risk of infection. While this is beneficial, involuntary face touching, especially around the mucosal regions, increases the risk of infection. Consequently, the use of disposable or reusable face masks was made mandatory. Although it is true that the use of a face mask is beneficial in reduction of the risk of infection, there remains certain issues with use of the face mask – the main issues being improper usage of face masks, prolonged usage of disposable face masks, and infrequent and inadequate washing of reusable masks. It should also be considered that poor handling of masks and frequent removal and reapplication of the same masks further increases the surface area of the face mask which is contaminated.

As face masks only cover the nose and mouth, there remains an exposure risk of the eyes and conjunctiva. This poses a risk of contact and entry for pathogens even whilst wearing a mask. In addition to this, upon removal of face masks and other personal protective equipment (PPE), there is the risk of contamination of skin surfaces^[2]. Errors in doffing (removal) procedures of PPE was studied by Okamoto et. al., (2019) whereby 125 participant healthcare workers (HCW) were enrolled. The findings demonstrated that 39.2% made multiple doffing errors and 36% were contaminated with multidrug resistant organisms^[3]. Lim et. al. (2015) identified a 20.6% error rate of donning of respirators or hoods with a 48.3% rate of contamination of the head, 6.9% contamination rate of the face, and 72.4% rate of contamination of the neck^[4].

There is a need for disinfection products that can be used to sanitize the face and its mucosal surfaces, ridding it of pathogens, including SARS-CoV-2.

A facial sanitiser would be a great tool to add to the current arsenal against the Covid-19 pandemic, as well as against other respiratory tract infections. HOCl is a secondary reactive oxygen species produced by neutrophils, macrophages, and mast cells. Physiologically HOCl is present in all human tissue systems, including the skin^[5].

Commercially produced HOCl has proven to be an effective and safe disinfectant, with rapid activity against a wide spectrum of microbes, including drug resistant bacteria and bacterial spores, fungi, viruses, prions, and amyloid seeds^[6,7].

In this review, the mechanism of action of HOCl will be briefly discussed alongside the safety of use of HOCl on the face. The potential benefits of using HOCl to reduce the number of pathogens will be discussed, and other potential benefits which may be associated with the use of HOCl will be summarised.

3.0. The Antimicrobial Mechanism of Action and Safety of HOCl

3.1. Mechanism of Action

Hypochlorous acid is a secondary reactive oxygen species (ROS). It is a naturally occurring molecule present in the human body, produced during the respiratory burst of phagocytosis. The molecule dissociates into free radicals – H^+ and OCl^- . Hypochlorite (OCl^-) is a potent free radical (oxidant) which rapidly causes damage to bacterial cell walls and cell contents^[8,9]:

1. Hypochlorite (OCl^-) reacts with membrane lipids and cell walls of pathogens resulting in:

- a. Peroxidation of polyunsaturated fatty acids and destruction of cross-linkages in cell walls
 - b. A chain reaction of peroxidation of membrane lipids and decreased membrane fluidity
2. Cellular dysfunction occurs due to inhibition of enzymes required for glycolysis, thus, pathogens, specifically bacteria, are unable to metabolise glucose to produce ATP resulting in:
 - a. An increase in the presence of free radicals, resulting in a change in intracellular redox potential further inhibiting glycolysis
 - b. The complete disruption of essential cellular functions and depletion of adenosine triphosphate (ATP)

Efficacy of HOCl has been demonstrated against *pseudomonas aeruginosa* and *Escherichia coli*^[10,11], poultry derived *salmonella spp.*^[12], *staphylococcus spp.*^[13], *enterococcus faecalis*^[14]. Sporidical activity has also been demonstrated^[14]. Virucidal activity against resistant organisms such as *norovirus spp.* was also shown^[15].

Testing of antimicrobial efficacy of HOCl has been sponsored by Aquaiox LLC, Loxahatchee, Florida, on multiple pathogens following the USP <51> testing protocol^[16]. Relevant pathogens tested include *Candida albicans*, *S. aureus*, and *S. epidermidis* demonstrated a reduction of >99.9999% with 15 seconds of contact. *P. aeruginosa* showed a reduction of >99.9999% with 60 seconds of contact and MRSA had a reduction of >99.999% with 60 seconds of contact. The 2009 Pandemic strain of H1N1 had a >99.963% reduction with 5 minutes of contact, and *M. bovis* demonstrated a >99.99% reduction with 10 minutes of contact. From the above results it is clear that Hypochlorous Acid (HOCl) will offer an additional defence mechanism to prevent microbial infection.

