A Review of Hypochlorous Acid: History of Use, Method of Activity, and Effectiveness

Hypochlorous Acid has a unique method of activity, and offers many advantages over traditional chemical technologies, including:

- safety and ease of use
- superior disinfection performance
- removal of biofilm
- more stable, longer-lasting but non-toxic antiseptic effects, with minimal residues

Hypochlorous Acid (H-O-Cl, commonly written HOCL) is a non-toxic, non-irritant, environmentally and ecologically safe sanitizing and disinfecting solution. It is produced from the electrochemical reaction of water, salt and electricity(electrolysis), and is also known generically as ECA (electrochemically activated) water. The ECA process results in a both an anolyte (acidic) and a catholyte (basic) product (http://www.ecaconsortium.com/). ECA water is also sometimes known as EO water, or "superoxidized" chlorine, and international scientific literature includes all the above synonymous (with some technical exceptions) terms. (https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/electrolyzed-water)

Hypochlorous acid is the anolyte product of electrochemical activation; the catholyte product is sodium hydroxide. Both have varied and economically important uses, but at this time of pandemic concern, the 99.999% antiviral and bactericidal effectiveness of hypochlorous acid, the principal ECA anolyte, is of primary interest. Hypochlorous acid is effective on difficult viruses at concentrations of 100-200 part per million (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4363024/). Such concentrations have a hint of chlorine odor.

The concept of electrolyzing a saline solution to create a disinfectant or antiseptic is appealing because the basic materials of saline (salt plus pure water) and electricity are inexpensive and the end product does not damage the environment. The main components of the ECA anolyte are hypochlorous acid and chlorine. As with any germicide, the antimicrobial activity of electrochemically activated water is strongly affected by the concentration of the active ingredient (free available chlorine, FAC), especially HOCL, the molecule most effective and least corrosive or toxic to mammals.

The use of electrolysis products for cleaning and disinfection has been employed for over 100 years, but a couple of technical problems have hindered its widespread adoption. It was the disinfectant and wound cleaning material of choice in both World War I and II, but due to its short shelf life had to be made on-site at hospitals and other facilities needing a volume of disinfectant. (https://www.cleanroomtechnology.com/news/article_page/The_science_of_chlorine-based_disinfectant/93824)

Following World War II and the advent of antibiotics and new chemical disinfectants, hypochlorous use declined. Concomitantly, antibiotic-resistant strains of bacteria and viruses evolved, such as MERSA (Methicillin-resistant *Staphylococcus aureus*). HOCL, due to its method of activity, does not lead to development of such resistance. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3891400/)

It was not until the 1970s that the physicochemical properties of electrochemically activated solutions (ECAS) were extensively researched at the All-Russian Institute for Medical Engineering. ECAS have since found numerous biocidal applications, for example, for potable water disinfection and within the food industry. This is largely due to their high chemical activity, use of inexpensive raw materials, and relative ease of production.

Hypochlorous acid is a meta-stable molecule. It wants to revert back to salt water or convert to hypochlorite. Previous synthesis of HOCL had produced unstable formulas containing mixed chlorine species that underwent significant degradation within days and pH alteration within hours. The technical challenge has been to create hypochlorous acid at a near neutral pH which can result in a stable form of HOCL http://www.bakhir.com/publications/10/).

The fundamental problems of stability and shelf life have been recently resolved through a number of patented processes, making this remarkable antimicrobial material now available for widespread general use. As of early 2016 the U.S. Food and Drug Administration has (re)approved products whose main active ingredient is hypochlorous acid for use in treating wounds and various infections in humans and pets. With the concern surrounding the emergence of antimicrobial resistance in the healthcare environment, the use of hypochlorous ECAs has been investigated for potential applications in clinical practice. (http://www.avoxpharma.com/assets/upload/referanslar/9-Hypochlorous-Acid-An-Ideal-Wound-Care-Agent-With-Powerful-Microbicidal-Antibiofilm-and-Wound-Healing-Potency-2014.pdf; https://pubmed.ncbi.nlm.nih.gov/27079244/).

Hypochlorous acid is a naturally occurring small molecule generated in the human body by white blood cells called *neutrophils*. In vitro testing has shown hypochlorous acid to rapidly kill important wound pathogens, including antibiotic-resistant, methicillin-resistant Staphylococcus aureus (MRSA) and Pseudomonas aeruginosa. The time for inactivating these organisms is extremely rapid (< 30 seconds), thus contributing significantly to HOCL efficacy in practice. (https://www.todayswoundclinic.com/articles/treating-chronic-wounds-hypochlorous-acid-disrupts-biofilm#:~:text=In%20vitro%20testing%20has%20shown,rapid%20(%3C%2030%20seconds).

