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Review

Toward Sustainable Chlorine Dioxide: Managing and Minimizing By-Product Generation

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Abstract: Chlorine dioxide (ClO_2) is a key oxidizing agent widely used in water treatment, pulp bleaching, and disinfection processes. Despite its recognized efficiency and its reduced formation of harmful chlorinated by-products compared to chlorine, the sustainability of its full life cycle, starting from production to end-use, remains underexplored. This review critically examines the industrial methods for ClO_2 synthesis, highlighting the chemical pathways and operational conditions that influence the formation of undesirable by-products such as chlorates, chlorites, and acidic effluents. In parallel, attention is given to disinfection by-products (DBPs) formed during ClO_2 application, which often share precursors or transformation routes with the compounds generated during production. This dual perspective reveals important chemical and regulatory overlaps, suggesting that upstream improvements in synthesis can have downstream benefits in reducing DBPs in treated waters. This review provides a comprehensive and system-level analysis of chlorine dioxide sustainability by introducing original comparative tables and innovative matrices that map production routes, by-product profiles, and mitigation strategies across different operational contexts. These visual tools aim to support decision-makers, researchers, and industry professionals in identifying optimal trade-offs between efficiency, environmental safety, and regulatory compliance. By adopting a by-product-centered lens across both production and application phases, this work offers new insights into circular opportunities and green chemistry innovations for ClO_2. Future directions are discussed with a focus on process integration, by-product valorization, and the alignment of industrial practices with emerging sustainability frameworks.

Keywords: chlorine dioxide; production methods; disinfection by-products; chlorite; chlorate; toxicity; mitigation strategies

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1. Introduction

Chlorine dioxide (ClO_2) has emerged as a powerful and versatile disinfectant with broad applicability across water treatment, industrial hygiene, medical sterilization, and food safety sectors [1], [2], [3], [4]. Initially introduced in the 1940s as a bleaching agent in the paper industry, its use has significantly expanded in recent decades due to growing concerns over the disinfection by-products (DBPs) associated with traditional chlorination methods [1], [4], [5], [6], [7], [8]. As a potent oxidizing agent, ClO_2 exhibits strong biocidal activity against a wide range of microorganisms, including bacteria, viruses, protozoa, and fungi, while exhibiting unique chemical behavior that distinguishes it from chlorine and other oxidants such as ozone or hydrogen peroxide [1], [4], [6], [7], [8]. One of the most notable advantages of ClO_2 lies in its selectivity and reaction mechanisms [9]. Unlike chlorine, which primarily acts through electrophilic halogenation and tends to form halogenated DBPs such as trihalomethanes (THMs) and haloacetic acids (HAAs)[10], ClO_2 oxidizes cellular components via single-electron transfer processes without halogenating organic molecules to the same extent [11]. This distinction leads to significantly lower levels of THMs and HAAs formation, an especially important benefit in the context of drinking water treatment, where these compounds

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are regulated due to their genotoxic and carcinogenic potential [12–15]. Another key advantage of chlorine dioxide is its broad operational pH range. While chlorine's disinfection efficacy diminishes considerably in alkaline environments (pH > 7.5), ClO_2 maintains its antimicrobial activity across a pH range of 4 to 10, making it more robust and adaptable to variable water conditions [13–15]. Moreover, it remains dissolved in water as a true gas rather than undergoing hydrolysis, contributing to its stability and consistent performance [16,17]. ClO_2's physical and chemical properties make it highly effective in both liquid and gaseous phases, allowing for flexible implementation in settings such as hospital disinfection, biofilm control in pipelines, due to its high water solubility, and decontamination of enclosed spaces [4], [18], [19], [20]. Compared to ozone, another powerful oxidant, chlorine dioxide demonstrates lower corrosivity and does not generate hazardous by-products like bromate (BrO_3^-) in bromide containing waters, an issue that has limited ozone's widespread adoption [21,22]. Despite its advantages, the use of chlorine dioxide is not without challenges. The generation and application of ClO_2 can lead to the formation of several inorganic by-products, most notably chlorite (ClO_2^-) and chlorate (ClO_3^-) ions, which result from its disproportionation and decomposition reactions [23]. Under specific conditions, especially in electrochemical generation processes or at high dosages, perchlorates (ClO_4^-) may also be produced [24]. These anions are of concern due to their potential effects on thyroid function and ecosystem toxicity, leading to regulatory scrutiny and the need for careful monitoring [5], [25], [26], [27]. Furthermore, secondary reactions involving ClO_2 and halide ions such as bromide (Br^-) or iodide (I^-) can give rise to halogenated organic by-products, including brominated trihalomethanes, iodoacetic acids, and other species known for their increased cytotoxicity and genotoxicity compared to chlorinated analogues [28]. This aspect has led to increased research into both the mechanisms of by-product formation and strategies to minimize their occurrence, including precursor removal, optimization of ClO_2 dose, and integration with other treatment technologies [29], [30]. Given the growing interest in sustainable and safe disinfection technologies, this review aims to provide a comprehensive and critical overview of chlorine dioxide's chemistry, production techniques, disinfection efficacy, and by-product formation. It stands out for its comparative and integrated approach, combining technical and environmental evaluation matrices with detailed tables that allow a direct comparison of production methods and their environmental implications. Special attention is devoted to the mechanisms of formation of both inorganic and organic disinfection by-products, including chlorinated, brominated, and iodinated species, as well as to their toxicological profiles and regulatory relevance. In addition to discussing current and emerging strategies for by-product mitigation, ranging from process optimization and electrochemical control to advanced oxidation/reduction processes and adsorption systems, this review also examines hybrid and combinatorial solutions that enhance treatment efficacy while minimizing health and environmental risks. The work is addressed to a broad audience including researchers, water treatment professionals, and regulatory bodies. By providing a technically rigorous yet accessible synthesis of the current knowledge, it aims to fill an existing gap in the literature, supporting the transition toward more efficient, compliant, and environmentally responsible disinfection practices.

2. Chlorine Dioxide: Properties and Mechanism of Action

2.1. Chemical Properties

Chlorine dioxide (ClO_2) is a yellow-green gas at room temperature with a pungent chlorine-like odor, commonly recognized by its intense oxidizing capacity [31]. With a molecular weight of 67.45 g/mol, it is significantly heavier than air (approximately 2.4 times denser), which influences its behavior in confined environments. Its molecular configuration, consisting of one chlorine atom in a +4 oxidation state bonded to two oxygen atoms, contributes to its high reactivity and distinctive properties compared to other oxidants such as chlorine, ozone, or hydrogen peroxide [5]. A hallmark of ClO_2 is its high water solubility, approximately 8 g/L at 25°C, which is 5 times higher than Cl_2 [32], and the amount of ClO_2 utilized in water treatment is less than that of Cl_2 [33], which occurs without hydrolysis. This is crucial, as many oxidants hydrolyze in aqueous solutions, altering their reactivity and stability. Instead, ClO_2 remains in solution as a true dissolved gas, granting it stability in various treatment environments. Moreover, unlike chlorine, ClO_2 functions as a selective oxidant and does not participate in chlorination reactions, which limits the formation of halogenated by-products such as trihalomethanes (THMs) and haloacetic acids (HAAs) [10]. Chang et al. (2000) [34] investigated the formation of trihalomethanes (THMs) (Figure 1) and haloacetic acids (HAAs) (Figure 2) under varying chlorine dioxide dosages and contact times, enabling a comparison with the formation patterns observed for chlorine [35], [36]

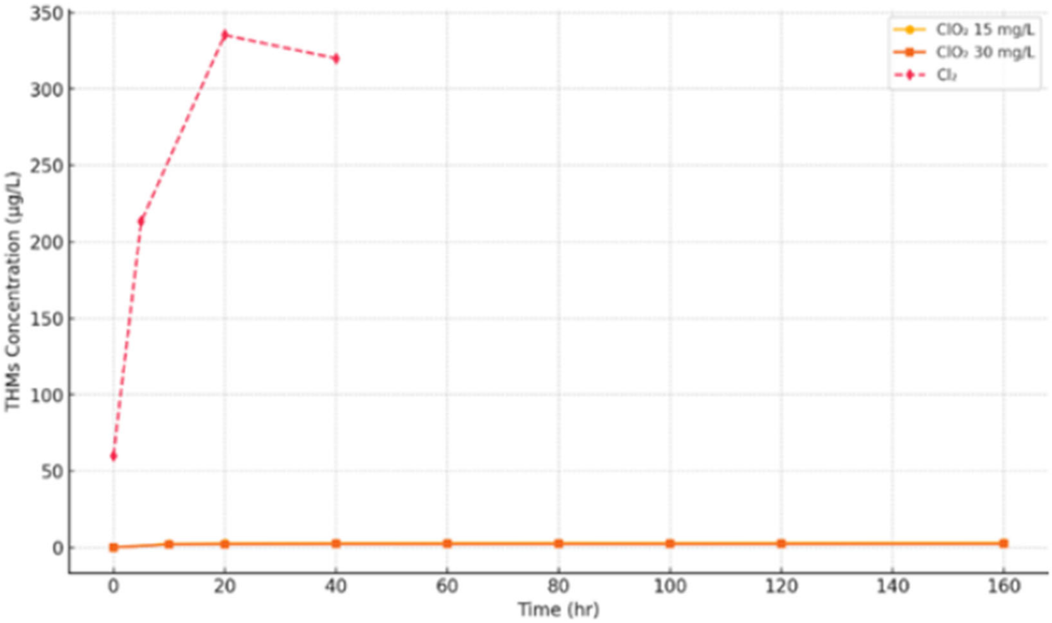

Figure 1. Residual percent of Total THMs at different contact time and ClO_2 (left) [34] and Cl_2 (right) [35] dosage.

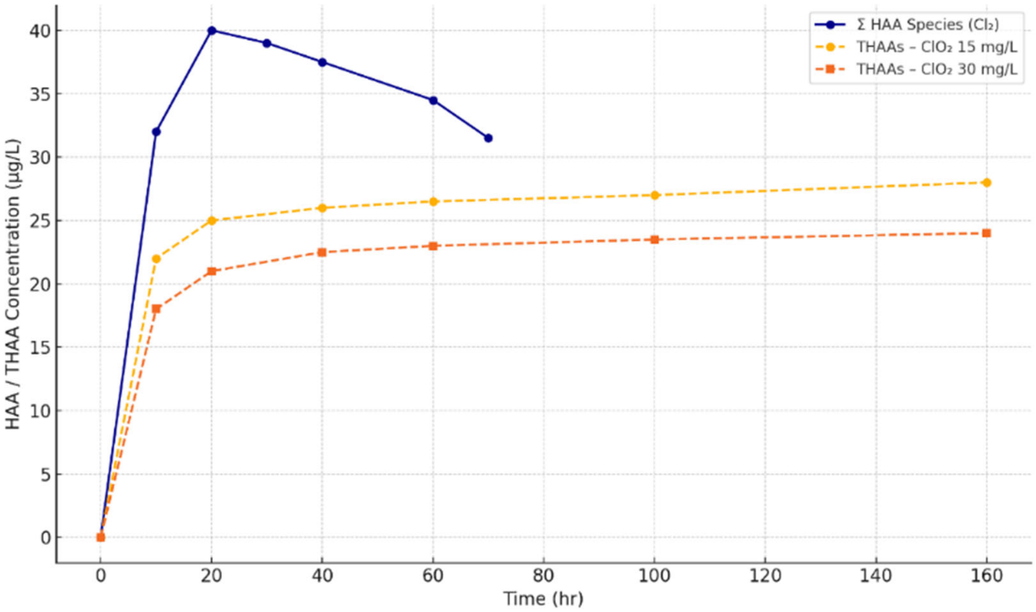

Figure 2. Residual percent of Total HAAs at different contact time and ClO_2 (left) [36] and Cl_2 (right) [36] dosage.

