

## A REVIEW OF CHLORINE DIOXIDE: EFFICACY, APPLICATIONS AND HEALTH IMPLICATION IN DISINFECTION

Yeshwanth Kamalakannan\*<sup>1</sup>

\*<sup>1</sup>M. Pharm, Department of Pharmaceutics. School of Pharmacy, Sathyabama Institute of Science and Technology. Chennai, Tamil Nadu – 600119.

Article Received on  
28 October 2024,

Revised on 18 Nov. 2024,  
Accepted on 08 Dec. 2024

DOI: 10.20959/wjpr202424-34876



\*Corresponding Author

Yeshwanth

Kamalakannan

M. Pharm, Department of  
Pharmaceutics. School of  
Pharmacy, Sathyabama  
Institute of Science and  
Technology. Chennai, Tamil  
Nadu – 600119.

### ABSTRACT

A potent, all-purpose antibacterial, chlorine dioxide (ClO<sub>2</sub>) is used extensively in water treatment, sterilisation, and disinfection. It is becoming a more alluring substitute for conventional disinfectants due to its special qualities, which include great stability at low doses and the lack of harmful byproducts. It is used in a variety of industries, including as healthcare, pharmaceuticals, and food safety, due to its efficaciousness in targeting bacteria, viruses, fungus, and other pathogens. It involves its oxidative characteristics, which cause cellular death by damaging the proteins, enzymes, and cell membranes that make up microorganisms. ClO<sub>2</sub> is a multipurpose disinfectant because of its ability to disrupt both aerobic and anaerobic bacteria. The safety profile of chlorine dioxide is further improved by the fact that it does not generate hazardous chlorinated byproducts as chlorine does. Chlorine dioxide has several benefits over conventional sterilising agents like hydrogen peroxide and chlorine. It does not damage surfaces or materials, has no residual toxicity, and is quite effective at

low doses. Furthermore, even when organic matter is present, it may penetrate biofilms and offer persistent disinfection. In addition to being environmentally benign, chlorine dioxide decomposes into non-toxic byproducts, making it appropriate for usage in delicate settings like hospitals and pharmaceutical production plants. Because of its many advantages, chlorine dioxide is a promising substitute for traditional disinfectants. Future project will investigate its potential in a new aerial sterilisation technique, which will enhance air-based disinfection in medical and pharmaceutical conditions.

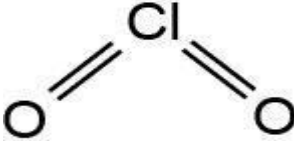
**KEYWORDS:** Chlorine dioxide, Sterilisation, disinfection, Industries, Chlorine.

## 1. INTRODUCTION

A strong oxidising agent, chlorine dioxide (ClO<sub>2</sub>) has attracted a lot of interest due to its many uses in water treatment, bleaching and disinfection. Chlorine dioxide was first created in 1814 by the British chemist Sir Humphrey Davy, and since then, it has developed from a curious laboratory experiment to an essential part of many industrial operations. It is a useful instrument for public health and safety because of its special chemical characteristics, which enable it to efficiently eradicate bacteria, viruses, and fungus. Chlorine dioxide works especially well as a disinfectant in drinking water, where it is a safer substitute for conventional chlorine. Chlorine dioxide breaks down into non-toxic compounds, reducing the dangers to the environment and human health, in contrast to chlorine, which can create hazardous disinfection byproducts.

Through a process that involves the oxidation of biological components, chlorine dioxide damages the integrity of microbial cell membranes and causes cell death. Its effectiveness spans a broad pH and temperature range, increasing its adaptability in a variety of contexts.<sup>[1]</sup> Chlorine dioxide usage is not risk-free, despite its advantages. High amounts can cause respiratory irritation as well as other health problems. Thus, to guarantee safe use, strict control and oversight are necessary. In order to maximise its usage in industrial and public health applications, ongoing research is examining the balance between its antibacterial qualities and possible toxicity. Chlorine dioxide continues to be a crucial research topic in the disinfectants increases.<sup>[2]</sup>

