SARS-CoV-2 pharmaceutical drugs: a critical review on the environmental impacts, chemical characteristics, and behavior of advanced oxidation processes in water

Monserrat Castañeda-Juárez1, Ivonne Linares-Hernández1, Verónica Martínez-Miranda1, Elia Alejandra Teutli-Sequeira1,2, Luis Antonio Castillo-Suárez1,3, Ana Gabriela Sierra-Sánchez1

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Abstract
This review summarizes research data on the pharmaceutical drugs used to treat the novel SARS-CoV-2 virus, their characteristics, environmental impacts, and the advanced oxidation processes (AOP) applied to remove them. A literature survey was conducted using the electronic databases Science Direct, Scopus, Taylor & Francis, Google Scholar, PubMed, and Springer. This complete research includes and discusses relevant studies that involve the introduction, pharmaceutical drugs used in the SARS-CoV-2 pandemic: chemical characteristics and environmental impact, advanced oxidation process (AOP), future trends and discussion, and conclusions. The results show a full approach in the versatility of AOPs as a promising solution to minimize the environmental impact associated with these compounds by the fact that they offer different ways for hydroxyl radical production. Moreover, this article focuses on introducing the fundamentals of each AOP, the main parameters involved, and the concomitance with other sources and modifications over the years. Photocatalysis, sonochemical technologies, electro-oxidation, photolysis, Fenton reaction, ozone, and sulfate radical AOP have been used to mineralize SARS-CoV-2 pharmaceutical compounds, and the efficiencies are greater than 65%. According to the results, photocatalysis is the main technology currently applied to remove these pharmaceuticals. This process has garnered attention because solar energy can be directly utilized; however, low photocatalytic efficiencies and high costs in large-scale practical applications limit its use. Furthermore, pharmaceuticals in the environment are diverse and complex. Finally, the review also provides ideas for further research needs and major concerns.

Keywords COVID-19 · Hydroxyl radical · Sulfate radical · COVID-19 drugs · Mineralization

Introduction
On March 11th, 2020, the World Health Organization (WHO) declared a global pandemic the coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was discovered in December 2019 in Wuhan, China (Khezri et al. 2021). The novel virus has caused more than 552 million infections and more than 6.347 million deaths worldwide as of July 11, 2022. COVID-19 is the third zoonotic epidemic of the twenty-first century (Nasir et al. 2021) and is more easily transmitted between people, especially in dense population places (Teymoorian et al. 2021).

At the beginning of the pandemic, no vaccine or specific therapeutic drugs were available, and “repurposed” drugs were used, which are defined as drugs that have been used to treat similar kinds of viruses. Moreover, due
to the COVID-19 pandemic, the use of certain drugs has increased, such as antibiotics (Usman et al. 2020), antiepileptics, analgesics, anticancers, antidiabetics, antiallergics, antidepressants, antidiarrheals, and antipyretics, to protect themselves by self-medication (Teymoorian et al. 2021; Galani et al. 2021).

The human body only metabolizes approximately 60–70% of the active pharmaceuticals, and the residual metabolites and unmetabolized pharmaceutical are excreted in urine at 55–80%, followed by feces at 4–30% (Moratalla et al. 2021). As a consequence of the unprecedented use of those pharmaceuticals, they have been detected in the environment, particularly in wastewater, which can cause negative effects such as genotoxicity, aquatic toxicity, and bacterial resistance development (Teymoorian et al. 2021). As a result of the pandemic, the environment and the public’s health are exposed to new types of permanent pharmaceuticals; therefore, the SARS-CoV-2 pandemic has negative direct and indirect impacts on water and wastewater quality.

These compounds cannot be effectively and fully removed from wastewater using conventional methods due to their chemical properties and stability (Jelic et al. 2011; Bijlsma et al. 2021). On the other hand, the number of studies published to date on the removal of new SARS-CoV-2 pharmaceuticals in the pandemic and their environmental impacts is quite low.

For this reason, this paper critically reviews currently available knowledge on advanced oxidation processes (AOPs) and their potential to remove these pharmaceutical drugs. The present review focuses on analyzing the characteristics of AOPs, identifying the main trends in this area that will help future research and providing guidance for new researchers.