2.2. Antimicrobial Mechanism of Action

The antimicrobial properties of chlorine dioxide are the result of its selective oxidation of key bio-molecular targets [9], [37]. ClO_2 shows a preference for electron-rich sites in proteins and other cellular structures [1], [2], [3], [4]. It reacts rapidly with amino acids such as cysteine [38], tyrosine [4], [39], [40], methionine [41], and tryptophan [38], [42], disrupting enzymatic functions and protein integrity. These reactions ultimately lead to loss of cell membrane integrity, disruption of osmotic balance, and cell death [38], [42]. As demonstrated in studies such as those by Ogata (2007), ClO_2 modifies side chains of susceptible amino acids, denaturing proteins critical for microbial survival. Its action also includes oxidation of iron-sulfur clusters within respiratory enzymes, thereby inhibiting cellular respiration and ATP production [43], [44]. Though ClO_2 is less reactive with nucleic acids compared to proteins, it can still induce oxidative damage to RNA and DNA, including nucleotide modification and strand breakage, which impairs microbial replication and viability [45], [46], [47]. Another significant feature is ClO_2's efficacy against biofilms, which are microbial communities embedded in a protective matrix of extracellular polymeric substances. Biofilms pose a substantial challenge in both medical and industrial contexts, often resisting conventional disinfection. ClO_2's high solubility and small molecular size enable it to penetrate the biofilm matrix, oxidize microbial membranes, and inactivate embedded cells, unlike, for example, ozone, does not react with the extracellular polysaccharides that make up the biofilm matrix [18]. The selectivity of ClO_2 based on organism size has also been quantitatively described. According to Noszticzius et al. (2013)[37], the time required to inactivate bacteria is of the order of milliseconds: 2.9 ms for spherical bacteria and 4.4 ms for cylindrical ones with a 1 μm diameter. The extremely short contact time needed for microbial inactivation makes ClO_2 efficient and fast acting, while its limited tissue penetration due to volatility ensures minimal harm to multicellular organisms.

2.3. Antiviral Properties

In addition to its antibacterial and antifungal capabilities, chlorine dioxide is an effective antiviral agent against a broad range of viruses, including both enveloped and non-enveloped types. Its antiviral action primarily involves the oxidation of viral capsid proteins, disrupting the structure required for host-cell recognition and entry. In enveloped viruses such as SARS-CoV-2 or influenza, ClO_2 targets the envelope glycoproteins, such as the spike protein, impairing their ability to bind host receptors [48], [49], [50]. Empirical studies support these mechanisms. In enveloped viruses, it acts on viral genoma damaging the Rna stopping its replication [51]. Watamoto et al. (2013)[52] demonstrated that a 0.02% ClO_2 solution could disinfect Hepatitis C virus-contaminated dental tools in under 10 minutes. Xue et al. (2013)[53] showed that ClO_2 outperforms chlorine in inactivating rotavirus and influenza H1N1, achieving 4-log reductions at low concentrations and short contact times. Miura and Shibata (2010) confirmed similar results at just 0.03% ClO_2 for H1N1. For enterovirus EV71, antiviral activity was significant at concentrations as high as 84.65 mg/L. Girard et al (2016)[54] reported over 98% microbial reduction on produce surfaces using 5–20 mg/L ClO_2. While bacterial inactivation was more effective at lower concentrations, higher doses were required for complete viral disinfection, highlighting dose-dependent efficacy. Moreover, temperature and pH adjustments can enhance virucidal activity, granting flexibility in designing effective disinfection protocols [55]. Taken together, these findings underscore ClO_2's role as a broad-spectrum antimicrobial and antiviral agent. Its non-chlorinating oxidation mechanism, pH-independent activity, and reduced by-product formation make it a compelling alternative to traditional disinfectants for water treatment, food sanitation, and medical sterilization applications.

3. Comparative Evaluation of Chlorine Dioxide and Alternative Disinfectants

To provide a comprehensive understanding of chlorine dioxide's performance relative to other commonly employed disinfectants, this section presents a structured comparison with ozone (O_3), ultraviolet (UV) radiation, hydrogen peroxide (H_2O_2), and peracetic acid (PAA). These agents are widely used in water treatment, food processing, and healthcare environments, each offering unique benefits and limitations. Wang et al. (2024) [56] have conducted a comprehensive study on the differences between chlorine dioxide and other disinfectants, consulting an extensive bibliography. The comparative evaluation considers key parameters such as antimicrobial efficacy, disinfection by-products, operational costs, and environmental impact, crucial criteria for selecting an optimal disinfection strategy tailored to specific regulatory and practical contexts. Chlorine dioxide demonstrates strong biocidal activity across a wide range of pathogens, including resistant protozoa and biofilm-associated microbes, due to its penetration ability and selective oxidation mechanisms [18], [19], [20]. Ozone, as a powerful oxidant, shows rapid inactivation but lacks residual disinfection [57], [58], [59], [60], [61], [62], [63]; UV irradiation is efficient for inactivating bacteria and viruses but can be hindered by water turbidity [60], [64]. Hydrogen peroxide, while less potent on its own, is effective when combined with UV or ozone in advanced oxidation processes. Peracetic acid (PAA) is a powerful disinfectant, effective against bacteria, viruses, and spores by releasing active oxygen and disrupting cell membranes [65], [66]. A major advantage of ClO_2 over chlorine is its lower tendency to form halogenated organic DBPs such as trihalomethanes (THMs) and haloacetic acids (HAAs) [6], [58],[67], [68], [69]. However, it does produce inorganic DBPs like chlorite and chlorate, which must be monitored [23], [26]. Ozone can form bromate, a regulated carcinogen, when bromide is present [60], [65], [66]. UV treatment generates no chemical by-products but may cause nitrite formation under certain conditions. H_2O_2 breaks down into benign substances, making it attractive for environmentally sensitive applications. Monarca et al. (2002)[67] reported that by-products isolated from river waters treated with PAA were predominantly carboxylic acids, which are not recognized as being mutagenic, and that are formed through the oxidation of natural organic matter in the water. Table 1 presents an overview of disinfection by-products generated by various disinfectants. Table 2 is also essential to understanding the regulatory framework for these by-products.

Table 1. Disinfection Byproducts from Various Disinfectants, not only Ozone, UV and Hydrogen Peroxide [10], [35], [59], [70], [71].

Disinfectant	Organohalogenic Disinfection Byproducts	Inorganic Disinfection Byproducts	Non-Halogenic Disinfection Byproducts
Chlorine (Cl_2) / Hypochlorous Acid (HOCl)	Trihalomethanes, halogenic acetic acids, haloacetonitriles, hydrated chlorine, chloropicrin, chlorophenol, N-chloramines, haloform, bromonitromethane	Chlorates (mainly from hypochlorite application)	Aldehydes, alkanes, benzene, carboxylic acids
Chlorine Dioxide (ClO_2)	Haloacetonitriles, cyanogen chloride, organic chloramines, acids, chlorohydrins, haloketones	Chlorite, chlorate	Not known
Chloramines (NH_2Cl, etc.)	Haloacetonitriles, cyanogen chloride, organic chloramines,	Nitrite, nitrate, chlorate, hydrazine	Aldehydes, ketones

	acids, chlorohydrins, haloketones		
Ozone (O_3)	Bromoform, monobromoacetic acid, dibromoacetic acid, dibromoacetone, cyanogen bromide	Chlorate, iodate, bromate, hydrogen peroxide, iodoacetic acid, iodobromoacetic acid, peroxides, ozonates	Aldehydes, ketones, ketoacids, carboxylic acids
Ultraviolet (UV) Rays	None	Nitrite, nitrate (from nitrate photolysis)	Aldehydes, organic acids
Hydrogen Peroxide (H_2O_2)	None	Peroxides, oxygen radicals	Aldehydes, organic acids
Peracetic Acid (PAA)	None	None	Carboxylic acids

Table 2. Comparison of Legislative Regulations on the Limit Concentrations (mg/l) of Trihalomethanes [72].

By products	**EPA (2003)**	**WHO (2004)**	**Europe (98/83/EC)**	**Italy (D. Lgs. 31/01)**
THMs	0.8		0.1	0.03
Chloroform		0.2	(0.15 until 11/08)	
Bromoform		0.1		
Dibromochloromethane		0.1		
Dichlorobromomethane		0.06		

Table 3 shows that ozone has the highest oxidizing power among these disinfectants and its oxidation potential is 1.39, 1.52, 1.62, and 1.78 times more oxidant than hypochlorous acid, chlorine, chlorine dioxide, and monochloramine, respectively [74]. These values are in accordance with the CT parameter that gives a measure of the disinfectant power, as can be seen in Table 4. CT is the product of the disinfectant concentration and the detention time [75]. ClO_2 has a standard redox potential of 0.954 V, which is lower than that of ozone (2.07 V) and chlorine (1.36 V), yet its mechanism of action compensates for this lower voltage. It does not operate via a free radical chain reaction but rather acts as a stable free radical due to its unpaired electron. This radical stability underpins its broad-spectrum disinfection while minimizing secondary reactions [76].

Table 3. Oxidation power of some oxidizing-disinfectants of drinking water at 25 °C, relative to hydrogen electrode [73].

Oxidant-Disinfectant	**Oxidation Potential, V**
Ozone	2.07
Hydrogen peroxide	1.77
Hypochlorous acid	1.49
Chlorine Dioxide	1.28
Monochloramine	1.16

Table 4. CT values of drinking water disinfectants to inactivate 99% of some pathogens at pH between 6 and 7 except for chloramines with pH between 8 and 9 [73].

	Chlorine	Chlorine Dioxide	Chloramine	Ozone
E. Coli	0.034–0.05	0.4–0.75	95–180	0.02
Rotavirus	0.01–0.05	0.2–2.1	3810–6480	0.006–0.05
G. Lambia Cyst	47–150	-	-	0.5–0.6
G. Muris	30–630	7.2–18.5	1400	1.8–2.0

Table 5 illustrates an immediate comparison between chlorine dioxide and alternative disinfectants. ClO_2 systems require on-site generation due to its instability, contributing to moderate costs. Ozone treatment incurs higher costs due to energy consumption and the need for specialized equipment. UV systems involve moderate costs that scale with water quality and the frequency of lamp replacement. The cost of H_2O_2 depends on dosing requirements and often increases when used in tandem with other oxidants or UV light [71], [77].

ClO_2 has a manageable environmental impact if DBPs are properly controlled and residuals are treated. Ozone, despite its high efficacy, poses environmental concerns if released into the atmosphere and can generate bromate in bromide-rich waters. UV treatment is environmentally benign, leaving no residuals. H_2O_2 is also environmentally favorable, decomposing into water and oxygen without accumulating in treated systems. The table below summarizes the main characteristics of chlorine dioxide and its alternatives, serving as a basis for the discussion that follows.

Table 5. Comparative Table on Alternative Disinfectants.

Parameter	Chlorine Dioxide (ClO_2)	Ozone (O_3)	Ultraviolet (UV)	Hydrogen Peroxide (H_2O_2)	Peracetic Acid (PAA)
Antimicrobial efficacy	Broad-spectrum (bacteria, viruses, protozoa); effective against biofilms	Very high; rapidly inactivates most pathogens	Effective for bacteria and viruses; limited for protozoa and turbid water	Moderate; often used in combination with other agents	Highly effective against a broad spectrum of microorganisms, including bacteria, viruses, fungi, and spores.
Operational costs	Moderate; on-site generation required	High; energy-intensive, complex systems	Moderate; dependent on water quality and lamp maintenance	Variable; combined use increases total costs	Generally higher than chlorine or chlorine dioxide but can be cost-effective in certain applications due to its effectiveness at lower concentrations.

Environmental footprint	Relatively low; by-products degrade over time	Potential bromate risk; ozone is a greenhouse gas if released	Minimal; no chemical residue	Low; breaks down into non-toxic compounds	Biodegradable and breaks down into acetic acid and water, with minimal long-term environmental impact when used properly.
Application notes	Stable across wide pH range; does not react with ammonia	Must be generated in situ; unstable	Effectiveness reduced by turbidity and suspended solids	Sensitive to light and heat; used in advanced oxidation processes	Often used in food processing, water treatment, and sanitation; effective in both cold and hot water applications; requires careful handling due to its corrosive nature.