**Table 1: DRUG PROFILE.**

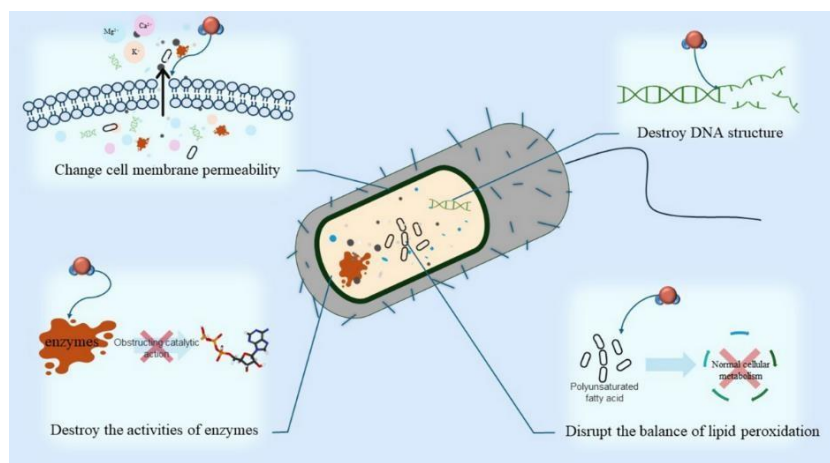
CONTENT	CHLORINE DIOXIDE
Structure	 <p><b>Figure: 1 structure of Chlorine dioxide.</b></p>
Chemical formula	ClO <sub>2</sub>
IUPAC Name	Chlorine Dioxide
	Beyond 11°C, Chlorine dioxide turns into a yellow-green gas; above 11°C degrees Celsius and -59°C, it appears to be a reddish-brown fluid.
Melting point	-59°C
Boiling point	11°C

Molecular weight	67.45 g/mol
pKa	ClO <sub>2</sub> (chlorine dioxide) has a high acidic pH value of it dissolves in water, a combination of chloric as well as chlorous acid develops, Thus ClO <sub>2</sub> is a combined anhydride.
Solubility	Chlorine is soluble in water
Uses	Chlorine dioxide is used for microbiological control in cooling towers and for the disinfection

## 2. MECHANISM OF ACTION

The most important method that chlorine dioxide (ClO<sub>2</sub>) has antimicrobial effects is because of its potent oxidising capabilities, which allow it to interfere with cellular structures and activities in a range of pathogens, including viruses, fungi, and bacteria. The production of reactive oxygen species (ROS), which cause oxidative stress in microbial cells, is the mechanism of action. Cell death is the ultimate effect of this oxidative stress, which also causes protein denaturation, cell membrane disintegration, and nucleic acid damage. Particularly, ClO<sub>2</sub> interacts with amino acids and other parts of the cell to produce covalent connections that change the structure and function of proteins and impede vital metabolic functions.<sup>[3]</sup> Chlorine dioxide is quickly absorbed in the gastrointestinal system when taken orally, and peak plasma concentrations are usually seen within an hour after consumption. ClO<sub>2</sub> and its byproducts, such as chlorite, chlorate, and chloride are dispersed throughout the body after absorption, with notable buildup in organs such as the kidneys, lungs, liver, and spleen. Chlorine dioxide is mostly eliminated by urine and faeces after 72 hours of ingestion, according to its pharmacokinetic profile. Because of its short half-life in the blood, ClO<sub>2</sub> requires cautious dosage in order to sustain therapeutically useful concentrations. The dosage, the method of administration, and individual differences in the makeup of the gut microbiota all affect the pharmacodynamics of chlorine dioxide.<sup>[4]</sup> Despite the strong antibacterial activity of ClO<sub>2</sub>, its safety profile is an important factor to take into account. When exposed to chlorine dioxide, adverse consequences might include more severe responses including haemoglobinuria and methemoglobinemia, especially at larger dosages, as well as gastrointestinal problems like nausea, vomiting, and diarrhoea. These side effects highlight how crucial it is to follow dose recommendations and keep an eye out for any possible toxicity. According to preliminary research, ClO<sub>2</sub> may impede viral entrance by oxidising cysteine residues in the virus's spike protein, which stops the virus from attaching to the host cell's angiotensin-converting enzyme 2 (ACE2) receptor. To completely clarify chlorine dioxide's safety and effectiveness in this role, however, and to create uniform guidelines for

its application in clinical settings, more research is required. In general, optimising chlorine dioxide's use in industrial and medicinal settings requires an understanding of its pharmacokinetic profile and mechanism of action.<sup>[10]</sup>