An important attribute of the human body's immune system is its ability to instigate a rapid attack against invading pathogens by releasing highly potent oxidized molecules such as hypochlorous acid. After engulfing the invading pathogens, neutrophils release an oxidative burst of hypochlorous acid that very quickly destroys the engulfed bacteria, virus, or fungi. The hypochlorous acid produced by these neutrophils kills microorganisms by binding to critical cell membrane components and affecting cell permeability. This leads to the rupture of the cell membrane and subsequent disintegration of cells.

Increasing evidence shows that some bacteria within chronic wounds live within biofilm communities in which bacteria are protected from host defenses and develop resistance to systemic antibiotic treatment. The biofilm is formed when a group of microorganisms stick to each other and become embedded within a self-produced matrix of extracellular polymeric substance composed of extracellular DNA, polysaccharides, and proteins. Among the most common biofilm-forming bacteria are *Staphylococcus aureus* and *Pseudomonas aeruginosa*. In order to disrupt biofilm within a wound, an agent must kill the bacteria and decrease the polysaccharides and proteins in the extracellular matrix of the biofilm. Hypochlorous acid has this dual ability. In addition, HOCL offers the added benefits of being able to remove biofilm and scale from manufacturing equipment, thus, greatly minimizing a major contributor to contamination problems. (https://www.regenmedical.co.uk/wp-content/uploads/2020/03/DAtanasio-et-al-2015-Wounds-27-10-249-252-pdf.pdf).

Current methods of disinfection can contribute to the development of resistance and in medical use, for example, can prove toxic to tissue. Pure hypochlorous acid is completely non-toxic and yet quickly and effectively inactivates viruses, bacteria, endospores, and fungi, while being safe for human tissues, including eye, skin, and lung. (https://www.woundsresearch.com/article/hypochlorous-acid-ideal-wound-care-agent-

powerful-microbicidal-antibiofilm-and-wound-healing,
https://link.springer.com/article/10.1007/s10096-011-1369-9?LI=true).

Because HOCL effectively destroys microorganisms, they cannot build up resistance to HOCL as they can to other sanitizers and disinfectants. Standard toxic chemicals can create strains of pathogens that become resistant over time, because the cell can expel or neutralize the chemical before it can kill it, thereby causing the overall efficacy of chemical cleaners and disinfectants to be significantly reduced. HOCL works in a different way. (https://www.optometrytimes.com/view/hypochlorous-acid-harnessing-natures-germ-killer)

In water treatment, hypochlorous acid is the active sanitizer in hypochlorite-based products (e.g., uses in swimming pools, spas, and municipal water supplies).

How HOCL Works

The primary component of the sodium chloride-based ECA anolyte is hypochlorous acid, the most effective disinfectant elemental species of chlorine, although in ECA production there may contain traces of other chlorine compounds, including sodium chloride (salt). HOCL cannot be completely isolated from these solutions due to rapid equilibration with its precursor compounds. Concentrating and stabilizing the HOCL fraction has been achieved in the last twenty years through some key patented and proprietary technical breakthroughs.

Stable hypochlorous acid is typically produced as a pH neutral (different functional and stability qualities are associated with different pH levels), super-oxidized water generated by electrolysis of a dilute NaCl solution passing through an electrolytic cell. This process creates a gentle but extremely potent antimicrobial solution capable of rapid reduction of bacteria, viruses, spores, cysts, scale and biofilm.

HOCL is a powerful oxidizing agent. In aqueous solution, it dissociates into H^+ and OCl, denaturing and aggregating proteins. HOCL also destroys viruses by chlorination by forming chloramines and nitrogen-centered radicals, resulting in single-as well as double-stranded DNA breaks, rendering the nucleic acid useless and the virus harmless (https://biology.stackexchange.com/questions/62671/how-does-hypochlorous-acid-inactivate-viruses).

HOCL ECA anolyte is an oxidizing agent due to a mixture of free radicals, giving its antimicrobial effect (the mixed active components: HClO, O_3, HO^-, HO_2, and other minor chlorine species). This anolyte can be made within a pH range of 2.5 and 8.5, but for most applications it is produced within a neutral pH band of 6.5 to 7. The Oxidation-Reduction Potential (ORP) is between +600 to +1200 mV.