4. Products by Chlorine Dioxide Production Methods

The industrial synthesis of chlorine dioxide has diversified considerably to meet the growing demand for high-purity, cost-effective, and environmentally sustainable disinfectants. The various methods, developed for ClO_2 generation, are typically classified based on the precursor material used, sodium chlorite ($NaClO_2$) or sodium chlorate ($NaClO_3$), each offering specific advantages and limitations. The operational context, scale, and required purity level dictate the choice of production route.

4.1. Sodium Chlorite-Based Methods

Sodium chlorite-based methods are particularly favored for on-site generation systems due to their relatively straightforward chemistry and superior control over by-product formation. ClO_2 is generated from chlorite ions using chemicals, electrochemicals, and biocatalysts, and from the reaction of chlorite with chlorine gas Cl_2 or hydrochloric acid (HCl) [78], [79], [80]. These methods are extensively employed in municipal water disinfection, food sanitation, and healthcare applications, where high-purity ClO_2 is essential.

a) Acidic Sodium Chlorite Reaction

One of the most prevalent approaches involves the acidification of sodium chlorite with hydrochloric acid (HCl), forming ClO_2 alongside sodium chloride and water as by-products:

$$5NaClO_2 + 4HCl \rightarrow 4ClO_2 + 5NaCl + 2H_2O \tag{1}$$

This method allows for high conversion efficiencies, typically 95–98%, when operated under optimized conditions: HCl concentration of 10–20 M, temperature range of 20–40 °C, and pH maintained below 3. In this method, the content of chlorine is high, the purity of chlorine dioxide is low, and the pollution is severe [81], [82]. However, secondary disproportionation pathways that may yield undesirable chlorate or chlorine gas if not properly managed accompany the reaction:

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$$4HClO_2 \rightarrow 2ClO_2 + HClO_3 + HCl + H_2O \quad (2)$$

$$5ClO_2^- + 2H^+ \rightarrow 3ClO_3^- + Cl_2 + H_2O \quad (3)$$

To mitigate these reactions, critical process controls are necessary. These include maintaining a strong excess of hydrochloric acid (about 300% of stoichiometric needs), using softened water to avoid calcium carbonate scaling, and providing vigorous mixing to optimize mass transfer and yield.

b) Chlorine + Sodium Chlorite Method

Another widely implemented strategy involves generating chlorine gas in situ by reacting sodium hypochlorite (NaClO) with HCl, followed by its reaction with sodium chlorite:

$$NaClO + 2HCl \rightarrow Cl_2 + NaCl + H_2O \quad (4)$$

subsequently reacts with sodium chlorite to form chlorine dioxide

$$2NaClO_2 + Cl_2 \rightarrow 2ClO_2 + 2NaCl \quad (5)$$

This two-step process enables compact generation systems that can run continuously and are suitable for mobile units or decentralized facilities. A notable enhancement was introduced in FR Patent No. 2,855,167 [83], where an electro chlorinator generates NaClO on-site, lowering operational costs and reducing storage needs. Key operational parameters for this method include temperatures between 25–50 °C, pH below 3, and excess chlorine dosing (approximately 10%) to maintain reaction efficiency and pH control. While efficient, this method poses risks of chlorinated by-product formation if chlorine carryover occurs, necessitating scrubbing or gas-liquid separation units [83].

c) Electrochemical Generation

Electrochemical generation of ClO_2 from sodium chlorite represents a clean and scalable method suitable for high-purity applications and small-scale application where chemical handling must be minimized [84], [85]. As described by US Patent No. 6,869,518[86] the anodic oxidation of chlorite ions proceeds as follows:

$$2Na^+ + 2ClO_2^- \rightarrow 2Na^+ + 2ClO_2 + 2e^- \quad (6)$$

coupled with water reduction at the cathode:

$$2H_2O + 2e^- \rightarrow H_2 + 2OH^- \quad (7)$$

The overall reaction is:

$$2Na^+ + 2ClO_2^- + 2H_2O \rightarrow 2ClO_2 + H_2 + 2OH^- \quad (8)$$

This acid-free process avoids many of the issues associated with corrosive environments and provides a route for on-demand ClO_2 generation in sensitive applications. Systems utilizing mixed metal oxide (MMO) and boron-doped diamond (BDD) electrodes have demonstrated exceptional selectivity and efficiency. Notable studies include works by Pillai et al. (2009), et al. (2015b), Mostafa et al. (2018), and Souza et al. (2016) [84], [87], [88], [89], which explored variations in electrode materials and cell configurations to enhance yield and minimize side reactions.

d) Carbonic Acid Method

An innovative, low-impact alternative to conventional acidification employs carbon dioxide (CO_2) to generate ClO_2 from sodium chlorite through carbonic acid formation:

$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^- \quad (9)$$

followed by acidification of the chlorite solution

$$5ClO_2^- + 4H^+ \rightarrow 4ClO_2 + Cl^- + 2H_2O \quad (10)$$

As described in CN Patent No. 1,295,142, this method circumvents the use of corrosive acids, reducing infrastructure corrosion and scaling risk. Typical operation includes short CO_2 injection periods (~2 min) followed by reaction incubation (~10 min) at pH levels of 4–6 as described by US Patent No. 6,761,872 [90]. This approach has gained attention for use in agricultural applications and groundwater remediation, where residue-free disinfection is critical.

e) Phosphoric acid method

Less common but noteworthy methods include the phosphoric acid-chlorite approach, where ClO_2 gas is generated by mixing sodium chlorite solution and phosphoric acid:

$$15NaClO_2 + 4H_3PO_4 \rightarrow 12ClO_2 + 6H_2O + 3NaCl + 4Na_3PO_4 \quad (11)$$

Shirasaki et al. (2016) [91], for example, uses 3.35% sodium chlorite solution (Purogene, Fuji Techno Service Co., Ltd., Sendai, Japan) and 85% phosphoric acid (Kanto Chemical Co., Inc., Tokyo, Japan) without dilution.

4.2. Sodium Chlorate-Based Methods

The most common industrial method for producing ClO_2 is the reduction of sodium chlorate ($NaClO_3$) in an acidic medium with a reducing agent. There are several reduction methods, such as the sulphuric acid method, the hydrogen peroxide method, the sulphur dioxide method, the sodium chloride method, the hydrochloric acid method, the methanol method, and so on [92], [93], [94]. The choice of reducing agent affects reaction conditions, by-products, and efficiency. In addition, in the study of Chen et al. (2005) [95], urea was used as a reducing agent in the medium of sulphuric acid to reduce alkali chlorate in place of CH_3OH and H_2O_2 for producing ClO_2. The conversion of alkali chlorate and the purity of chlorine dioxide are both over 95% [95]. In all commercial processes, the most commonly used acids have been sulphuric (H_2SO_4) and hydrochloric (HCl). Consequently, the most common byproducts are sodium sulphate (Na_2SO_4), recovered as neutral crystalline sodium sulphate, sodium sesquisulphate ($Na_3(SO_4)_2$) or dissolved in an acidic effluent, and sodium chloride (NaCl) in a crystalline form or in an internally recycled solution, but also ClO_2^-, ClO_3^-, Cl_2 and Cl_2O. The conditions for producing ClO_2 from sodium chlorite can be better controlled than those for sodium chlorate, but chlorite is more expensive and unstable, and therefore, from an industrial point of view, sodium chlorate is a more suitable feedstock [96].

a) Sulphur Dioxide Reduction (Mathieson Process)

In this process, developed in 1950 by the Olin-Mathieson Chemical Corporation, an SO_2-air mixture is introduced into an aqueous solution of $NaClO_3$ and sulphuric acid (H_2SO_4), producing ClO_2 with minimal chlorine contamination.

$$2NaClO_3 + SO_2 + H_2SO_4 \rightarrow 2ClO_2 + 2NaHSO_4 \quad (12)$$

However, secondary disproportionation pathways that may yield undesirable sodium chloride or chlorine gas if not properly managed accompany the reaction:

$$2NaClO_3 + 5SO_2 + 4H_2O \rightarrow Cl_2 + 2NaHSO_4 + 3H_2SO_4 \quad (13)$$

This method requires a relatively high SO_2 concentration (10–12%), 22–35 mg/L of sodium chlorate and concentrated acid solutions to achieve a reasonable reaction rate [90], [97]. Despite its lower chlorine by-product content and despite the fact that this process produces sulphuric acid and so reduces the amount of acid required, the process suffers from sulphur dioxide contamination and reduced efficiency. Key operational parameters for this method include temperatures between 50–70°C, an acid concentration of 6 M [97] and a reaction time of 10 minutes.

b) Hydrochloric Acid Reduction

In this method, hydrochloric acid reacts with sodium chlorate. The main reaction is:

$$2NaClO_3 + 4HCl \rightarrow 2ClO_2 + Cl_2 + 2NaCl + 2H_2O \quad (14)$$

There are two problems with this method: the formation of elemental chlorine (Cl_2), which requires removal or neutralization, and corrosion issues due to strong acidic conditions. Using hydrochloric acid, the chlorine content is high, the purity of the chlorine dioxide is low, and the contamination is severe [98], [99]. The parameters of the process include temperatures between 50–80°C, pH below 2, an acid concentration of 4–8 M, and a reaction time of 5–10 minutes.

c) Hydrogen Peroxide Reduction

Hydrogen peroxide (H_2O_2) can serve as a reducing agent to convert $NaClO_3$ into ClO_2 under strong acidic conditions [99], [100], [101]. The main reaction is:

$$2NaClO_3 + H_2O_2 + 2H_2SO_4 \rightarrow 2ClO_2 + 2NaHSO_4 + O_2 + 2H_2O \quad (15)$$

The reaction produces oxygen as a by-product, making it more environmentally friendly than other processes, but the excess oxygen generation may reduce ClO_2 yield and it requires precise control to prevent side oxidation reactions. Some studies describes the electrochemical production of chlorine dioxide from sodium chlorate and hydrogen peroxide produced in a single electrochemical cell [102], [103], [104]. The operating conditions of the process include temperatures between 40–60°C and an acid's concentration of 3-6M and hydrogen peroxide at 33% [99].

d) Methanol-Based Process (R8 Process)

The methanol process is the most widely used method for the production of chlorine dioxide in the newly built reduction plants in the world, at present [105]. It is an industrial approach that converts $NaClO_3$ using methanol (CH_3OH) in the presence of sulphuric acid. The reaction formula [101] is:

$$6NaClO_3 + CH_3OH + H_2SO_4 \rightarrow 6ClO_2 + 2NaHSO_4 + CO_2 + 5H_2O(16).$$

The reaction is composed of three steps [106]. First, chlorate reacts with sulphuric acid to form $H_2ClO_3^+$ (equation 17). The second step leads to the formation of formaldehyde and $H_2ClO_2^+$ (equation 18), that then in the third step reacts with chlorate to form chlorine dioxide (equation 19):

$$ClO_3^- + 2H^+ \rightarrow H_2ClO_3^+ \ (17)$$

$$H_2ClO_3^+ + CH_3OH \rightarrow H_2ClO_2^+ + HCHO + H_2O \ (18)$$

$$H_2ClO^+{}_2 + ClO^-{}_3 \rightarrow O_2Cl-ClO_2 + H_2O \rightarrow 2ClO_2 + H_2O(19) \quad [106]$$

However, the reaction is accompanied by secondary reactions like the formation of formaldehyde (HCOH) and formic acid (HCOOH): chlorate oxidizes methanol in a stepwise manner, first forming formaldehyde, then formic acid, and finally carbon dioxide [107], [108], [109], [110]. The oxidation of formic acid to carbon dioxide is very slow step so it does not react easily rather volatilize and escape along with highly volatile methyl formate and chlorine dioxide. The incomplete oxidation of methanol to formic acid is represented as:

$$12NaClO_3 + 3CH_3OH + 8H_2SO_4 \rightarrow 12ClO_2 + 4Na_3H(SO_4)_2 + 3HCOOH + 9H_2O(20)$$