**Fig. 1: Application for chlorine dioxide and how it work as a disinfectant.**

### 3. METHOD DEVELOPMENT AND VALIDATON

**1. Fredy saguti, *et al.*, (2023)** in drinking water treatment facilities, chlorine and chlorine dioxide are commonly used as disinfectants. A study assessed the effectiveness of these disinfectants in inactivating human adenovirus type 2 (HAdV2), simian rotavirus SA11 (RVSA11), and echovirus 20 (E30) in purified water from a plant that prepares drinking water. According to the findings, within two minutes of contact, chlorine reduced E30 by 3-log<sub>10</sub>, RV SA11 by 2-3-log<sub>10</sub>, and HADV2 by 3-4-log<sub>10</sub>. In contrast, chlorinedioxide was more efficient in rendering undetectable despite inactivating E30 by 4-log<sub>10</sub> and RV SA11 BY 3-log<sub>10</sub>.<sup>[11]</sup> These findings are valuable for determining which disinfection systems are most suitable for wastewater reuse and for assessing the risks associated with chlorine and chlorine dioxide treatment processes.

**2. Kadota Chisaki *et al.*, (2023)** the antiviral properties of chlorine dioxide (ClO<sub>2</sub>) against the infectious bronchitis virus (IBV) and avian influenza virus (AIV) were assess in both gaseous and liquid forms (ClO<sub>2</sub> gas dissolved liquid). Suspension experiments (10 ppm) and carrier testing in dropping/wiping procedures (100 ppm) were conducted to assess ClO<sub>2</sub> action in liquid form. Within 15 seconds of treatment, virus levels in the suspension test fell below the detection limit<sup>[12]</sup>, even an organic component was present. The carrier examinations dropping procedure dropped AIV and IBV to below the detection limit in 1 and 3 minutes, respectively.

**3. Audry Peredo-Lvoillo, *et al.*, (2023)** ClO<sub>2</sub> is currently being touted as a potential anti-SARS-cov-2 medication for people since it has its unique ability to oxidize cysteine amino acids in the spike protein sequences that comprise the SARS-associated this prevents subsequent contact with the Angio tension- converting enzyme type 2 receptor found in alveolar cells.<sup>[13]</sup> Further research into the dependability and efficacy of ClO<sub>2</sub> in healthy and sick persons would be beneficial in justifying its function as an anti- SARS-cov-2 agent.

**4. Albaharna Husssain *et al.*, (2023)** Flexible Bronchoscopes, Laryngoscope blades, and rigid nasal endoscopes were used to evaluate chlorine dioxide wipes. Following contact with patients who tested positive for COVID-19, the endoscopes were cleaned using the wipes. If the post-procedure pre- disinfection swab tested positive for the COVID-19 virus using RT-PCR, the scope of the research was covered.<sup>[14]</sup> Between July 2021 and February 2022, we examined 38 samples for 19 individuals (scopes) both before and after they were cleaned with chlorine dioxide wipes.

**5. Obinata Kaoru *et al.*, (2022)** Ozone and chlorine dioxide gases are useful ways to prevent aerosol infections in indoor air. Ozone, however, needs comparatively the elevated levels for how its works may damage individuals around.<sup>[15]</sup> Nonetheless, the aqueous solution and mild levels of chlorine dioxide gas are minimizing aerosol infiltration of the responsible bacteria and it is anticipated that they will be extremely safe, effective in preventing infections, and economical when used in conjunction with a high- efficiency particulate air filter.

**6. Lim YC, *et al.*, (2022)** the purpose of this study was to thoroughly examine and assess chlorine dioxide's disinfecting effectiveness and safety.<sup>[16]</sup> Of the 33 included research, 14 examined chlorine dioxide's effectiveness as a disinfectant, 8 examined its safety and toxicity in people and animals, and 15 examined its effects, including its usage in water treatment disinfection.