3.2. Safety

The potential for HOCl to damage mammalian cells appears to be present. However, inherent mechanisms in human cells are in place in order to prevent cellular damage. The physiological protective mechanism is based on the antioxidant defence mechanism. As HOCl is a ROS (oxidant), the antioxidant defence mechanism of human cells protects against the oxidative stress caused by HOCl. Activation of enzymes causes cellular lysis. Human cells make use of a group of defence mechanisms collectively known as the Antioxidant Defence System (ADS)^[9,17]. Microbial cells, however, do not have this defence mechanism and for this reason HOCl is effective against microbes, but safe for human cells.

This specific quality is what renders HOCl safe for use in humans while making it toxic to microbes. SkinSafe, developed by Mayo Clinic, designates HOCl as hypoallergenic, irritant free, eyelid and lip safe, safe for teens and safe for babies^[18].

Antioxidants are molecules which slow down or prevent oxidation of other molecules. The mechanism of action of antioxidants are as follows:^[19]

1. Removal of radical intermediate species
2. Blocking secondary production of toxic metabolites and inflammatory mediators
3. Converting free radicals into less toxic compounds
4. Blocking chain propagation of secondary radicals

5. Repairing molecular injury
6. Enhancing the endogenous antioxidant system function of exogenous antioxidants
7. Inhibiting other oxidation reactions by being oxidised themselves

As such, there are two classes of antioxidants – enzymatic and non-enzymatic antioxidants. Enzymatic antioxidants include superoxide dismutases, catalases, glutathione system, thioredoxin system. Non-enzymatic antioxidants include ascorbic acid (vitamin C), glutathione and thiocyanate, tocopherols and tocotrienols (Vitamin E), beta-carotene (Carotenoids – provitamin A).

The Antioxidant Defence System (ADS) is what protects the body from oxidative damage. The presence of the ADS alone makes HOCl safe for use in humans and other species that make use of this kind of system.

3.3. The Face as a Harbour for Respiratory Infections

The entry points to the nose, mouth and eyes are key regions which predispose infections of the upper respiratory tract. Microorganisms proliferate on the surface of the skin, and constant touching of the face, nose, mouth, and eyes results in an increase in presence of the number and variety of microorganisms present. The major causative agents for upper respiratory tract infections (URTIs) are viral in nature, although not limited to viruses alone^[20].

Microorganisms involved in the pathogenesis of upper respiratory tract infections include *rhinovirus*, *respiratory syncytial virus (RSV)*, *parainfluenza virus*, *coronavirus*, *influenza viruses*, *adenovirus*, *enterovirus*, *S. aureus*, *S. pneumoniae*, *H. influenzae*, *P. aeruginosa*, *M. catarrhalis*, *E. coli*, *K. pneumoniae*, *N. gonorrhoeae*, among other pathogens.

SARS-CoV-2 is a pathogen of interest in recent times which causes upper respiratory tract infections. Wim Van Damme et. al.(2021) discuss the relationship of inoculum dose and disease severity of SARS-CoV-2 due to three possible factors:

1. At an individual level: “viral dose in inoculum is related to severity of disease (dose-dependent relationship)”
2. At a cluster level: “Severity of disease is related to transmission potential” leading to clusters of mild cases and clusters of severe cases.
3. At a community level: “In certain contexts, chains of severe cases can build up through intensive transmission with high inoculum to severe local outbreaks, which can result in large-scale intensive epidemics, while this is less likely in other contexts”

This theory plays out in practice on three levels:^[21]

1. Individual level: A person infected with a small dose viral inoculum will on average develop milder disease than a person infected with a high viral inoculum and vice versa. This is independent of other well known risk factors for severity of disease, mainly old age, and comorbidities, such as diabetes.
2. Cluster level: A person with asymptomatic infection or mild disease, will on average spread lower dose of the virus, and is less likely to transmit disease; and when the person transmits, the newly infected person is more likely to have a mild disease compared to a person infected by a severely ill person, who spreads on average higher

doses of the virus. This causes clusters and chains of milder cases or more severe cases.