In the chloride dioxide production a phenomenon known as "white-out" can occur, when ClO_2 production suddenly ceases due to an imbalance in chloride ion concentration. In methanol-based chlorine dioxide production, these reactions occur:

$$HClO_3 + HCl \rightarrow HClO_2 + HClO \ (21)$$

$$HClO_3 + HClO_2 \rightarrow 2ClO_2 + H_2O \ (22)$$

$$HClO + CH_3OH \rightarrow HCl + HCHO + H_2O \ (23)$$

The undesirable side reaction is the decomposition of hypochlorous acid (HClO). The relative rates of reactions 21 and 23 are critical for avoiding whiteout. If reaction 21 (which consumes chloride) is faster than reaction 23 (which generates chloride), the process becomes unstable and white-out occurs [111]. The methanol process has the advantages of simple operation, effortless control, high production efficiency, low one-time investment, average operating cost, and no catalyst in production [112], and, according to Europe Patent 0,535,113, it is an alternative solution to the white-out. Despite high efficiency (>95%), it can suffer from incomplete oxidation, leading to formic acid accumulation, which affects overall process stability. The key operational conditions of the process are temperatures between 60–80°C and pressures between 100–300 mmHg.

e) Sodium Chloride - Sodium Chlorate Method (Rapson R2 process)

The Rapson R2 process employs sodium chloride as reductive agent. The stoichiometry [113], [114], [115], [116][117] of the reaction is:

$$2NaClO_3 + 2NaCl + 2H_2SO_4 \rightarrow 2ClO_2 + 2Na_2SO_4 + Cl_2 + 2H_2O \quad (24)$$

Deshwal and Lee (2004) [118] have studied the kinetic of the reaction. They says that reaction's rate follows the equation:

$$-12\frac{dNaClO_3}{dt} = k\left[NaClO_3\right]\left[NaCl\right]^2\left[H_2SO_4\right]^{\gamma},$$

with the reaction order concerning acid (y) being surprisingly high (12-14), indicating strong acidity dependence. Such a high order (12-14) might seem unusual, but this has been previously reported in industrial processes. The presence of sodium ions lowers the effective acidity of the solution [119], [120], [121], [122]. To correct for this, the acidity function $\left(-H = log\left(h\right)\right)$ is adjusted: $-H_{corrected} = -H + 0.12\left[NaClO_3\right]$. Instead of using sulfuric acid concentration directly, the corrected acidity function (h) is used in the rate law: $\frac{dx}{dt} = A\ exp\left(-E_a RT\right)\ \left[NaClO_3\right]\left[NaCl\right]^2\left(h\right)^{\gamma}$ [118]. This adjustment led to a reaction order with respect to acid = 2.4, much more reasonable than the extremely high 12-14 order found when using molar concentration directly. The reaction also shows significant temperature dependence, with an activation energy of 81.84 kJ/mol, a pre-exponential factor $A = 2.403\times10^{2}$ (for rate equation with [H_2SO_4]). So with corrected acidity function (recommended): $\frac{dx}{dt} = 2.639\times10^{7}\,exp\left(\frac{-9944.6}{T}\right)\left[NaClO_3\right]\left[NaCl\right]^2\left(h\right)^{2.4}$ [118]. So at the end it is corrected to say that two important parameters of this process are temperature and acid concentration.

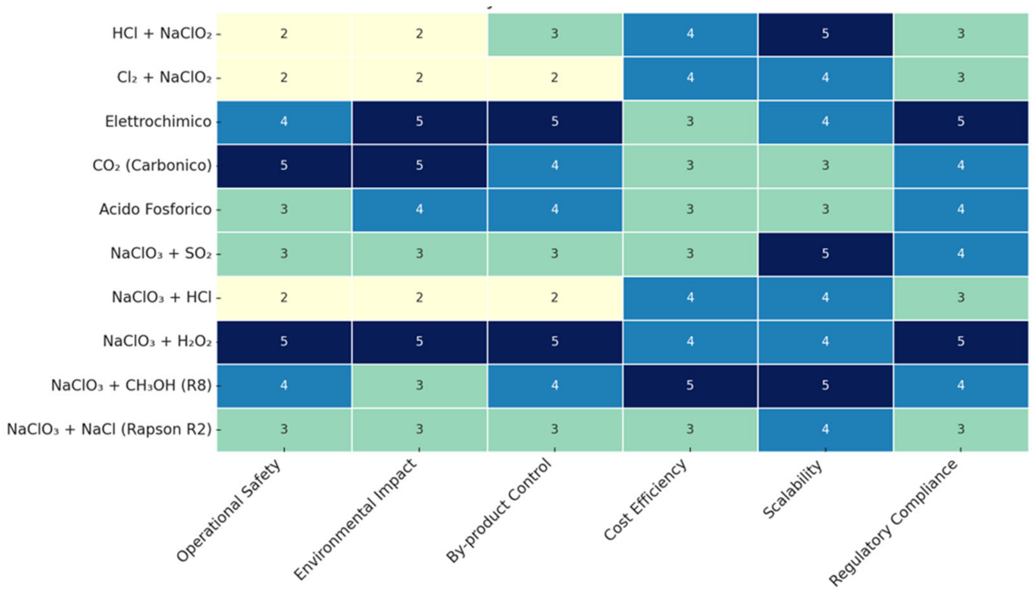
5. Comparative Evaluation Framework

To support a comparative assessment of chlorine dioxide (ClO_2) generation methods, we developed two complementary decision matrices: one focused on sustainability and regulatory alignment, the other on technical and operational feasibility. Each method was evaluated across six criteria using a scoring scale from 1 (optimal) to 5 (least favorable), based on an integrated review of scientific literature, industrial data, and relevant regulations. This dual-framework approach balances scientific rigor with practical applicability. The first matrix emphasizes environmental sustainability and regulatory compliance. Operational safety accounts for the chemical risks involved, favoring low-hazard approaches such as electrochemical or CO_2-based systems, while penalizing those involving strong acids or chlorine gas. Environmental impact considers emissions, energy demand, and waste production, with low-residue technologies receiving better scores. By-product control evaluates the formation and mitigation of chlorite, chlorate, and perchlorate. Cost efficiency reflects both reagent affordability and system complexity, while scalability assesses adaptability to various applications [98], [123–125]. Regulatory compliance is judged based on alignment with WHO, EPA, and EU standards, with higher scores applied to methods requiring post-treatment to meet legal thresholds. Technologies such as electrochemical or H_2O_2-based generation stand out for their low emissions and minimal by-product formation, whereas conventional acid-based methods are penalized due to safety and compliance challenges. The second matrix addresses implementation challenges. Cost reflects direct chemical and operational expenses [98], [123–125]. By-products considers typical residuals formed during standard operation. Operating temperature and pressure point out energy intensity and technical constraints, with ambient-condition processes ranked more favorably. Acidic conditions/pH assesses the corrosiveness of the chemical environment and its implications for materials and safety. Chemical efficiency measures the conversion yield of ClO_2, favoring high-performance and selective reactions. Figure ambient conditions with moderate pH requirements, such as those based on carbonic acid or sodium chlorite, show strong implementation potential. In contrast, routes involving methanol or hydrochloric acid may impose higher demands in terms of chemical handling and safety measures. In Table 6 there are the criterions used to create the matrices. To account for varying levels of performance, intermediate scores (2 to 4) were used. A score of 2 indicates strong performance under specific conditions but limited generalizability. A 3 reflects average, acceptable operation without distinctive strengths. A 4 denotes clear limitations or trade-offs, such as increased environmental management needs or borderline regulatory compliance, that do not constitute outright failure but warrant consideration.

Table 6. Descriptive criteria explaining matrices in Figures 3 and 4.

Criterion	Score 1 (Optimal)	Score 5 (Least Favorable)
Operational Safety	No corrosive agents, no gas release	Toxic reagents (Cl2), exothermic risks, strong acids
Environmental Impact	Low emissions, low energy, benign by-products	High waste load, VOCs, persistent by-products
By-product Control	Minimal ClO2-, ClO3-, ClO4-	High or unstable by-product formation
Cost Efficiency	Low-cost reagents, minimal system complexity	Expensive inputs, intensive infrastructure
Scalability	Modular, adaptable to multiple scales	Suitable only for large, fixed systems
Regulatory Compliance	Intrinsically within legal thresholds	Exceeds MCLs without further treatment
Cost (Tech Matrix)	Widely available, low-cost chemicals	Specialized or costly reagents
By-products (Tech Matrix)	Low reactivity with NOM, minimal secondary species	Persistent or hazardous residuals
Operating Temperature	Ambient (20–30°C)	High (>50°C)
Operating Pressure	Atmospheric	Requires pressurization
Acidic Conditions / pH	Neutral to mildly acidic (pH > 4)	Highly acidic (pH < 2), corrosive
Chemical Efficiency	>90% ClO_2 yield, low side products	Low conversion, unstable intermediates

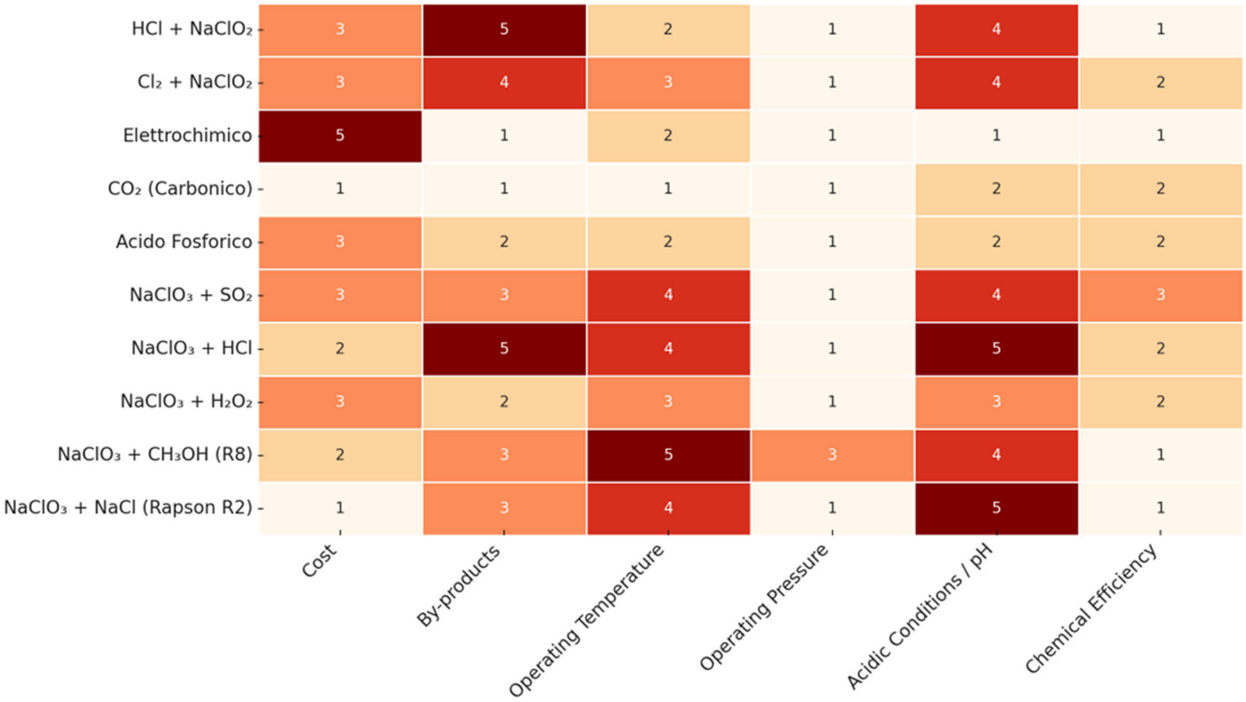
Figure 3 provides an overview of the environmental and policy-related strengths and weaknesses of each method. Technologies such as electrochemical or H_2O_2-based generation stand out for their low emissions and minimal by-product formation, whereas conventional acid-based methods are penalized due to safety and compliance challenges.