**7. Ruiping Wei *et al.*, (2022)** ClO<sub>2</sub> repressed the early stage of the virus life cycle, as evidenced by the fact that its inhibitory action happened during viral attachment rather than entrance.<sup>[17]</sup> When ClO<sub>2</sub> was added before to, concurrently with, or following viral infection, it demonstrated a strong anti-ASFV impact.

**8. Sevda Jalali Milani *et al.*, (2022)** The SARS-cov-2 virus was detected in sewage using the viral concentration approach, followed by an RT-qPCR test.<sup>[18]</sup> The ability and efficacy of UV disinfection, ozone, and chlorination in eradicating the virus that causes SARS-cov-2 in

wastewater was assessed.

**9. N. Hatanaka *et al.*, (2021)** To possess each chemical's antiviral action, evaluating SARS-CoV-2 viruses were medications with varying concentrations of sodium hypochlorite and ClO<sub>2</sub>, and a 50% tissue culture infectious dose was calculated.<sup>[19]</sup>

**10. Michele Totaro, *et al.*, (2021)** the efficacy of ClO<sub>2</sub> used in clinical and community settings to eradicate bloodborne, enteric, and respiratory viruses is the main topic of this narrative synthesis. In less than five minutes, 0.5-1.0 mg/L of ClO<sub>2</sub> decreased influenza viruses by 99.9%. Sewage containing Sars-CoV-2 was eradicated at higher concentrations (20 mg/L). in less than 30 minutes, ClO<sub>2</sub> concentrations ranging 0.2 to 1.0 mg/L guaranteed a minimum of 99% viral reduction of Ad40, HAV, Coxsackie B5 virus, and other enteric viruses.<sup>[20]</sup> To sum up, ClO<sub>2</sub> is a flexible virucidal agent that works well in a variety of environmental matrices.

**11. Yuexian Ge, *et al.*, (2021)** The purpose of this study is to provide a summary of the processes and dynamics of ClO<sub>2</sub> inactivation with viruses. Viral inactivation rates rise two stage: a tailing phase after an initial fast inactivation with viruses. Viral Inactivation rates rise with temperature or pH, but exhibit distinct patterns when dissolved organic matter (DOM) concentrations rise.<sup>[21]</sup>

**12. M Wittmann, *et al.*, (2020)** In this editorial, we suggest that high purity aqueous chlorine dioxide (ClO<sub>2</sub>) solutions be used to examine the potential for creating and executing antiviral procedure. This proposal's goal is to start studies that could result in the development of useful and efficient antiviral treatments. In order to do this, we will first go over several significant characteristics of the ClO<sub>2</sub> molecule that make it a useful antiviral agent. After that, we will go over some previous findings about the use of ClO<sub>2</sub> solutions to stop the propagation of viral infections.<sup>[22]</sup>

#### 4. DISCUSSION

A strong antibacterial, chlorine dioxide (ClO<sub>2</sub>) has attracted a lot of interest due to its many uses in water treatment and disinfection. It is a useful tool in many industries, including wastewater management, food safety, and healthcare, because of its special oxidative qualities, which allow it to efficiently target a variety of pathogens, including bacteria, viruses, and fungus. Chlorine dioxide functions at lower concentrations than conventional disinfectants, which improves its safety profile and reduces the possibility of hazardous byproducts. Its promise as an antiviral drug has been demonstrated by recent studies that have

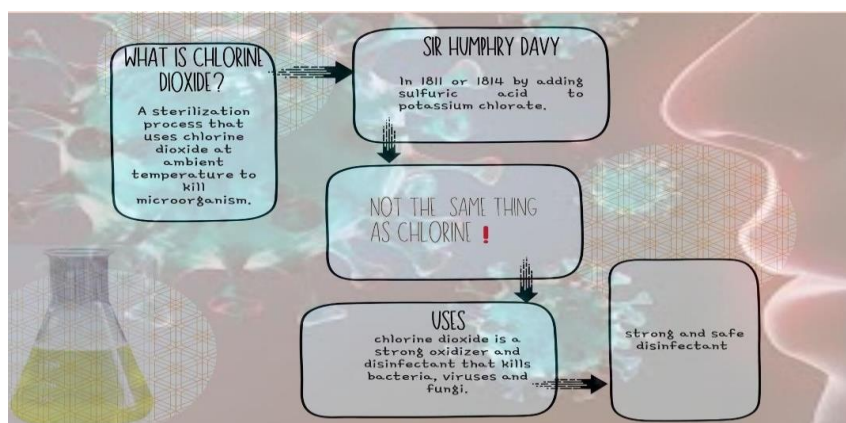
shown its efficacy against certain viruses, such as the avian influenza virus and the infectious bronchitis virus.

