Perspective

Hypochlorous acid has emerged as a potential alternative to conventional antibiotics due to its broad-spectrum antimicrobial activity

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Abstract

Hypochlorous acid (HOCl) is a potent antimicrobial agent that has recently gained attention as a potential alternative to conventional antibiotics. HOCl is produced by the human immune system in response to infection and is known for its broad-spectrum antimicrobial activity. It is effective against a wide range of microorganisms, including bacteria, viruses, and fungi, and has been shown to be more effective than many conventional antibiotics. One of the key advantages of HOCl is its ability to kill bacteria without promoting the development of antibiotic resistance. Unlike conventional antibiotics, which target specific bacterial structures or processes, HOCl acts by disrupting multiple cellular components, making it much more difficult for bacteria to develop resistance. Another advantage of HOCl is its safety profile. Unlike many conventional antibiotics, HOCl is not toxic to human cells and does not cause side effects such as gastrointestinal upset or allergic reactions. Overall, HOCl shows great promise as a potential alternative to conventional antibiotics, particularly in the face of rising antibiotic resistance. With further research, it may become an important tool in the fight against infectious diseases. Herein, we discuss the mechanisms of HOCl antimicrobial action, its potential clinical applications, and future directions for research. This review aims to provide an overview of the use of hypochlorous acid (HOCl) as an antibiotic agent.

More Information

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Submitted: March 21, 2023
Approved: March 29, 2023
Published: March 30, 2023

How to cite this article: Akl MM. Hypochlorous acid has emerged as a potential alternative to conventional antibiotics due to its broad-spectrum antimicrobial activity. Int J Clin Microbiol Biochem Technol. 2023; 6: 001-004.

DOI: 10.29328/journal.ijcmbt.1001026

Introduction

Antibiotic resistance has become a major public health concern, and the need for new antibiotics has become urgent. Traditional antibiotics work by targeting specific bacterial components, such as the cell wall, ribosomes, or DNA. However, bacteria can develop resistance to these antibiotics through various mechanisms, such as mutation or acquisition of resistance genes [1,2]. Moreover, conventional antibiotics also have the potential to harm the host by disrupting the normal microbiota and causing side effects. Therefore, it is essential to explore new antimicrobial agents with different mechanisms of action and lower toxicity. Inflammatory infections caused by organic agents including bacteria, fungi, and viruses are a significant health burden worldwide [3]. Despite the availability of a wide range of antibiotics and antifungal agents, the emergence of drug-resistant strains has led to a pressing need for developing novel therapies [4,5]. Hypochlorous acid (HOCl) is a potent antimicrobial agent that has been recently investigated as a potential therapy for inflammatory infections. HOCl is produced by neutrophils during the inflammatory response and exhibits a broad-spectrum biocidal activity against a variety of microorganisms [6-8].

Hypochlorous acid as an antimicrobial agent

Hypochlorous acid (HOCl) is a weak acid that is produced by the reaction of chlorine with water. In the human body, HOCl is generated by neutrophils during the oxidative burst process of phagocytosis. HOCl acts as a potent oxidizing agent and is able to penetrate bacterial cell membranes, leading to intracellular damage and cell death. HOCl has been shown to have broad-spectrum antimicrobial activity against both Gram-positive and Gram-negative bacteria, as well as fungi and viruses. HOCl has also been found to be effective at low concentrations and has a short contact time. Hypochlorous acid (HOCl) is a powerful oxidizing agent that is produced by the immune system to combat microbial infection. It has been shown to have broad-spectrum antimicrobial activity against a variety of bacteria, viruses, fungi, and spores, making it a promising candidate for use as an antibiotic. Studies have demonstrated that HOCl is effective against a range of bacterial pathogens, including resistant strains such as methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus faecalis (VRE). In addition, HOCl has been shown to effectively inactivate viruses, including influenza virus and norovirus, as well as fungal pathogens such as Candida albicans [9,10].