3. Community level: In certain contexts, such as dense urban centres with a moderate climate, during the season that people live mostly indoors, the potential for intensive transmission and explosive outbreaks is higher than in rural areas, or in regions with a hot and humid climate where people live mostly outdoors. Hence, a cascade of intensive transmission is more likely in certain contexts than others.

This model is based on other pathogens which show dose-dependent severity, such as:

- Influenza virus
- Coronavirus (seen with MERS and HCoV-229E)
- Human immunodeficiency virus (HIV)
- Measles
- *Mycobacterium tuberculosis* (TB)
- *Streptococcus pneumoniae*

It is of note that the inoculum dose-dependent hypothesis needs further investigation in order to be well established, and medical experts need to pay close attention to these factors^[21].

3.0. Dermatological Benefits of Hypochlorous Acid

The use of alcohol-based sanitisers has increased since the onset of the Covid-19 pandemic, resulting in an increase in the incidence of contact dermatitis and allergic contact dermatitis associated with the use of alcohol-based sanitisers^[22]. The incidence of allergic contact dermatitis increased with use of other non-alcohol-based hand sanitisers (such as chlorhexidine and quaternary ammonium compounds).

4.0. Potential Benefit of HOCl on the Face and Skin

Due to the efficacy and safety of HOCl, it is proposed for facial sanitisation, as well as sanitisation of nasal and oral cavities. Due to its own endogenous nature, HOCl is inherently safe, as demonstrated in numerous international studies^[24-29].

5.0. Discussion

Literature indicates that HOCl is efficacious against a wide range of microorganisms. This, alongside knowledge of the mechanism of action provides insight into the antimicrobial properties which may bypass the potential of microbial resistance against HOCl. The range of microorganisms killed by HOCl are all significant microbes which cause dermatological or respiratory tract infections. As such, it can be deduced that use of HOCl as a facial sanitiser would decrease incidence of the skin conditions mentioned. The safety of HOCl to mammalian cells has been demonstrated on sensitive cells. As HOCl with a concentration of 200 ppm (0.2%) and 210 ppm (0.21%) has been proven safe using Vero cells, it can be concluded that HOCl is safe to use as a facial sanitiser^[29]. In addition to the potential ability of preventing upper respiratory tract infections, HOCl has further potential benefits with the potential to treat a range of dermatological disorders, such as acne vulgaris, seborrheic dermatitis, and atopic dermatitis. Furthermore, a range of cutaneous conditions associated with the use of PPE and alcohol-based sanitisers can see a benefit from the use of HOCl. As such, the combined benefits of HOCl use further potentiates the use of the compound as a

facial sanitiser. HOCl has a proven efficacy against biofilms, and as such, the presence of epithelial biofilms would be eradicated, alongside conditions associated with them^[30-32]. Use of a facial sanitiser, in addition to vaccination, and the arsenal of hand sanitiser and masks, further improves protection against and prevention of the spread of SARS-CoV-2. The inoculum dose-dependent relationship with severity of infection postulation brings to consideration that any reduction of SARS-CoV-2 numbers on the face and mucosal surfaces will be beneficial with reduction of both risk of infection and severity of ongoing infection. The potential administration forms of HOCl for the purpose of a facial sanitisation could be by the use of a spray due to ease of application, as well as the ability to use the spray for sanitisation of masks and hands as well. Alternative methods of sanitisation could be by use of a gel formulation. This method would result in increased dermatological benefits; however, ease of use and sanitisation of masks would not be possible with this method. Thus, there is the potential benefit of a facial sanitiser, and HOCl may be a suitable compound with this regard.

6.0. Data Availability

All article and book references are available online and can easily be found using their respective DOI references. Reference 29 (Kabamba & Malatji, 2020) is available on request.

7.0. Conflicts of Interest

Dr. Avis Aman Nowbuth is Head of Research at BSafe^{HOCl}. Dr. Josh Barrie Armstrong was contracted to assist and review the integrity of the data by BSafe^{HOCl}. Professor Pieter Fourie and Professor Thomas Cloete were additionally contracted to verify data integrity and fact checking.

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A preprint has previously been published.^[33]

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