Additionally, as the need for effective disinfectants rises, research on chlorine dioxide remains a critical area of study in the quest for safer and more potent antimicrobial treatments. Nevertheless, there are hazards associated with using chlorine dioxide, even with its benefits. Strict control and supervision are required during application since high concentrations might cause respiratory irritation and other health problems. In order to maintain chlorine dioxide's effectiveness as a disinfectant in the face of new public health issues, it is imperative that ongoing research be conducted to balance its antimicrobial activity with safety.

## 5. CONCLUSION

In conclusion, chlorine dioxide ( $\text{ClO}_2$ ) is a strong and adaptable antimicrobial agent that has a lot of promise for use in a variety of fields, such as food safety, healthcare, and water treatment. Often at lower concentrations than conventional disinfectants, its special oxidative qualities allow for efficient disinfection against a variety of pathogens, such as bacteria, fungus, and viruses. Despite its well-established effectiveness, cautious handling and continued study are necessary to reduce any possible health hazards brought on by excessive concentrations.  $\text{ClO}_2$  is a viable answer in the search for safer and more effective antimicrobial treatments, as the need for efficient disinfectants in developing.

## 6. GRAPHICAL ABSTRACT



## 7. ACKNOWLEDGEMENTS

The management of the Sathyabama Institute of Science and Technology, Jeppiaar Nagar, Sh 49A, Chennai, Tamil Nadu 600119, India, is greatly appreciated by the writers for their

support.

I would want to express my profound gratitude to my amazing mentor for his inspirational remarks.

## 8. CONFLICT OF INTEREST

Regrading this paper, the authors state that they have no relevant conflict of interest.

## 9. REFERENCE

1. Qingdong X, Guangming, *et al.*, Study on subchronic toxicity of chlorine dioxide and by-products in water. *J. Environ. Sci. Health A Tox. Hazard Subst. Environ*, 2006 Eng. 41(7): 1347–1353.
2. White C.W, Martin J.G, Chlorine gas inhalation: human clinical evidence of toxicity and experience in animal models. *Proc. Am. Thor. Soc*, 2012; 7(4): 257–263.
3. Andrés CMC, Lastra JMPdI, Andrés Juan C *et al.*, Chlorine dioxide: friend or foe for cell biomolecules? A chemical approach. *Int J Mol Sci*, 2022; 23: 15660. <https://doi.org/10.3390/ijms232415660>.
4. Arellano-Gutiérrez G, Aldana-Zaragoza EH, Pérez-Fabián A. Intestinal perforation associated with chlorine dioxide ingestion: and adult chronic consumer during COVID-19 pandemic. *Clin J. Gastroenterol* 2021; 14: 1655–60. <https://doi.org/10.1007/s12328-021-01527-y>
6. Bathina G, Yadla M, Burri S *et al.* An unusual case of reversible acute kidney injury due to chlorine dioxide poisoning. *Ren Fail*, 2013; 35: 1176–8. <https://doi.org/10.3109/0886022X.2013.819711>.
7. Bercz J, Jones L, Garner. L *et al.*, Subchronic toxicity of chlorine dioxide and related compounds in drinking water in the nonhuman primate. *Environ Health Perspect*, 1982; 46: 47–55. <https://doi.org/10.1289/ehp.824647>.
8. Burela A, Hernández-Vásquez A, Comandé D *et al.*, Chlorine dioxide and chlorine derivatives for the prevention or treatment of COVID-19: a systematic review. *Rev Peru Med Exp Salud Publica*, 2020; 37: 605–10. <https://doi.org/10.17843/rpmesp.2020.374.6330>.
9. Buschini A, Carboni O, Furlini M *et al.*, Sodium hypochlorite-, chlorine dioxide-, and peracetic acid-induced genotoxicity detected by the Comet assay and *Saccharomyces cerevisiae* D7 tests. *Mutagenesis*, 2004; 19: 157–62. <https://doi.org/10.10193/mutage/geh012>.