## Pharmaceutical drugs used in the SARS-CoV-2 pandemic: chemical characteristics and environmental impact

SARS-CoV-2 changes over time, and some changes may affect its properties, such as how easily it spreads, disease severity, vaccine performance, the pharmaceutical drugs used, and public health and social measures employed. SARS-CoV-2 variants need to be monitored to improve antiviral treatments and vaccination (Darvishi et al. 2021). The WHO established the following variants to date: Alpha, Beta, Gamma, Delta, Eta, Iota, Kappa, Lambda, Mu, and Omicron. Table 1 shows the pango lineage and date of designation (WHO, 2022).

Depending on the viral load, the lungs, cardiovascular tissue, kidneys, upper respiratory, and gastrointestinal tract can be affected (Biswas et al. 2021). Currently, no effective drug treatment is available for fighting SARS-CoV-2 (Tarazona et al. 2021); however, the existing pharmaceutical drugs approved or in development for treating infections caused by HIV, hepatitis B and C virus, and influenza were repurposed based on therapeutic experiences with SARS and MERS (Dheyab et al. 2021) called “repurposed pharmaceutical drugs.” These pharmaceuticals include antiviral agents, antimalarial drugs (Midassi et al. 2020), immune response regulators, modifiers of the intracellular environment, viral RNA polymerase inhibitors, protease inhibitors, monoclonal antibodies, corticosteroids, and antibiotics. These are the main pharmaceutical drugs used around the world, but other pharmaceutical compounds have been used (Awadasseid et al. 2021; Sarkar et al. 2020; Bergman et al. 2021; Jan et al. 2021). Furthermore, SARS-CoV-2 patients present another complication, including mental health disequilibrium, and approximately 48% of patients manifest psychological diseases (Tingbo 2020).

### Table 1  SARS-CoV-2 variants established by WHO

| WHO label | Earliest documented samples | Date of designation | Pango Lineage |
|-----------|-----------------------------|---------------------|---------------|
| **Variants of concern** | | | |
| Alpha | UK, September 2020 | 18-Dec-2020 | B.1.1.7 |
| Beta | South Africa, May 2020 | 18-Dec-2020 | B.1.351 |
| Gamma | Brazil, November 2020 | 11-Jan-2021 | P.1 |
| Delta | India, October 2020 | 11-May-2021 | B.1.617.2 |
| Omicron | November 2021 | 24-Nov-2021 | B.1.1.529 |
| **Variants of interest** | | | |
| Eta | December 2020 | 17-March-2021 | B.1.525 |
| Iota | USA, November 2020 | 24-March-2021 | B.1.526 |
| Kappa | India, October 2020 | 4-April-2021 | B.1.617 |
| Lambda | Peru, December 2020 | 14-June-2021 | C.37 |
| Mu | Colombia, January, 2021 | 30-Aug-2021 | B.1.621 |
Moreover, the pandemic has influenced people’s mental health worldwide, leading to an increase in depressive episodes, anxiety, and insomnia (Olff et al. 2021; Allan et al. 2020; Bareeqa et al. 2021), and depression affects approximately 300 million individuals (Faquih et al. 2019). As a consequence, psychiatric drugs such as sertraline, carbamazepine, fluoxetine, and citalopram are highly consumed (Teymoorian et al. 2021).

Table 2 summarizes the main pharmaceutical drugs used during the SARS-CoV-2 pandemic and shows the chemical properties and chemical structure. These pharmaceutical drugs are derived from quinolones (chloroquine and hydroxychloroquine) with good solubility (Gosu et al. 2016; Race et al. 2020) and chemical stability, fluoroquinolones (ciprofloxacin), and macrocyclic lactones (Ivermectin) which are hydrophobic and have low volatility and solubility