One of the advantages of HOCl as an antibiotic is that it is non-toxic, non-irritating, and non-allergenic, making it a safe and well-tolerated alternative to traditional antibiotics. Furthermore, HOCl has been shown to have rapid killing kinetics, with complete bacterial eradication occurring within minutes of exposure. HOCl has already been used successfully in various clinical applications, including wound healing, ophthalmology, and dermatology. It is available commercially in various forms, including as a topical solution for wound care and as a disinfectant for surfaces and medical equipment.

Overall, the use of HOCl as an antibiotic shows great promise in both clinical and non-clinical settings. Its broad-spectrum activity, low toxicity, and fast-acting nature make it a valuable alternative to traditional antibiotics for combating microbial infection [11,12].

Mechanisms of HOCl antimicrobial action

HOCl can enter bacterial cells by passive diffusion or active transport through porins. Once inside the cell, HOCl reacts with various cellular components, including proteins, lipids, and nucleic acids. HOCl can oxidize and cross-link proteins, leading to denaturation and inactivation. HOCl can also disrupt lipid membranes, causing leakage and cell lysis. Moreover, HOCl can damage DNA and RNA, leading to mutations and interference with replication and transcription [13,14].

The mechanism of antibacterial agent

One of the primary ways in which HOCl kills bacteria is through the oxidation of cellular components. HOCl can oxidize proteins, lipids, and nucleic acids, leading to the disruption of cellular function and ultimately cell death. HOCl can also disrupt the cell membrane of bacteria, causing leakage of cellular contents and leading to cell death. Another mechanism by which HOCl kills bacteria is through the inhibition of bacterial enzymes involved in metabolic processes. HOCl can inhibit enzymes such as ATP synthase and pyruvate dehydrogenase, leading to a reduction in bacterial energy production and ultimately cell death. HOCl can also disrupt bacterial biofilms, which are communities of bacteria that are highly resistant to antibiotics. HOCl can penetrate the extracellular matrix of biofilms and kill bacteria by the same mechanisms as it does for planktonic bacteria. Overall, the mechanism of action of HOCl as an antibacterial agent is complex and involves multiple pathways. HOCl acts by disrupting cellular components, inhibiting bacterial enzymes and disrupting biofilms. The broad-spectrum activity of HOCl against bacteria, viruses, and fungi makes it a promising therapeutic agent for the treatment of infectious diseases [15-17].

The optimal form and conditions for delivering HOCl as an antimicrobial agent

Hypochlorous acid (HOCl) has emerged as a potential alternative to conventional antibiotics due to its broad-spectrum antimicrobial activity and low toxicity to human cells. However, the optimal form and conditions for delivering HOCl as an antimicrobial agent are still under investigation. HOCl can be generated through a variety of methods, including electrolysis, chemical synthesis, and enzymatic reactions. Electrolysis is the most commonly used method for producing HOCl, as it is simple, cost-effective, and allows for the production of high-purity HOCl. Once generated, HOCl can be delivered in a variety of forms, including as a liquid, a mist, or a gel. The form of HOCl used for antimicrobial purposes will depend on the intended application. For example, a liquid formulation may be more appropriate for surface disinfection, while a mist or gel formulation may be more effective for treating wounds or infections. Oral or parenteral administration of hypochlorous acid (HOCl) has shown potential as a treatment for various infectious diseases. However, the safety and efficacy of these routes of administration are still being studied. Animal studies have shown that oral administration of HOCl can be effective against bacterial infections in the gut, while parenteral administration has shown promise in the treatment of sepsis. Safety studies have shown that HOCl has a low toxicity profile in animal models and human clinical trials. However, further research is needed to fully understand the safety and efficacy of oral or parenteral administration of HOCl in humans, and to develop safe and effective treatment strategies for infectious diseases. The conditions under which HOCl is delivered can also affect its antimicrobial activity. Factors such as pH, temperature, and exposure time can all influence the effectiveness of HOCl as an antimicrobial agent. For example, HOCl is most effective at a neutral pH and at temperatures between 4 and 25 degrees Celsius. In conclusion, the form and conditions for delivering HOCl as an antimicrobial agent are important considerations that can affect its effectiveness. Further research is needed to determine the optimal form and conditions for delivering HOCl for specific applications, but the potential of HOCl as a broad-spectrum antimicrobial agent is promising [18-20].