	Operational Safety	Environmental Impact	By-product Control	Cost Efficiency	Scalability	Regulatory Compliance
HCl + NaClO₂	2	2	3	4	5	3
Cl₂ + NaClO₂	2	2	2	4	4	3
Elettrochimico	4	5	5	3	4	5
CO₂ (Carbonico)	5	5	4	3	3	4
Acido Fosforico	3	4	4	3	3	4
NaClO₃ + SO₂	3	3	3	3	5	4
NaClO₃ + HCl	2	2	2	4	4	3
NaClO₃ + H₂O₂	5	5	5	4	4	5
NaClO₃ + CH₃OH (R8)	4	3	4	5	5	4
NaClO₃ + NaCl (Rapson R2)	3	3	3	3	4	3

Figure 3. Comparative matrix of chlorine dioxide production's methods focusing on safety, environmental problems, regulatory aspects and scalability.

Figure 4 provides an overview of the operating conditions associated with different chlorine production methods, along with a comparative analysis of their costs, to offer a comprehensive perspective on these aspects. Production routes operating under ambient conditions and moderate pH requirements, such as those based on carbonic acid or sodium chlorite, exhibit strong potential for practical implementation. Conversely, methods involving methanol or hydrochloric acid tend to require more stringent chemical handling protocols and safety measures.



	Cost	By-products	Operating Temperature	Operating Pressure	Acidic Conditions / pH	Chemical Efficiency
HCl + NaClO₂	3	5	2	1	4	1
Cl₂ + NaClO₂	3	4	3	1	4	2
Elettrochimico	5	1	2	1	1	1
CO₂ (Carbonico)	1	1	1	1	2	2
Acido Fosforico	3	2	2	1	2	2
NaClO₃ + SO₂	3	3	4	1	4	3
NaClO₃ + HCl	2	5	4	1	5	2
NaClO₃ + H₂O₂	3	2	3	1	3	2
NaClO₃ + CH₃OH (R8)	2	3	5	3	4	1
NaClO₃ + NaCl (Rapson R2)	1	3	4	1	5	1

Figure 4. Comparative matrix of chlorine dioxide production's methods focusing on operative conditions.

Processes that utilize hydrochloric acid (HCl) or molecular chlorine (Cl_2) as reagents are negatively assessed in the matrix shown in Figure 3, receiving high penalty scores for operational safety and regulatory compliance. This evaluation is supported by the data reported in the relevant

Safety Data Sheets (SDS), which highlight significant health hazards and corrosivity. The environmental impact of these methods is further exacerbated by the potential formation of hazardous by-products, including Cl_2 gas, chlorate, and, to a lesser extent, perchlorate. From a technical perspective (Figure 4), these processes are also disadvantaged: the need to operate under strongly acidic conditions ($pH < 2$) and at elevated temperatures (>50 °C) necessitates corrosion-resistant materials and increased energy input (Cornelius 1943). An alternative method involves the electrochemical generation of chlorine dioxide (ClO_2) from sodium chlorite, relying on electrically controlled redox mechanisms and eliminating the use of hazardous reagents. According to the available SDS, chlorite is classified as an oxidizer and should be handled with care, though it does not pose the same level of risk as Cl_2 or HCl. This approach receives high scores in Figure 3 for "operational safety" and "by-product control", as it avoids the formation of chlorate and perchlorate when properly managed [84,87,88]. Nevertheless, its reliance on a stable power supply may present a limitation in settings with inadequate infrastructure. Despite this, the method's high chemical efficiency and environmental compatibility make it one of the most promising options. Reduction of chlorate via the in situ formation of carbonic acid from CO_2 offers a low-impact strategy. This method is notable for its lack of corrosive or toxic agents, absence of VOCs, and mild operating conditions (moderate pH, ambient temperature), yielding optimal scores across most of the criteria in Figure 3. Similarly, the technical matrix (Figure 4) highlights advantages such as low energy requirements, absence of elevated pressure, and ease of handling. However, the lower chemical yield compared to stronger reducing agents may limit its scalability for industrial applications [86], [126]. In contrast, sulfur dioxide (SO_2) reduction is heavily penalized in both matrices [127]. High scores for operational risk, inhalation toxicity, reagent instability, and sulfate by-product formation make this "chemical bond" particularly unfavorable. SDS data confirm respiratory hazards associated with SO_2, while the acidic waste stream requires additional post-treatment and increases operational costs. Consequently, this method receives the lowest ratings for "environmental impact", "regulatory compliance", and "cost". The use of hydrogen peroxide (H_2O_2) as a chlorate reductant, in the presence of sulfuric acid, provides a reasonable compromise between efficiency and environmental impact. Scores reported in Figure 3 reflect the lower toxicity of peroxide compared to other reducing agents, as well as the production of oxygen as the main by-product. SDS documentation indicates limited hazards when handled correctly. In Figure 4, the method also performs well in terms of conversion efficiency and by-product control, although it still requires acidic conditions and moderate temperatures. Major limitations include reagent stability and operational costs related to the handling of oxidants [99–101]. Finally, the use of methanol stands out for its high efficiency in chlorate reduction, with yields exceeding 95%. However, significant safety concerns arise from its flammability and toxicity, as reported in SDS documents. Moreover, the formation of secondary by-products, including formic acid, formaldehyde, and VOCs, results in a notable environmental burden. These issues justify the unfavorable scores in Figure 3 under the "by-product control" and "environmental impact" criteria. Nonetheless, the high chemical yield and scalability contribute to a more favorable rating in the technical matrix (Figure 4), despite the need for vacuum conditions and moderate temperatures (60–80 °C) [128].

6. Industrial Methods and Recent Advances

The industrial-scale production of chlorine dioxide (ClO_2) has undergone substantial transformation over the past few decades, driven by increasing demand for high-purity disinfectants with minimal environmental and health impacts. These advancements have led to the development of several proprietary production technologies that aim to enhance operational safety, reduce chlorine gas emissions, improve chemical conversion efficiencies, and minimize waste generation. Leading chemical manufacturers such as Nouryon (formerly AkzoNobel) and Eka Chemicals have pioneered some of the most widely implemented systems in this field.

6.1. Proprietary Vacuum-Based Systems

One of the most significant innovations in ClO_2 generation is the SVP-LITE® process, developed by Nouryon. This method utilizes methanol as a reducing agent under vacuum conditions, offering several benefits including a high conversion efficiency, limited formation of unwanted by-products such as elemental chlorine (Cl_2), and the production of manageable process residues such as formic acid and sodium sulfate. Operating under vacuum reduces the partial pressure of ClO_2, thereby stabilizing the gas phase and facilitating safe extraction and dilution prior to on-site application. The SVP-LITE® system is particularly well-suited for large-scale municipal water treatment facilities and pulp bleaching operations, where consistent ClO_2 demand justifies centralized, continuous production systems. A closely related technology, the SVP-SCW process, also employs methanol but is optimized for specific pulp and paper industry conditions. It maintains the core principles of vacuum operation and methanol reduction while tailoring reactor design and feed ratios to the requirements of chlorine-free bleaching processes, where color removal and fiber brightness must be carefully controlled. Despite the advantages of methanol-based systems, there are operational contexts in which organic by-product minimization is paramount, for example, in pharmaceutical, food processing, or high-purity water applications. In these scenarios, the SVP-HP process provides an attractive alternative. This technology replaces methanol with hydrogen peroxide (H_2O_2) as the reducing agent, generating oxygen gas (O_2) as the primary by-product alongside sodium sulfate. This reaction profile significantly reduces the risk of volatile organic compound (VOC) formation and simplifies effluent treatment processes. As with SVP-LITE®, the SVP-HP system also operates under vacuum, ensuring controlled ClO_2 handling and minimal emissions. To further accommodate varying plant configurations, Nouryon has introduced the HP-A® system, which adapts the hydrogen peroxide-based chemistry to atmospheric pressure conditions. While the atmospheric design may reduce certain capital costs and ease installation, it requires careful engineering to maintain safety and yield, particularly when managing ClO_2 gas extraction and dilution in open environments. A summary of the technologies developed and tested by Nouryon up to 2021 is presented in Table 7. The table reports the operating process conditions, the reducing agent used in the process, the by-products resulting from chlorine dioxide, and the by-products generated during production.

Table 7. Nouryon Chlorine dioxide technologies [128].

Technology	Process condition	Reducing agent	ClO2 by-product	Process by-product
SVP-LITE®	Vacuum	Methanol	Formic acid	Sodium Sulfate
SVP-SCW	Vacuum	Methanol	Formic acid	Sodium Sulfate
SVP-HP	Vacuum	Hydrogen Peroxide	Oxygen	Sodium Sulfate
HP-A®	Atmospheric	Hydrogen Peroxide	Oxygen	Sodium Sulfate

6.2. Emerging Technologies and Research Directions

Beyond these commercialized systems, recent innovations in ClO_2 generation technology aim to address emerging priorities in sustainability, energy efficiency, and decentralized production. Among these innovations is the exploration of membrane distillation techniques, which enable selective separation and purification of ClO_2 from reaction mixtures [5]. This method enhances product purity while potentially reducing energy input and chemical usage compared to traditional vacuum stripping systems. In parallel, electrochemical methods continue to gain interest for on-demand generation of ClO_2 with minimal precursor chemicals and waste streams. Recent research by Mostafa et al. (2018), Brito et al. (2015b), and Pillai et al. (2009) [84,87,88] has demonstrated the viability of advanced electrode materials, including boron-doped diamond (BDD) and mixed metal oxide (MMO) electrodes, in promoting efficient ClO_2 production with high Faradaic efficiency and low over potential losses. These electrochemical systems are especially valuable for remote or mobile disinfection units where logistical constraints limit the availability of concentrated chemical reagents. Another promising avenue involves further refinement of the carbonic acid reduction process, originally described in CN Patent No. 1,295,142 [126]. By using CO_2 gas as a soft acidifying agent, this method eliminates the need for hazardous mineral acids and significantly reduces the formation of chloride- or sulfate-containing effluents. Ongoing studies aim to optimize cycle times, CO_2 dosing strategies, and reactor designs to enhance ClO_2 yield while maintaining pH conditions that are compatible with sensitive downstream applications, such as produce washing or aquaculture [67]. The push toward green chemistry in disinfection technologies has also motivated efforts to reduce the carbon footprint of ClO_2 production by exploring renewable methanol sources, integrating solar-powered electrochemical cells, and developing closed-loop acid recovery systems. Additionally, several research groups are investigating automated control systems equipped with real-time monitoring of ClO_2 concentration, pressure, and by-product levels, which can dynamically adjust operational parameters to ensure maximum safety and efficiency.

6.3. Outlook and Industry Trends

As water treatment regulations grow increasingly stringent and public awareness of chemical residues continues to rise, the demand for high-purity, low-residue disinfectants like chlorine dioxide is expected to increase. Future industrial developments will likely focus on modular, decentralized ClO_2 generation systems that can be integrated directly into municipal, hospital, or food processing infrastructures. These systems will prioritize not only chemical efficiency but also occupational safety, automation, and environmental impact. Moreover, the combination of ClO_2 with other disinfection technologies, such as chlorine, ultraviolet (UV) light or advanced oxidation processes (AOPs), is under evaluation for synergistic pathogen inactivation and by-product reduction [30,124,129]. Such hybrid systems may become increasingly relevant in multi-barrier approaches to water safety and biofilm control, where chlorine dioxide's selectivity and membrane permeability are leveraged alongside complementary modes of microbial disruption.

7. Disinfection By-Products

The interaction of chlorine dioxide (ClO_2) with water matrices during disinfection processes leads to the formation of a distinct class of disinfection by-products (DBPs), primarily as a result of its selective oxidizing properties. Unlike chlorine, ClO_2 does not extensively chlorinate organic compounds; instead, it oxidizes them, typically yielding more biodegradable and less chlorinated DBPs [130], [131–133]. Nonetheless, various inorganic and organic by-products may still pose environmental and health concerns, depending on process conditions and water composition. Several factors influence the formation and speciation of these DBPs [116], [134]. Among these are the ClO_2 dosage, as higher doses generally promote increased by-product formation, and the contact time, since prolonged exposure enhances the conversion of ClO_2 into chlorite and chlorate. Temperature also plays a role, with higher values accelerating reaction kinetics. Alkaline conditions favor disproportionation reactions. Moreover, the presence of metals, halides, natural organic matter (NOM), or ammonia can alter reaction pathways. Residual ClO_2 persisting after treatment may continue to react downstream, leading to delayed DBP formation. One of the most prominent reactions of ClO_2 in aqueous environments is disproportionation, particularly at elevated pH, where ClO_2 decomposes into chlorite (ClO_2^-) and chlorate (ClO_3^-) ions via the reaction [30]:

$$2ClO_2 + 2OH^- \rightarrow ClO_2^- + ClO_3^- + H_2O \quad (25)$$

Chang et al. (2000) [34] studied DBP formation under two different levels of ClO_2 that were higher (15.0, 30.0 mg/l) of normal levels (0.1–5 mg/l), in order to simulate higher organic level, with a concentration of organic precursors of 5 mg-DOC/l at neutral (pH=7) conditions. They found that inorganic species increased with the dosage (mg-ClO2 added/mg initial DOC). In the portion of inorganic DBPs formation, shown in Figure 5, chlorite (ClO_2^-), chlorate (ClO_3^-), chloride (Cl^-) were the principal DBPs.