| Name                   | Chemical properties | Chemical structure | Pharmacological class of drug | Metabolite / absorption percentage on the body | Log Kow | Impacts on water and the environment |
|------------------------|---------------------|--------------------|-------------------------------|-----------------------------------------------|---------|-------------------------------------|
| Acyclovir              | C$_{7}$H$_{7}$N$_{3}$O$_{6}$ | 225.21 g/mol pKa 2.27 pKa 9.25 | Antiviral drugs | 9-carboxymethylmethylguanine 8-hydroxy-acyclovir (National Center for Biotechnology Information 2021e) | -1.10 | Inhibited the growth of the algae Raphidiellopsis subcapitata at concentrations of 2.5 to 20 mg/L (C$_{50}$=3.612 mg/L) Caused a significant fertility decrease in females of Cardioina dubia at concentrations of 2.5 to 20 mg/L (Almeida et al. 2021) |
| Amoxicillin            | C$_{18}$H$_{26}$ClN$_{3}$ | 356.4 g/mol pKa 2.69 | Antibiotic | Amoxicillin diketopiperazine 20-30-dione (Sun et al. 2016) | 0.87 | Cause antibiotic resistance, decreasing the effectiveness of available antibiotics Change microbial ecosystems potentially (Alkshe Demirenzie, Yildz, and Demirenze Yilmaz 2019) |
| Antibiotic             | C$_{20}$H$_{20}$N$_{3}$O$_{11}$ | 748.98 g/mol pKa 8.5 | Antibiotic | The principal route of biotransformation involves N-demethylation of the desoxamine sugar or at the 9a position on the macrolide ring (National Center for Biotechnology Information 2021a) | 4.02 | High concentrations (5–100 μg/L) inhibited algal growth (Chlorovula pervicaudata). Weaken the photosynthetic activities of algae by promoting heat dissipation, inhibiting the absorption and trapping of light energy (Mao et al. 2021). |
| Carbamazepine          | C$_{11}$H$_{12}$N$_{2}$O$_{4}$ | 23627 g/mol pKa 13.94 | Antiepileptic | Carbamazepine-10,11-epoxide (National Center for Biotechnology Information 2021f) | 2.45 | Acute toxicity on fish, algae, bacteria, and invertebrates (Ferrari et al. 2005) |
| Chloroquine            | C$_{31}$H$_{36}$ClN$_{6}$ | 319.872 g/mol pKa 10.1 | Antimalarial drug | Dihydrochloroquine (National Center for Biotechnology Information 2021g) | 3.03 | Persistent, bioaccumulate, and transfer to living organisms in intensified toxic forms owing to its antiviral and antibacterial characteristics (Alshehadi, Boudon, and Bonneval 2020) Carcinogenic, toxic and teratogenic |
| Ciprofloxacin          | C$_{15}$H$_{14}$N$_{2}$O$_{4}$ | 331346 g/mol pKa 6.89 | Antimicrobial Agents | Ofoxeracillin, Solociprofloxacin, Dexamethacycline, Ciprofloxacin Formylciprofloxacin (National Center for Biotechnology Information 2021h) | 0.28 | Inhibits active and growing microorganisms Important risk for the environment, especially for soil microbial ecology and microbial ecosystem services (Girardi et al. 2011) |
| Citalopram             | C$_{20}$H$_{21}$N$_{3}$O$_{5}$ | 324592 g/mol pKa 9.8 | Antidepressant | N-desmethylcitalopram Di-N-desmethylcitalopram citalopram-N-oxide Deaminated protonic acid (National Center for Biotechnology Information 2021i) | 3.5 | Causes free detachment from the substrate in two kinds of freshwater snails (Lymnaea stagnalis, Lymnaea alba) and snails (=Lymnaea stagnalis J.E.F.ing and E.T.) (Yilmaz 2019) | E50 = 1.15 mg/L Daphnia magna |
| Darunavir              | C$_{15}$H$_{16}$N$_{5}$S | 547665 g/mol pKa 13.59 | ENU | Ne reported | 1.89 | Environmental risk, focusing on chronic sublethal effects on fish (Tanamura et al. 2021) |
| Dexamethasone          | C$_{22}$H$_{27}$F$_{7}$O$_{3}$ | 392966 g/mol pKa 1.8 | Corticosteroids | 6β-hydroxycortisol 11-deoxycortisol (National Center for Biotechnology Information 2021j) | 1.83 | Effects on vertebrate growth, at 40–50 μg/L NOEC: 4 and 1 μg/L (Tanamura et al. 2021) |
| Azithromycin           | C$_{38}$H$_{72}$N$_{2}$O$_{12}$ | 748.98 g/mol | Antibiotic | 748.98 g/mol | 0.87 | Weaken the photosynthetic activities of algae by promoting heat dissipation, inhibiting the absorption and trapping of light energy (Mao et al. 2021). | 3.03 | Persistent, bioaccumulate, and transfer to living organisms in intensified toxic forms owing to its antiviral and antibacterial characteristics (Alshehadi, Boudon, and Bonneval 2020) Carcinogenic, toxic and teratogenic |
| Cimetidine             | C$_{14}$H$_{17}$N$_{3}$O$_{2}$ | 231551 g/mol pKa 5.01 | Antiproliferative | Cimetidine (National Center for Biotechnology Information 2021k) | 0.28 | Inhibits active and growing microorganisms Important risk for the environment, especially for soil microbial ecology and microbial ecosystem services (Girardi et al. 2011) |
| Dexamethasone          | C$_{22}$H$_{27}$F$_{7}$O$_{3}$ | 392966 g/mol pKa 1.8 | Corticosteroids | 6β-hydroxycortisol 11-deoxycortisol (National Center for Biotechnology Information 2021j) | 1.83 | Effects on vertebrate growth, at 40–50 μg/L NOEC: 4 and 1 μg/L (Tanamura et al. 2021) | 3.5 | Causes free detachment from the substrate in two kinds of freshwater snails (Lymnaea stagnalis, Lymnaea alba) and snails (=Lymnaea stagnalis J.E.F.ing and E.T.) (Yilmaz 2019) | E50 = 1.15 mg/L Daphnia magna |
and strong affinity for soil and organic matter (Nippes et al. 2021), synthetic steroids (dexamethasone) characterized by a four-membered hydrocarbon core (Kasal 2010), beta-lactams (amoxicillin) with amphoteric properties (Aksu et al. 2019; Anastopoulos et al. 2020), sulfonamides (sulfamethoxazole) (Larcher and Yargeau 2012), etc.