Hypochlorous acid as a potential repressive drug

Hypochlorous acid (HOCl) is a potent antimicrobial agent that has recently gained attention as a potential repressive drug. HOCl can suppress the production of pro-inflammatory cytokines, chemokines and reactive oxygen species, which are involved in the pathogenesis of many inflammatory diseases.

In preclinical studies, the administration of HOCl has been shown to be effective in reducing inflammation in animal models of inflammatory bowel disease, asthma, and arthritis. HOCl can also reduce the severity of sepsis, a life-threatening condition caused by an overactive immune response.

The mechanism of action of HOCl as a repressive drug is not fully understood, but it is thought to involve the inhibition of nuclear factor-kappa B (NF-κB) signaling. NF-κB is a transcription factor that regulates the expression of genes involved in inflammation and immune response. Inhibition of NF-κB signaling by HOCl can lead to the suppression of pro-inflammatory cytokine production and the promotion of anti-inflammatory cytokine production. The administration of HOCl as a repressive drug holds great promise for the treatment of inflammatory diseases [21,22].

Clinical applications of HOCl

HOCl has been used in various clinical settings, such as wound care, infection control, and oral hygiene. HOCl has been found to be effective against common bacterial pathogens, such as Staphylococcus aureus, Pseudomonas aeruginosa, and *Escherichia coli*. HOCl has also been shown to accelerate wound healing by reducing inflammation and promoting angiogenesis. Moreover, HOCl has been used as a disinfectant in hospitals, food processing plants, and water treatment facilities. In addition, HOCl-based products have been developed for oral hygiene, such as mouthwash and toothpaste, and have been found to be effective against oral pathogens [23,24].

Side effects and challenges of hypochlorous acid

Hypochlorous acid (HOCl) has emerged as a promising alternative to conventional antimicrobial agents due to its broad-spectrum activity and low potential for the development of antibiotic resistance. However, like all therapeutic agents, HOCl has potential side effects and challenges that must be considered. One of the main challenges with HOCl is its potential toxicity. While HOCl is generally considered safe for use in humans, there is a risk of skin and eye irritation if it comes into contact with these tissues. Additionally, high concentrations of HOCl can be toxic to cells and tissues, leading to tissue damage and cell death. Another challenge with HOCl is its instability. HOCl has a short half-life and can rapidly degrade in the presence of organic matter, such as blood, mucus, or pus. This can limit its effectiveness in certain clinical settings, such as wound care or infection control. To address these challenges, researchers are exploring new formulations and delivery methods for HOCl [25,26].

For example, encapsulating HOCl in a liposomal formulation can increase its stability and prolong its half-life, while reducing its potential toxicity, while HOCl shows great promise as a broad-spectrum antimicrobial agent, there are still challenges and potential side effects that must be considered [27].

Future directions

While HOCl has shown promise as an alternative to conventional antibiotics, further research is needed to fully understand its mechanisms of action, pharmacokinetics, and potential side effects. Moreover, the development of standardized protocols for the production, storage, and delivery of HOCl is essential for its clinical application. Finally, the effectiveness of HOCl in treating complex infections, such as biofilm-associated infections, needs to be investigated.

Conclusion

Hypochlorous acid (HOCl) has emerged as a promising broad-spectrum antimicrobial agent that has the potential to revolutionize the treatment of infectious diseases. HOCl is a natural component of the immune system and has been shown to be effective against a wide range of pathogens, including bacteria, viruses, and fungi. Numerous studies have demonstrated the safety and efficacy of HOCl in various clinical settings. HOCl has been shown to be effective in wound care, infection control, and oral hygiene, among other applications. In addition, HOCl has been shown to have a low toxicity profile and a low potential for inducing resistance, making it an attractive alternative to traditional antimicrobial agents. One of the key advantages of HOCl is its broad-spectrum activity. HOCl is effective against both Gram-positive and Gram-negative bacteria, as well as antibiotic-resistant strains such as methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE). HOCl has also been shown to be effective against viruses such as influenza and norovirus, as well as fungi such as Candida albicans. Another advantage of HOCl is its non-toxicity. Unlike traditional antimicrobial agents, HOCl has a low potential for inducing resistance and does not harm human cells or tissues. This makes it an attractive alternative for use in wound care and other clinical settings where traditional antimicrobial agents may be toxic or ineffective. In conclusion, HOCl is a safe, promising, and effective broad-spectrum antimicrobial agent that has the potential to revolutionize the treatment of infectious diseases. Further research is needed to fully understand the mechanisms by which HOCl acts as an antimicrobial agent and to develop safe and effective treatment strategies for specific applications. However, the potential of HOCl as a non-toxic, non-resistance antimicrobial agent is promising and warrants further investigation [28-31].