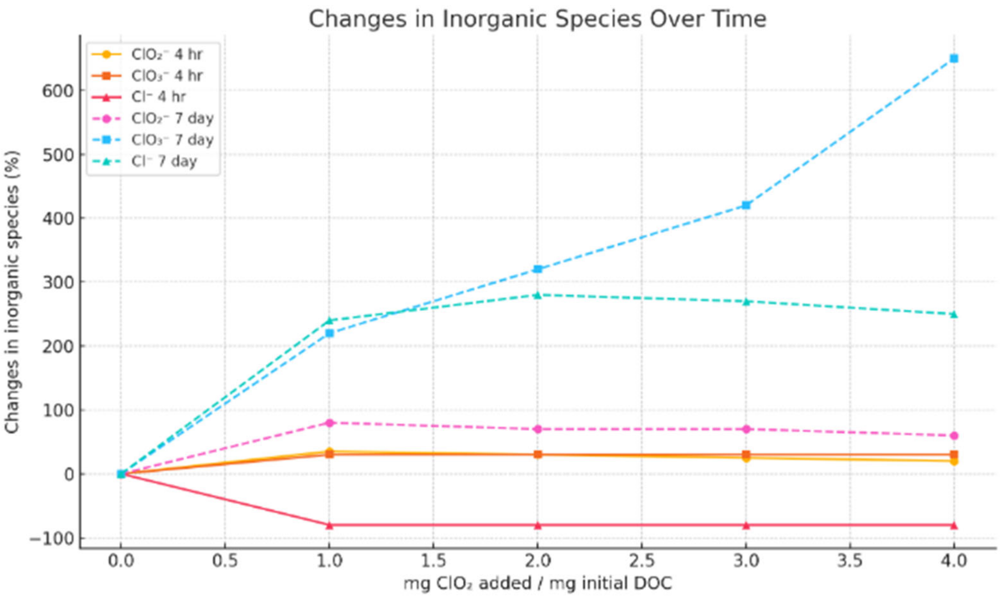


Figure 5. Variation of inorganic DBPs (HA=5 mg-DOC/l, pH=7) [34].

Chlorite is the predominant by-product, typically representing 40–60% of the reacted ClO_2, as reported by Werdehoff and Singer (1987)[135], and is often regarded as a key indicator for regulatory monitoring. Chlorate, by contrast, can form via several concurrent pathways: during the chemical generation of Chlorine dioxide, particularly when chlorine gas or sodium hypochlorite are used as precursors [135]; through photolytic degradation of ClO_2 under sunlight in open storage or treatment systems [136]; via alkaline hydrolysis at pH levels above 9 [137]; and through the oxidation of sodium hypochlorite during prolonged storage, especially at elevated temperatures [134], [138–140]. The radical-based mechanism for chlorate formation involves the transformation of chlorite (ClO_2^-) through interactions with highly reactive radicals like $Cl^{\cdot}$, $HO^{\cdot}$, or $ClO^{\cdot}$, leading to intermediate species ($ClO_2^{\cdot}$) (Equations 26–28) [141] that can be further oxidized to chlorate (Equations 29, 30) [129]:

$$ClO_2^- + Cl^\bullet \rightarrow Cl^- + ClO_2^\bullet \text{牋} k = 7.0\times10^9 M^{-1}s^{-1} \left(26\right)$$

$$ClO_2^- + HO^\bullet \rightarrow OH^- + ClO_2^\bullet \text{牋} = 7.0\times10^9 M^{-1}s^{-1} \left(27\right)$$

$$ClO_2^- + ClO^\bullet \rightarrow ClO^- + ClO_2^\bullet \text{牋} = 9.4\times10^8 M^{-1}s^{-1} \left(28\right)$$

$$ClO_2^\bullet + ClO^\bullet + H_2O \rightarrow ClO^-{}_3 + HClO + H^+ \text{牋} = 9.4\times10^9 M^{-1}s^{-1} \left(29\right)$$

$$ClO_2^\bullet + HO^\bullet \rightarrow ClO^-{}_3 + H^{+\text{牋}} k = 4.0\times10^9 M^{-1}s^{-1} \left(30\right)$$

Perchlorate (ClO_4^-) is a rarer but more concerning by-product. Its formation generally occurs under highly acidic conditions, or when high electric currents are used in electrochemical ClO_2 generators, especially in systems with inefficient mixing or incomplete reaction recirculation [5], [136]. It is formed by the reaction between ClO_3^- and $Cl^{\cdot}$ or $HO^{\cdot}$ [142].

$$ClO_3^- + 2HO^\bullet \rightarrow ClO_4^- + H_2O\ k = 1.0\times10^6 M^{-1}s^{-1} \left(31\right)$$

$$ClO_3^- + Cl^\bullet + H_2O \rightarrow ClO_4^- + 2HCl\ k = 1.0\times10^6 M^{-1}s^{-1} \left(32\right)$$

Industrially, perchlorate has been historically linked to contamination from propellants and explosives, but its occurrence in water treatment is now under close scrutiny. Despite ClO_2's reputation for producing fewer halogenated organic DBPs compared to chlorine, reactions with natural organic matter (NOM) can still yield potentially harmful substances. ClO_2 acts as a selective oxidant, preferentially reacting with electron-rich functional groups such as phenols and amines, leading to the formation of aldehydes (e.g., formaldehyde, glyoxal), carboxylic acids, and other low-molecular-weight oxidized products [143], rather than trihalomethanes (THMs) or haloacetic acids (HAAs) [144].

Importantly, the presence of halide ions, such as bromide (Br^-) and iodide (I^-), introduces additional complexity (Rougé 2018). While ClO_2 itself does not brominate or iodinate organic matter directly, its oxidizing action can convert Br^- and I^- into hypobromous and hypoiodous acid, which in turn react with NOM to form brominated and iodinated DBPs, compounds generally more toxic and less biodegradable than their chlorinated counterparts [145], [146–148][149]. This has been highlighted in recent studies including Rougé (2018) [150], which noted a reduction in NOM aromaticity and electron-donating groups following ClO_2 exposure.

7.1. Health and Environmental Effects

The health risks associated with ClO_2 and its by-products stem from both acute and chronic exposure. Although ClO_2 itself degrades rapidly and does not persist in the environment, the same cannot be said for chlorite, chlorate, and perchlorate, which are more stable and mobile in aqueous systems. Chlorine dioxide, in high concentrations, has been associated with adverse hematological and renal effects. According to the U.S. Environmental Protection Agency (2006) [31], ingestion of high doses can impair red blood cell function, reduce enzymatic activity, and disrupt normal renal filtration. Acute exposure may manifest as nausea, diarrhea, or oxidative stress, and in extreme cases, systemic toxicity [151]. Chlorite (ClO_2^-) is particularly problematic due to its oxidative potential, ability to interfere with thyroid hormone synthesis and to affect red blood cells’ oxygen transport ability [5]. It has been shown to induce hemolytic anemia by damaging erythrocyte membranes and inhibiting enzymes responsible for maintaining redox balance [143]. Chronic low-dose exposure has raised concerns regarding developmental and neurological effects, especially in infants and fetuses. Chlorate (ClO_3^-) shares similar toxico dynamic properties, notably its competitive inhibition of iodine uptake, a crucial element for thyroid function [5]. Its environmental stability is also notable. Studies by Sorlini and Collivignarelli (2005) [152] demonstrated that chlorates could persist in aquatic ecosystems, potentially accumulating in biota. Furthermore, van Wijk et al. (1998) [26] documented heightened sensitivity in algal species, revealing ecological vulnerability to even low chlorate concentrations. Perchlorate (ClO_4^-) is perhaps the most concerning due to its endocrine-disrupting potential. It has a high affinity for the sodium-iodide symporter (NIS), thereby blocking iodine transport into the thyroid gland and suppressing the synthesis of thyroxine (T_4) and triiodothyronine (T_3) [5]. Gordon (2001) linked perchlorate exposure to hypothyroidism, particularly in pregnant women, neonates, and young children, making its regulation a high public health priority. These inorganic DBPs have also been detected in foods, particularly fresh produce, as a result of ClO_2's use in post-harvest sanitation, packaging, and agricultural defoliation. Although concentrations are typically low, chlorate and perchlorate residues have been quantified in various fruits and vegetables [152]. Given the dietary exposure pathway, risk assessments are increasingly focused on cumulative intake across multiple sources.

7.2. Regulatory Aspects

Regulation of chlorine dioxide and its associated by-products reflects a growing recognition of their potential health risks, particularly for vulnerable populations. Both international guidelines and national standards have been developed to control concentrations in drinking water, food, and occupational settings. In the United States, the Environmental Protection Agency (EPA) has set a maximum contaminant level (MCL) for chlorite at 1.0 mg/L under the Disinfectants and Disinfection Byproducts Rule (DBPR). Exposure to chlorine dioxide in the workplace is also regulated: the OSHA permissible exposure limit (PEL) and EPA ambient air limit are both 0.1 ppm (8-hour time-weighted average), with a short-term exposure limit (STEL) of 0.3 ppm over 15 minutes. Perchlorate, while currently under monitoring, does not yet have an enforceable federal MCL, though discussions are ongoing. In the European Union, Directive 2020/2184 defines stricter thresholds: chlorite at 0.2 mg/L and chlorate at 0.7 mg/L in drinking water. The directive also references bromate, setting a conservative limit of 0.01 mg/L due to its known mutagenic potential. These values reflect the EU's precautionary stance and align with findings on thyroid and reproductive toxicity associated with these compounds. Italian regulations, specifically D. Lgs. 31/2001, conform to EU standards, enforcing a 0.2 mg/L limit for chlorite. Legislative Decree 18/2023 further outlines permissible limits for general inorganic constituents, though some parameters (e.g., bicarbonate) remain unregulated. The World Health Organization (WHO) has issued guideline values of 0.7 mg/L for both chlorite and chlorate, serving as an international reference point for drinking water quality, especially in developing nations or regions lacking specific national legislation. Some regional jurisdictions, like California, have implemented stricter advisory levels. The state's Office of Environmental Health Hazard Assessment (OEHHA) recommends a public health goal of 0.8 mg/L for chlorate [153] and a health advisory level of 18 µg/L for perchlorate, illustrating the divergence in risk tolerance across regions. For food applications, the European Commission (2020) introduced targeted maximum residue levels (MRLs) for chlorates and perchlorates in agricultural products. Perchlorate MRLs are set at 0.05 mg/kg for most fruits and vegetables. Chlorate levels vary: 0.3 mg/kg for dried fruits like dates, 0.7 mg/kg for olives, 0.1 mg/kg for nuts, and 0.05 mg/kg for general produce. These limits aim to protect consumers from cumulative exposure while balancing technological needs in food sanitation.

8. Strategies for Mitigating the Formation of Disinfection By-Products from Chlorine Dioxide Application

Effectively mitigating by-products generated during chlorine dioxide (ClO_2) production and application is essential for ensuring its sustainable use, safeguarding public health, and complying with increasingly stringent environmental regulations. As ClO_2 continues to be adopted in diverse sectors including drinking water treatment, food sanitation, and industrial disinfection, attention to its residuals, particularly chlorite (ClO_2^-), chlorate (ClO_3^-), and perchlorate (ClO_4^-), has become a central concern in water quality management. A comprehensive strategy must encompass both upstream preventive measures and downstream treatment technologies [29], integrating process engineering, chemistry, biology, and environmental monitoring.