The use of these pharmaceutical compounds has increased since 2020 and has been detected in the environment. In Catalonia, Spain (in 2020), amoxicillin and broad-spectrum antibiotics increased their use (Abelenda-Alonso et al. 2020). Hydroxychloroquine and chloroquine have also been widely used (Revilla et al. 2021). Da Silva et al. evaluated antimicrobial consumption in Brazil and found a 2500% higher rate of azithromycin consumption. Moreover, the usage of amoxicillin/clavulanate had a notably higher rate in all COVID-19 clusters (Da Silva et al. 2021). In Athens, Greece, the use of antiviral drugs increased 170%, hydroxychloroquine increased 387%, antibiotics increased 57%, and paracetamol increased 198% (Galani et al. 2021). In 2020, Nason et al. detected different chemicals and evaluated their trends in primary wastewater sludge from WWTPs, and sertraline, citalopram, and acetaminophen showed a clear increase (Nason et al. 2021). Kumar et al. (2020) estimated the metabolite favipiravir hydroxide presented in rivers and

### Table 2 (continued)

| Compound | CxHyNzOw | Molecular Weight (g/mol) | pKa | Type | Source | Notes |
|----------|----------|--------------------------|-----|------|--------|-------|
| Ivermectin | C48H74O14 | 875.10 g/mol | 12.47 | Antibiotic | Anthelmintic | LC50 values to bluegill sunfish and rainbow trout were 4.8 and 3.0 ppb respectively after 96 h. Highly toxic towards invertebrates, moreover, ivermectin is located in the sediments (Sanderson et al. 2007). Carcinogenic, toxic and teratogenic |
| Lamivudine | C8H11N3O3S | 229.256 g/mol | 13.83 | Antiviral | HIV, Hepatitis B | Ecological health risk at different trophic levels, to both flora and fauna, at concentrations found in the environment (Omotola et al. 2021) |
| Lopinavir | C37H48N4O5 | 628.81 g/mol | 13.59 | Antiviral | HIV | Lopinavir shows high bioaccumulation potential (Dunok et al. 2015). |
| Oseltamivir (Tamiflu) | C16H28N2O4 | 312.4 g/mol | 7.7 | Neuraminidase inhibitor | Induce a significant ecotoxicological risk in waterways and reported to be recalcitrant in sewage effluent (Jain et al. 2013) |

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and strong affinity for soil and organic matter (Nippes et al. 2021), synthetic steroids (dexamethasone) characterized by a four-membered hydrocarbon core (Kasal 2010), beta-lactams (amoxicillin) with amphoteric properties (Aksu et al. 2019; Anastopoulos et al. 2020), sulfonamides (sulfamethoxazole) (Larcher and Yargeau 2012), etc.