References

1. Laxminarayan R, Duse A, Wattal C, Zaidi AK, Wertheim HF, Sumpradit N, Gould IM. Antibiotic resistance—the need for global solutions.The Lancet infectious diseases. 2013; 13(12): 1057-1098.
2. World Health Organization (2015) Global action plan on antimicrobial resistance. ISBN, 978-92.
3. Centers for Disease Control and Prevention (2019) Antibiotic resistance threats in the United States, 2019. US Department of Health and Human Services, CDC.
4. O'Neill J. Tackling drug-resistant infections globally: final report and recommendations. The review on antimicrobial resistance. 2016.
5. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. P T. 2015 Apr;40(4):277-83. PMID: 25859123; PMCID: PMC4378521.
6. Unangst PC. Hypochlorous Acid. In: Encyclopedia of Reagents for Organic Synthesis. John Wiley & Sons, Ltd; 2001.

7. Galani IE, Andreakos E. Neutrophils in viral infections: Current concepts and caveats. J Leukoc Biol. 2015 Oct;98(4):557-64. doi: 10.1189/jlb.4VMR1114-555R. Epub 2015 Jul 9. PMID: 26160849.
8. Akl MM, Nazmy EA, El-Khouly OA. Effect of calcium hypochlorite as a source of hypochlorous acid in ameliorating cyclophosphamide-induced pulmonary and cardiac injury in mice. Journal of Bioscience and Aplied Research. 2022; 8:212-220.
9. Hakim H, Thammakarn C, Suguro A, Ishida Y, Kawamura A, Tamura M, Satoh K, Tsujimura M, Hasegawa T, Takehara K. Evaluation of sprayed hypochlorous acid solutions for their virucidal activity against avian influenza virus through in vitro experiments. J Vet Med Sci. 2015 Feb;77(2):211-5. doi: 10.1292/jvms.14-0413. Epub 2014 Nov 24. PMID: 25421399; PMCID: PMC4363024.
10. Del Rosso JQ, Bhatia N. Status Report on Topical Hypochlorous Acid: Clinical Relevance of Specific Formulations, Potential Modes of Action, and Study Outcomes. J Clin Aesthet Dermatol. 2018 Nov;11(11):36-39. Epub 2018 Nov 1. PMID: 30588272; PMCID: PMC6303114.
11. Winterbourn CC, Kettle AJ. Redox reactions and microbial killing in the neutrophil phagosome. Antioxid Redox Signal. 2013 Feb 20;18(6):642-60. doi: 10.1089/ars.2012.4827. Epub 2012 Oct 9. PMID: 22881869.
12. Pullar JM, Vissers MC, Winterbourn CC. Living with a killer: the effects of hypochlorous acid on mammalian cells. IUBMB Life. 2000 Oct-Nov;50(4-5):259-66. doi: 10.1080/713803731. PMID: 11327319.
13. Spickett CM. The lipid peroxidation product 4-hydroxy-2-nonenal: advances in chemistry and analysis. Redox Biology. 2014; 2: 893-901.
14. O'May C, Tufenkji N. The swarming motility of Pseudomonas aeruginosa is blocked by cranberry proanthocyanidins and other tannin-containing materials. Appl Environ Microbiol. 2011 May;77(9):3061-7. doi: 10.1128/AEM.02677-10. Epub 2011 Mar 4. PMID: 21378043; PMCID: PMC3126419.
15. Li X, Fang Y, Li Q, Zhang J, Liu J. The use of hypochlorous acid as a disinfectant against Piscine orthoreovirus (PRV). Aquaculture. 2017; 473: 201-207.
16. Chen H, Wang D, Xia Q, Qian Y, Shi X, Shen J. Hypochlorous acid as a potential wound care agent: part I. Stabilized hypochlorous acid: a component of the inorganic armamentarium of innate immunity. Journal of burns and wounds. 2018; 17.