10. Campagna MV, Faure-Kumar E, Treger JA *et al.* Factors in the selection of surface disinfectants for use in laboratory animal setting. *J Am Assoc Lab Anim Sci*, 2016; 55: 175–88.
11. Saguti F, Kjellberg I, Churqui MP, *et al.*, The Virucidal Effect of the Chlorination of Water at the Initial Phase of Disinfection May Be Underestimated If Contact Time Calculations Are Used. *Pathogens*, 2023; 12(10): 1216.
12. Kadota C, Miyaoka Y, Kabir MH, *et al.* Evaluation of chlorine dioxide in liquid state and in gaseous state as virucidal agent against avian influenza virus and infectious bronchitis virus. *J Vet Med Sci*, 2023; 85(10): 1040-1046. doi:10.1292/jvms.23-0194.
13. Peredo-Lovillo A, Romero-Luna HE, Juárez-Trujillo N, *et al.*, Antimicrobial efficiency of chlorine dioxide and its potential use as anti-SARS-CoV-2 agent: mechanisms of action and interactions with gut microbiota. *J Appl Microbiol*, 2023; 134(7): 1xad133. doi:10.1093/jambio/1xad133.
14. Albaharna H, Almubiereek H, Almualim M, *et al.*, Efficacy of chlorin dioxide wipes in disinfecting airway devices contaminated with Covid-19. *Front Cell Infect Microbiol*, 2023; 13: 1061647. Published 2023 Mar 22. doi:10.3389/fcimb.2023.1061647.
15. Obinata K. New Countermeasures Against Infections with/after COVID-19: Is Chlorine Dioxide a Useful and Safe Disinfectant?. *Juntendo Iji Zasshi*, 2022; 68(5): 465-472. Published, 2022 Oct 15. doi:10.14789/jmj.JMJ22-0030-R.
16. Jefri UHNM, Khan A, Lim YC, *et al.*, A systematic review on chlorine dioxide as a disinfectant. *J Med Life*, 2022; 15(3): 313-318. doi:10.25122/jml-2021-0180.
17. Wei R, Wang X, Cao Y, *et al.*, Chlorine Dioxide Inhibits African Swine Fever Virus by Blocking Viral Attachment and Destroying Viral Nucleic Acids and Proteins [published correction appears in *Front Vet Sci*, 2022 Jun 09; 9: 937653. doi:10.3389/fvets.2022.937653].
18. Jalali Milani S, Nabi Bidhendi G. A Review on the Potential of Common Disinfection Processes for the Removal of Virus from Wastewater. *Int J Environ Res*, 2022; 16(1): 9. doi:10.1007/s41742-021-00387-1.
19. Hatanaka N, Xu B, Yasugi M, *et al.*, Chlorine dioxide is a more potent antiviral agent against SARS- CoV-2 than sodium hypochlorite. *J Hosp Infect*, 2021; 118: 20-26. doi:10.1016/j.jhin.2021.09.006.
20. Totaro M, Badalucco F, Costa AL, *et al.*, Effectiveness of Disinfection with Chlorine Dioxide on Respiratory Transmitted, Enteric, and Bloodborne Viruses: A Narrative Synthesis. *Pathogens*, 2021; 10(8): 1017. Published 2021 Aug 12.

doi:10.3390/pathogens10081017.

21. Alvarez ME, Brien RT, Mechanisms of inactivation of poliovirus by chlorine dioxide and iodine. *Appl Environ Microbiol*, 1984; 44: 1064–1071.
22. Kály-Kullai K, Wittmann M, Noszticzius Z, Rosivall L. Can chlorine dioxide prevent the spreading of coronavirus or other viral infections? Medical hypotheses. *Physiol Int*, 2020; 107(1): 1-11. doi:10.1556/2060.2020.00015.