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Table 2 (continued)

| Drug           | Formula | Molecular Mass | pKa | pKa1 | pKa2 | pKa3 | pKa4 | pKa5 | pKa6 | pKa7 | pKa8 | pKa9 | pKa10 | pKa11 | pKa12 | pKa13 | pKa14 | pKa15 | pKa16 | pKa17 | pKa18 | pKa19 | pKa20 | pKa21 | pKa22 | pKa23 | pKa24 | pKa25 | pKa26 | pKa27 | pKa28 | pKa29 | pKa30 | pKa31 | pKa32 | pKa33 | pKa34 | pKa35 | pKa36 | pKa37 | pKa38 | pKa39 | pKa40 | pKa41 | pKa42 | pKa43 | pKa44 | pKa45 | pKa46 | pKa47 | pKa48 | pKa49 | pKa50 | pKa51 | pKa52 | pKa53 | pKa54 | pKa55 | pKa56 | pKa57 | pKa58 | pKa59 | pKa60 | pKa61 | pKa62 | pKa63 | pKa64 | pKa65 | pKa66 | pKa67 | pKa68 | pKa69 | pKa70 | pKa71 | pKa72 | pKa73 | pKa74 | pKa75 | pKa76 | pKa77 | pKa78 | pKa79 | pKa80 | pKa81 | pKa82 | pKa83 | pKa84 | pKa85 | pKa86 | pKa87 | pKa88 | pKa89 | pKa90 | pKa91 | pKa92 | pKa93 | pKa94 | pKa95 | pKa96 | pKa97 | pKa98 | pKa99 | pKa100 | pKa101 | pKa102 | pKa103 | pKa104 | pKa105 | pKa106 | pKa107 | pKa108 | pKa109 | pKa110 | pKa111 | pKa112 | pKa113 | pKa114 | pKa115 | pKa116 | pKa117 | pKa118 | pKa119 | pKa120 | pKa121 | pKa122 | pKa123 | pKa124 | pKa125 | pKa126 | pKa127 | pKa128 | pKa129 | pKa130 | pKa131 | pKa132 | pKa133 | pKa134 | pKa135 | pKa136 | pKa137 | pKa138 | pKa139 | pKa140 | pKa141 | pKa142 | pKa143 | pKa144 | pKa145 | pKa146 | pKa147 | pKa148 | pKa149 | pKa150 | pKa151 | pKa152 | pKa153 | pKa154 | pKa155 | pKa156 | pKa157 | pKa158 | pKa159 | pKa160 | pKa161 | pKa162 | pKa163 | pKa164 | pKa165 | pKa166 | pKa167 | pKa168 | pKa169 | pKa170 | pKa171 | pKa172 | pKa173 | pKa174 | pKa175 | pKa176 | pKa177 | pKa178 | pKa179 | pKa180 | pKa181 | pKa182 | pKa183 | pKa184 | pKa185 | pKa186 | pKa187 | pKa188 | pKa189 | pKa190 | pKa191 | pKa192 | pKa193 | pKa194 | pKa195 | pKa196 | pKa197 | pKa198 | pKa199 | pKa200 | pKa201 | pKa202 | pKa203 | pKa204 | pKa205 | pKa206 | pKa207 | pKa208 | pKa209 | pKa210 | pKa211 | pKa212 | pKa213 | pKa214 | pKa215 | pKa216 | pKa217 | pKa218 | pKa219 | pKa220 | pKa221 | pKa222 | pKa223 | pKa224 | pKa225 | pKa226 | pKa227 | pKa228 | pKa229 | pKa230 | pKa231 | pKa232 | pKa233 | pKa234 | pKa235 | pKa236 | pKa237 | pKa238 | pKa239 | pKa240 | pKa241 | pKa242 | pKa243 | pKa244 | pKa245 | pKa246 | pKa247 | pKa248 | pKa249 | pKa250 | pKa251 | pKa252 | pKa253 | pKa254 | pKa255 | pKa256 | pKa257 | pKa258 | pKa259 | pKa260 | pKa261 | pKa262 | pKa263 | pKa264 | pKa265 | pKa266 | pKa267 | pKa268 | pKa269 | pKa270 | pKa271 | pKa272 | pKa273 | pKa274 | pKa275 | pKa276 | pKa277 | pKa278 | pKa279 | pKa280 | pKa281 | pKa282 | pKa283 | pKa284 | pKa285 | pKa286 | pKa287 | pKa288 | pKa289 | pKa290 | pKa291 | pKa292 | pKa293 | pKa294 | pKa295 | pKa296 | pKa297 | pKa298 | pKa299 | pKa300 |
|----------------|---------|---------------|-----|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------| ------|
possible absorption in fatty tissues, soil, and sediments, and its low mobility favors the toxicity of these substances. Table 2 shows that azithromycin, chloroquine, citralopram, fluoxetine, hydroxychloroquine, lopinavir, ritonavir, and sertraline have bioaccumulation potential.