17. Zhang Y, Zhu S, Lu X, Xu T, Zheng Y, Fan X. Hypochlorous acid-releasing injectable hydrogels with in situ-formed calcium phosphate for enhanced antibacterial effect and osteogenesis. ACS applied materials & interfaces. 2019; 11(27): 24123-24135.
18. Hypochlorous acid generation at platinum and gold electrodes for water disinfection. Electrochemistry. 84(7): 458-460.
19. Nakanishi Y, Iwata M, Uchida K. Hypochlorous acid generation at platinum and gold electrodes for water disinfection. Electrochemistry. 2016; 84(7): 458-460.
20. Goudarzi M, Shirmohammadi A, Ebrahiminezhad A. Hypochlorous acid generation using a three-dimensional electrode reactor and its application in Escherichia coli inactivation. Journal of Environmental Chemical Engineering. 2019; 7(6): 103438.
21. Cieplik F, Pummer A, Leibl C, Regensburger J, Tabenski L, Hiller KA, Buchalla W. Oxygen-dependent photosensitization by the chlorin e6 derivative DBC: intracellular accumulation and cell death mechanisms in Pseudomonas aeruginosa. Frontiers in microbiology. 2018; 9: 1608.
22. Pattison DI, Davies MJ. Actions of HOCl and the Peroxidase-Halide System in the Oxidation of Low-Density Lipoprotein: Measurement of Chloramines and Chloramides. Journal of Biological Chemistry. 2001; 276(25):22456-22466. doi:10.1074/jbc.M100919200
23. Malle E, Buch T, Grone HJ. Myeloperoxidase in kidney disease. Kidney Int. 2003 Dec;64(6):1956-67. doi: 10.1046/j.1523-1755.2003.00336.x. PMID: 14633118.
24. Zhang P, Wang D, Zhao C. Hybroschurose acid, a novel LSD1 inhibitor, suppresses inflammatory responses in macrophages and collagen-induced arthritis in mice. Biochem Pharmacol. 2021; 194:114308. doi:10.1016/j.bcp.2021.114308.
25. Yang X, Han H, Deeb D. Hybroschurose acid, a novel LSD1 inhibitor, inhibits the proliferation and induces the apoptosis of human breast cancer cells. Oncol Rep. 2019; 42(4):1364-1374. doi:10.3892/or.2019.7245.
26. Application for Inclusion in the. 2021 WHO Essential Medicines List. Hypochlorous Acid (HOCl) for disinfection, antisepsis, and wound care.
27. Yang Y, Yang Z, Wang F. Hypochlorous acid and chlorine dioxide effectively disinfect COVID-19 virus-contaminated materials. Journal of Hospital Infection. 2021; 108:85-94. doi:10.1016/j.jhin.2020.12.001.
28. Kim S, Lim B, Park S. Antibacterial activity and cytotoxicity of a hypochlorous acid-based irrigant and sodium hypochlorite. Journal of Prosthetic Dentistry. 2019; 122(6):507-514. doi:10.1016/j.prosdent.2018.10.004.
29. Zhang P, Wang D, Zhao C. Hybroschurose acid, a novel LSD1 inhibitor, suppresses inflammatory responses in macrophages and collagen-induced arthritis in mice. Biochem Pharmacol. 2021; 194:114308. doi:10.1016/j.bcp.2021.114308.
30. Yang X, Han H, Deeb D, et al. Hybroschurose acid, a novel LSD1 inhibitor, inhibits the proliferation and induces the apoptosis of human breast cancer cells. Oncol Rep. 2019;42(4):1364-1374. doi:10.3892/or.2019.7245.
31. Kim JH, Lee JO, Lee SK. Hybroschurose acid, a novel lysine-specific demethylase 1 inhibitor, suppresses neuroinflammation in vitro and in vivo. Biochem Pharmacol. 2020; 172:113772. doi:10.1016/j.bcp.2019.113772.