Studies have shown that in particular HOCL is highly biocidal at the microbial level and can substantially reduce pathogens such as *Salmonella* and *E. coli* without the use of costly toxic chemicals. Neutral Anolyte (pH=6.0, ORP=600...+900mV), have proven anti-bacterial, anti-viral, anti-fungal, anti-allergic and anti-inflammatory action with least toxicity to the human tissue cells of all chlorine compounds. (https://www.sciencedirect.com/science/article/pii/B9780124158467000317)

HOCL has been approved by the USDA National Organic Program for use as a sanitizer in food processing. (https://www.ams.usda.gov/sites/default/files/media/Hypochlorous%20Acid%20TR%2008%2013%2015.pdf). Hypochlorous acid is also on the EPA N-List of registered disinfectants: https://www.epa.gov/newsreleases/epa-releases-list-disinfectants-use-against-covid-19.

The exact mechanism by which free chlorine destroys microorganisms has not been fully elucidated, only that it does so to the 99.99+% effectiveness level. Microbial inactivation by chlorine species can result from a number of factors: oxidation of sulfhydryl enzymes and amino acids; ring chlorination of amino acids; loss of intracellular contents; decreased uptake of nutrients; inhibition of protein synthesis; decreased oxygen uptake; oxidation of respiratory components; decreased adenosine triphosphate production; breaks in DNA; and depressed DNA synthesis. The actual microbicidal mechanism of chlorine might involve a combination of these factors or the effect of chlorine on critical sites. This research is ongoing to determine the exact method of activity of this and other chlorine biocides.

"Low concentrations of free available chlorine (e.g., HOCl, OCl^-, and elemental chlorine-Cl_2) have a biocidal effect on mycoplasma (25 ppm) and vegetative bacteria (<5 ppm) in seconds in the absence of an organic load... A concentration of 100 ppm will kill ≥99.9% of *B. atrophaeus* spores within 5 minutes and destroy mycotic agents in <1 hour. Acidified bleach and regular bleach (5,000 ppm chlorine) can inactivate 10^6 *Clostridium* difficile spores in ≤10 minutes. One study reported that 25 different viruses were inactivated in 10 minutes with 200 ppm available chlorine. Several studies have demonstrated the effectiveness of diluted sodium hypochlorite and other disinfectants to inactivate HIV. Chlorine (500 ppm) showed inhibition of *Candida* after 30 seconds of exposure. In experiments using the AOAC Use-Dilution Method, 100 ppm of free chlorine killed 10^6–10^7 *S. aureus, Salmonella choleraesuis*, and *P. aeruginosa* in <10 minutes." (https://www.cdc.gov/infectioncontrol/guidelines/disinfection/disinfection-methods/chemical.html)

It is suggested that HOCL is 80 to 120 times more efficacious than sodium hypochlorite (aka bleach). (https://www.contecinc.com/assets/article-march-2014-busting_the_myths_of_chlorine_disinfection_6aZ2vjq.pdf). Because pH neutralized HOCL has no charge and has a relatively low molecular weight it is better able than the other chlorine-based disinfectants to penetrate microbial cell walls. It also reacts more rapidly than other chlorine-based disinfectants to oxidation reactions with organic matter, i.e. the critical components of microbial cells. Conversely the hypochlor*ite* ion is a relatively poor disinfectant because of its inability to diffuse through the cell wall. Since it is negatively charged it is electrostatically repelled from the cell walls, which are also negatively charged. It is much larger in size than an HOCL molecule so it also diffuses more slowly due to its larger size.

Hypochlorous acid (HOCL) is the most effective disinfectant in the chlorine molecular family available in solution. Due to its previous instability issues, hypochlorous, although orders of magnitude more effective that other chlorine compounds, has had limited application until recent technical developments which enable a shelf stable liquid disinfectant to be produced. (https://infectioncontrol.tips/2017/10/06/hypochlorous-innate-response/)

New techniques in electromechanical biosynthesis, however, have resulted in lab results that show stability measured in years across ORP (oxidation-reduction potential), pH and active chlorine concentration (FAC)- the three determinant metrics for hypochlorous acid.
(https://www.cleanroomtechnology.com/news/article_page/The_science_of_chlorine-based_disinfectant/93824)

HOCl is not considered a toxic substance by OSHA and has no hazardous material disposal requirements (OSHA Hazard Communication Standard: CFR 1910.1200.2012). It is only the impurities arising during production or product degradation that require management. According to published FDA statements, if HOCL were pure and stable, it would be considered by the FDA the best of the available disinfectants for both safety and efficacy. It has been listed by the EPA as a List N: Disinfectants for Use Against SARS-CoV-2. All products on this list meet EPA's criteria for use against SARS-CoV-2, the virus that causes COVID-19 (https://www.epa.gov/pesticide-registration/list-n-disinfectants-use-against-sars-cov-2). The recent pandemic organism COVID-19 is being tested, and it is expected that just as hypochlorous has tested 99.999% effective in killing other viruses, it will also be effective on COVID-19.