Conventional systems are designed to remove degradable organic pollutants in the range of mg/L; however, pharmaceutical drugs are present at low concentrations (ng/L–μg/L) and released through domestic, hospital, and industrial effluents due to their characteristics, such as absorption capacity, chemistry form, volatilization, biodegradation, stability, and polarity (Albornoz et al. 2021), which can destabilize these systems.

**Advanced oxidation process**

Advanced oxidation processes (AOPs) are defined as processes that involve the generation and use of the hydroxyl radical (HO•) as a strong oxidant and unselectively attack organic molecules (Nasir et al. 2021). The HO• reacts with the dissolved constituents at rate constants in the range of 10^6–10^10 L/mol (Mouset et al. 2021), initiating a series of oxidation reactions, the constituents can be completely mineralized to CO₂, H₂O, and inorganic ions. These methods are considered environmentally friendly processes, highly efficient, and capable of oxidizing a wide range of contaminants (Saharan et al. 2014). AOPs include sonochemical oxidation, electrochemical oxidation, ozone (O₃), Fenton’s reagent (H₂O₂/Fe²⁺), and photocatalysis, and they can be combined with ultraviolet (UV) or solar irradiation, heat, or microwaves (Teymoorian et al. 2021; Ushani et al. 2020; Nasir et al. 2021). The generated free radicals, such as hydroxyl radicals (HO•), superoxide radicals (O₂−•), sulfate radicals (SO₄²−•), and holes (h+), play a significant role in pollutant degradation (Xia et al. 2020). Some of these technologies have been applied to remove pharmaceutical drugs used in the SARS-CoV-2 pandemic, and according to Table 3 and Fig. 1, dexamethasone is the main pharmaceutical compound treated by AOP in recent years.

**Photocatalysis**

The principle of this process is based on the excitation of the catalyst material by the irradiation of light to produce free radicals, which will destroy the pollutants adsorbed on its surface. Different compounds have been used as photocatalysts (Gogate and Pandit 2004): oxides such as TiO₂, ZnO, ZrO₂, CeO₂, Fe₂O₃, WO₃, and SrTiO₃; sulfides such as CdS and ZnS; and carbon-based materials (Nasir et al. 2021) such as fullerene and carbon nanotubes. When the materials are activated by radiation (visible or UV), the formation of pairs of electrons in the conduction band (e_{CB}−) and positive holes in the valence band (h_{VB}+) is promoted, as shown in Eq. 1. The energy required for the process depends on the band gap of the semiconductor (Andreozzi 1999). h_{VB}+ reacts with water molecules to form HO•, whereas e_{CB}− reacts with oxygen to form O₂−• (Yu et al. 2006) (Eqs. 2 and 3). These radicals react with the organic matter, or they might continue the chain of reactions to produce a greater number of radicals. In a few cases, the adsorbed pollutant molecules might be reduced directly because of the conduction band electrons (Thi et al. 2021), as shown in Fig. 2.

\[
\text{Catalyst}^{hv}e^{-}_{cb} + h^{+}_{vb} 
\]

\[
h^{+}_{vb} + H_{2}O \rightarrow HO^{•} + H^{+} 
\]

\[
e^{-}_{cb} + O_{2} \rightarrow O_{2}^{−•} 
\]

The disadvantages of photocatalysis are the lifespan of the electron/hole pair (nanoseconds) and the band gap of the materials. To expand to the visible light region (solar irradiation, λ > 400 nm) or inhibit electron/hole pair recombination, methodologies have been developed to modify the electronic band structure of catalysts, such as the electrodeposition method (S. Zhang et al. 2013), impregnation (Simamora et al. 2012; Wu et al. 2009), precipitation (Chen et al. 2013), sol–gel (Arun and Sankaran 2016; Gotostos et al. 2014; Pronin et al. 2014), photoreduction (Chen et al. 2012), and ultrasonic impregnation (Chong et al. 2016). The main factors influencing photocatalytic performance include the size, specific surface area, pore volume, pore structure, crystalline phase, and exposed surface (Nakata and Fujishima 2012).