8.1. Toxicological Characterization of Chlorine Dioxide and Its By-products

A rigorous understanding of the toxicological profiles of ClO_2 and its primary by-products is essential to contextualize regulatory limits and assess potential human health risks. While ClO_2 is generally regarded as an effective and selective disinfectant, its oxidative nature and reactive by-products necessitate detailed evaluation of exposure thresholds, particularly through ingestion or inhalation. For ClO_2 itself, studies have demonstrated a relatively moderate acute toxicity profile. The oral LD_{50} (lethal dose for 50% of the population) in rats is approximately 94 mg/kg body weight, as reported by the World Health Organization [153]. Sub-chronic studies in African green monkeys indicated a NOAEL (No Observed Adverse Effect Level) of 24 mg/L in drinking water, equivalent to approximately 0.34 mg/kg-day, without observable systemic toxicity [153]. However, in rodent studies, morphological alterations in erythrocytes and reduced osmotic fragility were observed at all tested concentrations, suggesting a LOAEL (Lowest Observed Adverse Effect Level) below 24 mg/L [154–156]. These findings support the necessity of strict exposure limits for ClO_2 in potable water. Chlorite, the primary reduction product of ClO_2, exhibits a more pronounced toxicological concern, especially due to its hematological and thyroid effects. Chronic exposure studies in rats identified a NOAEL of 8 mg/L (corresponding to 0.7 mg/kg-day), while a LOAEL of 100 mg/L (9.3 mg/kg-day) was associated with renal pathology [157]. These effects justify the establishment of stringent guideline values in drinking water, typically set at or below 0.7 mg/L. Chlorate, formed through disproportionation or as a contaminant in ClO_2 generation, presents a slightly less toxic profile but still warrants concern. Although no specific NOAEL or LOAEL values were conclusively established in primate studies, chlorate was not found to induce thyroidal or oxidative stress-related effects in the same manner as chlorite. Nevertheless, the oral LD_{50} in rats exceeds 5000 mg/kg, indicating a relatively low acute toxicity but unknown chronic risks at environmentally relevant concentrations [158]. Perchlorate, though a less prevalent by-product, is of particular interest due to its interference with iodine uptake and subsequent effects on thyroid function. In human case reports, doses of 5–12 mg/kg/day over periods of several months through oral exposure have been associated with serious hematological disorders, such as aplastic anemia and agranulocytosis, and renal and hepatic troubles. Human studies suggest a NOAEL of 0.3 mg/kg-day and a LOAEL of 3.0 mg/kg-day, based on thyroid weight alterations in rodents [159]. The dietary LD_{50} in mice is reported to be approximately 3621 mg/kg/day, further underscoring its potential for toxicity at elevated exposure levels [160]. These quantitative data support the rationale for current regulatory thresholds and underscore the importance of incorporating toxicological evidence into disinfection strategy design and monitoring protocols. They also highlight the need for continued research into chronic low-level exposure effects and cumulative risks from simultaneous exposure to multiple by-products.

8.2. Strategies

A foundational aspect of by-product mitigation is the precise control of ClO_2 generation parameters. The efficiency and design of the ClO_2 generator play a pivotal role: poorly designed or outdated systems are prone to incomplete reactions and excessive side-product formation. Modern systems emphasize closed-loop control with real-time sensors that continuously monitor pH, temperature, and reagent concentrations, ensuring ClO_2 is produced under optimal conditions. For example, maintaining slightly acidic environments (pH 3–5) prevents the excessive formation of chlorate, which is promoted under highly acidic or alkaline conditions. Reagent stoichiometry is equally critical: excess chlorine or sodium hypochlorite can lead to the undesired formation of Cl_2 gas or elevate chlorate levels through secondary oxidation. Similarly, hydrogen peroxide, while sometimes used to boost reaction efficiency, can accelerate disproportionation pathways unless carefully dosed. Implementing short contact times and using softened water can further minimize by-product formation, as carbonate precipitation may catalyze side reactions and disrupt process stability. In addition in literature several methods for chlorites and chlorates removal are described:

a) Adsorption on GAC

Post-treatment adsorption, particularly using granular activated carbon (GAC), represents a mature and well-documented approach to removing chlorite and chlorate. GAC offers both physical adsorption and catalytic reduction capacity. GAC can remove chlorite as a result of absorption and chemical reduction [161]: as the absorptive sites are occupied, chemical reduction on the GAC surface becomes the main removal mechanism [162]. Sorlini and Collivignarelli (2005) [152] demonstrated that GAC facilitates the decomposition of chlorite into radical species (Cl, ClO) through reactions with free radicals on its surface; these intermediates subsequently react to form chloride as the final product, with no evidence of chlorate formation [162–164]. Surface chemistry plays a vital role: acidic or metal-doped carbons show higher affinity for oxychlorine species. Recent studies have highlighted that modified GAC, particularly when treated with cationic surfactants or impregnated with metal oxides (e.g., Fe or Mn), exhibits enhanced performance even in the presence of natural organic matter or nitrate [165]. Base-acid regeneration cycles can restore sorption capacity while promoting in-situ decomposition of chlorate via acid-mediated redox reactions. O'Brien et al. (2005) [166] demonstrated that acid washing with HCl can convert adsorbed chlorate into harmless chloride and gaseous chlorine under controlled conditions, providing a potential pathway for material reuse.

b) Chlorite ions reduction with Ferrous Iron

Reduction reactions with ferrous iron (Fe^{2+}) are a cost-effective and efficient means of transforming chlorite into chloride, especially in water treatment systems already utilizing iron-based coagulants. Qi et al. (2020) [98] demonstrated that a Fe^{2+}: ClO_2^- ratio of ~3.3:1 (mg/mg) enables near-complete removal within one minute. At higher pH, the formation of $Fe(OH)_3$ as a precipitate contributes additional coagulation benefits, removing suspended solids and enhancing overall water clarity [166]. The combination of Fe^{2+} dosing with UV/chlorine advanced oxidation processes (AOPs) creates synergistic pathways for contaminant breakdown. As described by Cassol et al. (2022) [167], the reaction generates highly reactive species such as $ClO^{\cdot}$ or $OH^{\cdot}$ radicals, which facilitate both micropollutant and chlorate degradation, all while maintaining low residual concentrations compliant with WHO guidelines (<0.7 mg/L).

c) Electrochemical systems

Electrochemical systems have garnered increasing attention as scalable, reagent-free options for chlorate and perchlorate removal. These systems function by reducing oxychlorine species at the cathode through proton-coupled electron transfer, often facilitated by high-surface-area electrodes such as boron-doped diamond (BDD) [167], graphite [87], or titanium [168], [169] coated with mixed metal oxides (MMO), hybrid electrodes, for detection of halogenate ion species in aqueous solutions, modified with electroactive silver nanoparticles [170]. Studies have shown that chlorate can be efficiently converted to chloride via multi-step pathways involving ClO_2^{-} intermediates [170], [171]. Mohammad et al. (2010) further demonstrated that the presence of triiodide (I_3^{-}) enhances this autocatalytic mechanism, accelerating the reaction in both acidic and near-neutral media [172]. As energy efficiency improves and renewable energy sources are incorporated, electrochemical systems are expected to become key components of sustainable water treatment infrastructure.

d) Advanced Oxidation/Reduction Processes (AOPs/ARPs)

Advanced oxidation and reduction processes represent some of the most versatile and effective methods for managing ClO_2 by-products in complex matrices [173]. The oxidation process based on sulfate relies on the activation of S(IV) to form sulfite radical ($SO_3^{\cdot -}$) via one-electron transfer by transition metal ions (e.g., Fe^{2+}, Mn^{2+}, Co^{2+}, Cu^{2+}) [174–176], various oxidants (e.g., bromate, hexavalent chromium, ferrate, potassium permanganate) [177], [178–180], UV-light [181], and electricity [182]. Subsequently, the generated SO_3^{-} is converted to $SO_5^{\cdot -}$, $SO_4^{\cdot -}$, and even $OH^{\cdot}$ under aerobic conditions [174], [175,176,178–182]. The processes rely on the generation of short-lived radicals, such as $OH^{\cdot}$, $SO_4^{\cdot -}$ and e_{aq}^{-}, capable of breaking down a wide range of pollutants. UV-activated sulfite systems are particularly well-suited for reducing chlorate in acidic wastewaters [183], while persulfate-chlorite hybrids can simultaneously regenerate ClO_2 and degrade organic and inorganic contaminants. Persulfate activation ($S_2O_8^{2-}$) under heat or UV produces $SO_4^{\cdot -}$[184], which is more selective and stable than $OH^{\cdot}$, allowing for targeted reactions with chlorate and chlorite. Moreover, coupling these processes with ClO_2 generation can create self-sustaining treatment loops [93]. However, to ensure efficacy, the scavenging effects of dissolved oxygen, nitrate, or bicarbonate must be carefully managed.

e) Underdeveloped technologies: Heterogeneous Catalysis for reduction processes, Biological Treatments and Membrane Separation Techniques

The catalytic reduction of oxychlorine species using noble metal catalysts, particularly platinum and palladium supported on zeolites, offers a promising route for high-efficiency treatment. These systems operate under mild conditions and can convert over 99% of chlorate into chloride without generating harmful by-products [28]. The underlying mechanism involves proton-coupled electron transfer on the catalyst surface, with reaction rates enhanced by optimizing metal dispersion and acid site density [185–187]. Continued research into catalyst regeneration and longevity will be vital for widespread implementation in both industrial and municipal settings. Anaerobic bioremediation presents a low-energy, environmentally friendly solution for perchlorate and chlorate reduction. Certain bacteria, including strains of Dechloromonas, Azospira, and Propionivibrio, can use these oxychlorine ions as terminal electron acceptors, reducing them to chloride during respiration [188–190], [191–193]. Bioreactors tailored to support these microbial communities, such as fluidized bed systems or fixed-film biofilters, have demonstrated high efficiency even at low contaminant concentrations. Supplementing these systems with electron donors like acetate or hydrogen gas enhances performance, or with iron salts which act as reducing agents and coagulants [163]. It has proven hydrogen's value as a reducing agent in wastewater and drinking water treatment [194], [195]. Moreover, combining biological reduction with coagulation or filtration enables integrated removal of microbial biomass and residual disinfectants. Membrane processes like reverse osmosis

(RO) [196], nanofiltration (NF) [196–198], and electrodialysis (ED)[199] offer precise separation of residual disinfectants and by-products, especially in settings where ultrapure water is required. RO systems can reject >90% of chlorite and chlorate ions but are sensitive to fouling, necessitating robust pre-treatment and regular maintenance [200].

f) Precipitation for chloride removing

Chemical precipitation, although less common, can be applied in niche settings to target chloride via the formation of insoluble salts such as AgCl or CuCl after chloride's generation by chlorate transformation. In the AgCl process, silver nanoparticles, in the presence of H_2O_2, oxidize Ag(0) to Ag(I), which complexes with Cl^- to form AgCl with major efficiency under alkaline conditions [201]. In the CuCl process, Cu(0) reacts with Cu(II) to form Cu(I), which then reacts with Cl^- to generate CuCl, with efficiency improving at higher temperatures and with increased Cu(II) concentrations [61,202,203]. Moreover, UV irradiation can enhance the removal efficiency by generating Cl· that reacts with Cu(0) [204], [205].These methods are generally reserved for point-of-use systems or laboratory-scale processes due to cost and complexity constraints. To assist in the evaluation of available technologies, Table 8 summarizes key mitigation strategies, their targeted by-products, and performance characteristics.

Table 8. Mitigation strategies, their targeted by-products, and performance characteristics.