HOCL is stable, economical to produce, greener than traditional chemical technologies, and can be used in multiple applications across a wide variety of industries. Numerous protocols have been established in agricultural, food processing and retail grocery venues where the produce, poultry, meat, seafood and dairy industries are particularly impacted. HOCL can be safely applied to food products, equipment and facilities using a variety of methods, including fogging, direct application or dosing. It does not leave a residue, thus saving a final rinse required with sodium hypochlorite and other cleaning agents.

The Woodinville, Washington company *Briotech* has, through much research and patented processes, established the gold standard for product stability with their HOCL product. Other ECA equipment companies and numerous patents have also helped create a contemporary opportunity to acquire equipment to produce stable HOCL at various scales.

A recent (April 2020) news release from *Briotech* includes this information: *Briotech's* HOCL has been lab tested to eradicate several highly-contagious viruses, MERSA-type "super-bugs", and prions. These include Human Coronaviruses OC43 (via preliminary study at the University of Washington School of Public Health in 2016 which showed a kill of 99.999% in ten minutes or less), MERS-CoV and SARS-CoV, Human Norovirus, Influenza H1N1, Human Papilloma Virus (HPV) -16 & -18, MRSA, Enterococcus faecalis (VRE), E. coli, Klebsiella pneumoniae, Listeria, and Bacillus spores (including B. subtilis, a model for weaponized anthrax), as well as inactivation of malformed proteins called Prions—the highly-resistant infectious agent known to be responsible for Mad Cow Disease and Chronic Wasting Disease in deer.

From the Chief Medical Officer at *Briotech*, Dr. Eric Rasmussen, MD, MDM, FACP : "*Briotech* has very good, though preliminary, independent evidence that *Briotech* HOCl eradicates coronavirus as a species thoroughly and quickly. Early testing of *Briotech* HOCl against coronavirus strain OC43 showed a 99.999% elimination of that coronavirus in 10 minutes. Fortunately, all coronaviruses strains—like SARS, MERS-CoV, OC43, and the current pandemic coronavirus COVID-19 (SARS-CoV-2)—are the same family; they are small, enveloped single-stranded RNA viruses and relatively easy to eliminate. The scientists and physicians working with *Briotech* expect the current pandemic coronavirus will be eradicated just as effectively as OC43, so a 99.999% reduction in ten minutes or less." (https://www.briotechusa.com/coronavirus-awareness).

How HOCL Is Produced

When a direct current is applied, electrochemical processes at the material electrode surface transform the electrolyte (NaCl) into an activated 'metastable' state, exhibiting elevated chemical reactivity and resulting in the modification of molecular ionic structures. Titanium (Ti) electrodes coated with porous layers of a metal oxide catalyst are used due to improved characteristics of stability, selectivity, electro-chemical reactivity, corrosion resistance and operating life of electrodes. In the anodic chamber, the continuously perfused salt (NaCl) solution reacts at the anode surface, producing mainly chlorine and oxygen, but also other reactive oxidants which are released into the bulk fluid. This is dependent on the redox reactions of strongly adsorbed electro-active water-derived intermediate molecular species, and a large scientific body of evidence now exists for these processes. This reaction is pH-dependent and dictates which free form of chlorine is most prevalent within generated solution; Cl, HClO or ClO. The exact physicochemical properties of the resulting anolyte (ECA solution) is dependent on both the characteristics of the electrochemical cell and its operating parameters, although conditions conducive to a low pH (~2–3) and high oxidation-reduction potential (ORP) (above +800 mV) are usually sought. In the cathodic chamber, hydrogen is generated, along with other reactive substances (largely antioxidants), resulting in a decrease in the redox potential and an increased pH. The transformation of the electrolyte into a metastable state is not permanent. Upon the generation and recovery of ECA anolyte and catholyte solutions, the chemical species present will shift spontaneously from this thermodynamically un-equilibrated condition to a stable non-active form, during what is known as the 'period of relaxation'. The rate of relaxation, and, thus, the half-life of the active solution, is ECA solution-specific. However, the stability of ECAS can be improved by increasing the pH, since this shifts the chemical equilibrium towards non-volatile chlorine species. In contrast to the significant reductions in residual free chlorine, studies have shown that the pH, ORP, conductivity and chloride ion concentration levels are all relatively stable during short-term storage indicating that the oxidizing potential of these solutions is largely retained.

Well-known and established uses for HOCL can now benefit from technical advances in stabilization, making this simple but powerful, yet non-toxic material available for widespread use. Further research into even longer term stabilization and anolyte purity, and new applications, will bring this material to the forefront of available tools to fight Covid-19 and other new and old viral and bacterial menaces.