Technology / Process	Operational Safety	Targeted By-Products	Mechanism	Operational Complexity	Removal Efficiency	Typical Application Context
pH and Reagent Optimization	High	Chlorite, Chlorate, Perchlorate	Controls stoichiometry and pH to prevent side reactions	Low	Moderate	ClO_2 generation in municipal treatment systems
Granular Activated Carbon (GAC) Adsorption	Medium	Chlorite, Chlorate	Adsorption + catalytic surface reduction (enhanced with modified GAC)	Medium	High (especially modified GAC)	Post-treatment for potable water
Ferrous Iron (Fe^{2+}) Reduction	High	Chlorite	Direct chemical reduction to chloride	Low	High	Integrated with coagulation in drinking water treatment
Electrochemical Systems	Variable (depending on design)	Chlorate, Perchlorate	Cathodic reduction via high surface area electrodes	Medium–High	High	Decentralized or high-tech treatment facilities
Advanced Oxidation/ Reduction Processes (AOPs/ARPs)	Medium	Chlorate, Chlorite	Radical generation ($SO_4^{\cdot-}$, $OH^{\cdot}$, etc.) for selective degradation	High	Very High	Industrial effluents, complex wastewater

Heterogeneous Catalysis (Pt/Pd on zeolites)	High	Chlorate	Catalytic reduction via proton-coupled electron transfer	Medium	Very High (>99%)	Advanced municipal and industrial treatment systems
Anaerobic Biological Treatment	High	Chlorate, Perchlorate	Microbial respiration (e.g., *Dechloromonas*)	Medium	High (but slow kinetics)	Groundwater remediation, agricultural runoff
Membrane Techniques (RO, NF, ED)	High	Chlorite, Chlorate	Physical separation using semi-permeable membranes	High	Very High (>90%)	Ultrapure water, pharmaceutical or high-end applications
Chemical Precipitation (AgCl, CuCl)	Medium	Chloride	Formation of insoluble salts under controlled chemical conditions	High	High (niche efficiency)	Point-of-use systems, lab-scale or experimental processes
ClO_2 + **Ozone Combination**	Medium	Reduced Chlorite, but increased Chlorate	O_3 oxidizes ClO_2^-, regenerating ClO_2	Medium	Moderate	Surface waters with high organic content

Given the complex nature of ClO_2 disinfection by-products, many systems benefit from integrated approaches that combine multiple technologies. These hybrid solutions can offer synergistic benefits, improving both efficacy and operational resilience. Table 9 outlines selected integrated strategies.

Table 9. Integrated Approaches to Minimize Disinfection By-Products in Chlorine Dioxide-Based Treatment Systems.

Integrated Strategy	Combined Components	Synergistic Benefit	Application Scope
ClO_2 + GAC + UV/Cl_2 AOP	ClO_2 for disinfection, GAC for DBP removal, UV/ Cl_2 for residuals	Reduces chlorite + chlorate + organic DBPs	Surface water, high NOM content
ClO_2 pre-oxidation + Fe^{2+} dosing + filtration	Pre-disinfection + chemical reduction + particle removal	Enhanced pathogen control + DBP mitigation	Drinking water with moderate turbidity
Electrochemical ClO_2 generation + membrane filtration	On-site ClO_2 + NF/RO for polishing	Residual control + high-quality effluent	Industrial or pharmaceutical water production
Bioreactor + ClO_2 residual disinfection	Biological reduction of DBPs + final disinfection	Reduces perchlorate/chlorate + ensures microbial safety	Decentralized systems, groundwater reuse

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PS- ClO_2 hybrid + real-time monitoring	ClO_2 + activated persulfate + automated controls	Optimized dosing, minimized DBP formation	Smart water networks, energy-intensive facilities

As global water treatment systems evolve to meet tighter regulatory standards and higher performance expectations, innovation in ClO_2 generation and by-product mitigation will remain a priority. The integration of continuous-flow micro reactors and electrochemical generators powered by renewable energy (e.g., solar PV) represents a promising direction. Real-time monitoring platforms equipped with optical sensors, spectrophotometers, or electrochemical probes enable proactive management of ClO_2 residuals and associated by-products. Machine learning models trained on historical water quality data can predict by-product spikes, enabling automated adjustments in dosing, pH control, or secondary treatment activation.

9. Research Gaps and Future Outlook

Despite the extensive use of chlorine dioxide (ClO_2) in water disinfection and industrial sanitation, several critical knowledge gaps persist. Key among these are the incomplete understanding of its by-product formation pathways, the long-term environmental impacts of its use, and its potential integration with advanced treatment technologies. This review has highlighted both the benefits and trade-offs of various ClO_2 generation methods, but further research is essential to inform regulatory developments and to optimize treatment designs in light of evolving environmental and public health challenges. While ClO_2 is generally associated with lower levels of trihalomethanes (THMs) and haloacetic acids (HAAs) compared to chlorine, recent studies suggest that reaction pathways involving radicals ($Cl•$, $Cl_2•^-$) and dissolved organic matter (DOM) may produce emerging DBPs not yet well characterized [206]. Detailed kinetic and molecular-level studies are needed to elucidate the formation mechanisms, speciation, and toxicity of these by-products under varying conditions of pH, DOM composition, and light exposure [207]. Chlorate (ClO_3^-) and perchlorate (ClO_4^-) remain the main inorganic DBPs of concern in ClO_2-based systems [208]. Although mitigation strategies, including UV/sulfite, zero-valent iron, and biological filtration have been proposed, there is a clear need for systematic evaluations of their effectiveness across different water matrices and operational regimes. Research should aim to develop scalable, robust, and integrated treatment trains capable of minimizing these DBPs without compromising microbial inactivation. The apparent simplicity and operational flexibility of ClO_2 generation may obscure significant hidden costs, including those related to material corrosion, degradation, and containment of residuals [123], [209]. Comprehensive life-cycle assessments (LCA) and total cost of ownership (TCO) analyses comparing ClO_2 with alternative disinfectants are scarce, and such evaluations are crucial to guide utility planning [210–214]. Future studies should integrate economic, environmental, and health impact modelling to support informed decision-making by utilities and regulators. Additionally, ClO_2 applications often fall within regulatory grey zones, as regional and national standards for chlorite, chlorate, and brominated DBPs are not harmonized. There is a pressing need for comparative analyses of existing regulatory thresholds (e.g., EPA, WHO, EU directives) in relation to specific ClO_2 generation and application techniques. Such efforts could support the development of more adaptive, globally aligned regulatory frameworks that promote safe and sustainable disinfection practices. The integration of with emerging advanced oxidation processes (AOPs) or smart, sensor-driven monitoring systems (e.g., real-time DBP sensors, AI-based control) remains largely unexplored [215], [216]. Studies should investigate how ClO_2 can be effectively embedded into multi-barrier treatment strategies, either as a primary oxidant or as a synergistic agent in conjunction with UV, ozone, or catalytic systems, particularly in decentralized, reuse-oriented, or low-resource contexts. One particularly promising area of future research lies in the combined use of ultraviolet (UV) irradiation with chlorite and ClO_2. Although UV has been extensively studied for its capacity to inactivate pathogens and degrade DBPs, its coupling with chlorite- and ClO_2-based systems is still insufficiently understood. Initial evidence suggests that UV can enhance chlorite decomposition, potentially generating reactive chlorine species that may synergistically improve disinfection or facilitate the degradation of organic by-products [217]. Furthermore, UV exposure may mitigate chlorate formation by promoting the photoreduction of ClO_2 to chloride, thus lowering the accumulation of toxic residues [30], [217]. However, more detailed studies are required to clarify the kinetics of these processes and to define optimal UV dosages and exposure times across diverse water chemistries. Moreover, the potential advantages of UV– ClO_2 integration in water reuse systems, high-purity applications, or decentralized treatment schemes should be rigorously evaluated. These hybrid approaches may offer significant gains in treatment efficiency, cost-effectiveness, and environmental sustainability, especially in regions where advanced treatment infrastructure is limited or where climate resilience is a priority.

Discussion

This comparative assessment reveals the multifaceted trade-offs between chlorine dioxide (ClO_2) and alternative disinfection technologies such as ozone, ultraviolet (UV) radiation, and hydrogen peroxide. Chlorine dioxide distinguishes itself for its broad-spectrum antimicrobial efficacy, which extends to bacteria, viruses, and protozoa [2], [4], and its ability to remain effective across a wide pH range [13], [14]. This pH-independence gives ClO_2 a distinct operational advantage in variable water chemistries where traditional disinfectants like chlorine may lose effectiveness. ClO_2 tends to produce fewer regulated halogenated organic by-products, such as trihalomethanes (THMs) and haloacetic acids (HAAs), compared to chlorine [10], [67]. However, it leads to the formation of inorganic by-products such as chlorite (ClO_2^-) and chlorate (ClO_3^-), which pose toxicological and regulatory challenges [23], [26]. Effective by-product management, such as UV-assisted reduction or the use of ascorbic acid [18], [184], is therefore essential for ClO_2 to remain a sustainable option in water treatment applications. Compared to ozone, ClO_2 offers superior storage stability and can be generated on-site under controlled conditions. Ozone, although a powerful oxidant with rapid kinetics, must be generated in situ and can form bromate (BrO_3^-), a known carcinogen, in bromide-rich waters [59]. UV disinfection is highly effective against a wide range of pathogens, including Cryptosporidium and Giardia, and is free of chemical additives. However, it lacks residual effect, making it less suitable in systems prone to microbial regrowth [64]. Environmentally, ClO_2 exhibits a moderate footprint. Its precursors, such as sodium chlorite, are manageable with proper handling, and its gaseous form allows for efficient dosing. Nonetheless, the downstream removal or minimization of ClO_2^- and ClO_3^- increases process complexity. Hydrogen peroxide, typically used in advanced oxidation processes (AOPs), offers a cleaner by-product profile but requires combination with UV or ozone for full microbial inactivation, raising costs [218]. Recent findings highlight the synergistic potential of combining UV with ClO_2 or ClO_2^-. UV photolysis of chlorite leads to the formation of reactive species such as $ClO^{\cdot}$, $Cl^{\cdot}$, and $OH^{\cdot}$, which can enhance degradation of contaminants and disinfection efficiency [219], [220]. Such integration improves the removal of organic micropollutants and reduces chlorate formation by driving ClO_2^- toward less harmful products [221]. Future research should focus on the optimization of UV– ClO_2^- systems, especially for decentralized and water reuse settings. Applications in which chlorite and UV are co-applied have shown promising results in the removal of emerging contaminants and in reducing residual toxicity [30], [184]. Additionally, the development of real-time monitoring systems for DBPs [215] and AI-assisted control strategies could enhance safety and performance. In conclusion, ClO_2 remains a robust and flexible disinfectant when properly managed, particularly in systems requiring strong residuals and broad-spectrum activity. However, its by-products, particularly chlorite and chlorate, necessitate the deployment of hybrid treatment chains and regulatory vigilance. The combination of ClO_2 with UV technologies emerges as a powerful tool to enhance efficacy while reducing environmental and health risks, indicating a promising direction for sustainable water disinfection.

Conclusions

The comparative analysis presented in this review confirms that while chlorine dioxide represents a viable alternative to traditional disinfectants, owing to its high biocidal potential and its ability to operate under a wide range of conditions, it is also associated with various challenges related to the formation of inorganic residuals. The review provides an original contribution to the literature on chlorine dioxide by presenting a systematic and comparative analysis of production methods, the challenges related to by-product formation, and corresponding mitigation strategies. The summary tables and comparative matrices outlined in the document clearly demonstrate how the production methods for ClO_2 can impact the quality of the final product and the type of by-products generated. In particular, systems based on electrochemical processes or the use of milder reducing agents (e.g., hydrogen peroxide or CO_2) provide excellent results in terms of operational safety and residual control, compared to traditional methods that rely on strong acids or chlorine-based reactions. Simultaneously, the review highlights that the techniques for removing chlorites, chlorates, and perchlorates, essential for mitigating the risks associated with ClO_2, offer significant benefits, especially when integrated within advanced treatment systems (e.g., modified activated carbon adsorption, oxidation/reduction processes, and electrochemical systems). In summary, the overall findings support the adoption of a multidimensional approach in selecting the disinfection method, whereby the correct combination of production systems and removal technologies enables the full potential of chlorine dioxide to be harnessed while minimizing its environmental and health-related drawbacks, making this technology a competitive and sustainable solution for future applications.

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