Conventionally, the photocatalyst is suspended in aqueous solution; to avoid the use of powder, which entails its subsequent separation from water, the photocatalyst can be immobilized on supports such as glass beads, glass spheres, glass microspheres, pebbles, sand, natural pumice, and ceramics such as alumina, perlite, poly(dimethylsiloxane), and zeolites (Castañeda-Juárez et al. 2019). Photocatalysis is a process with a high rate of decomposition of contaminants and can be used at room temperature and pressure and natural or neutral pH without the need for modification and has been applied to remove different pharmaceutical drugs, including antidepressants (Lin et al. 2017), anti-inflammatories (Lin et al. 2017; Rizzo et al. 2009; Calza et al. 2006; Achilles et al. 2010; Castañeda-Juárez et al. 2019), antibiotics (Lin et al. 2017; Elmolla and Chaudhuri 2010; Pronin et al. 2014), and analgesics (Gotostos et al. 2014; Mocetezuma et al. 2012).

The photocatalysis process has been applied to remove different SARS-CoV-2 pharmaceuticals according to Table 3: lamivudine, ivermectin, dexamethasone,
| AOP            | Pharmaceutical drug | Conditions | Efficiency/toxicity | By-product | Advantages and disadvantages |
|----------------|---------------------|------------|---------------------|------------|------------------------------|
| Photocatalysis | Lamivudine (An et al. 2011) | TiO₂ = 1.0 g/L, pH = 6.7, lamivudine = 60 µM, high-pressure mercury lamp (GGZ-125, Shanghai Yaming Lighting, Emax = 365 nm, 0.38 mW/cm²) | 87.1% | m/z values: 246: monohydroxylated intermediates, 262: dihydroxylated derivatives, 136: photohole attack at N3, 112: photohole attack at N3, 129: oxidized by HO•, 69: opening of aromatic ring | Advantages: Catalyst must be recovered, Is effective to mineralize organic compounds, High oxidation capacity, Immobilizing the catalyst solve the recovery issues, The process is stable. Disadvantages: The bandgap of catalyst limits the use of solar irradiation, Modification of catalyst increase the cost, Poor capability for carrier charge separation |
|                | Ivermectin (Havlíková et al. 2016) | TiO₂ = 2 g/L, UV Camag lamp (366 nm), room temperature (25 °C), aerobic conditions using a bubbling air pump, 5 h, pH 5 | 92.5% | DII1 ivermectin monosaccharide C₂₅H₅₂O₁₁ (MW 730.4), m/z 741.3 and 633.3, DII2 ivermectin aglycone C₁₃H₂₀O₆ (MW 586.4), m/z 608.8 and m/z 373.9, DII3 yielded the protonated ion [M+Ti]+ (m/z 649.1) | |
|                | Dexamethasone (Pazoki et al. 2016) | Ag coated TiO₂ (1.5 g/L), 35 °C, pH = 3, dexamethasone = 5 mg/L, UV lamp 100 ≤ λ ≤ 280 nm, visible lamp 400 ≤ λ ≤ 700 nm | 77.6% UV light irradiation, 63.8% VIS light irradiation | Mineralization of two carbon atoms, formation of a ketone group continued by the concerted losses of the HF molecule and of the H₂O molecules | |
|                | Dexamethasone (Ghenaatgar et al. 2019) | Dexamethasone = 25 mg/L, catalyst dosage 500 mg/L, catalyst: WO₃ and ZrO₂, Lamps: UVC (254 nm), UVA (365 nm), halogen (more than 380 nm) | 180 min UV light, 81.16% UV/ZrO₂, 75.64% BLB/ZrO₂, 69.36% halogen/ZrO₂, 47% UV/VO, 100% BLB/WO₃ (120 min), 100% halogen/WO₃ (120 min) | 100% halogen/WO₃ (120 min) | |
|                | Azithromycin (Čizmić et al. 2019) | Nanostructured TiO₂ film deposited on a borosilicate glass substrate, UV-C lamp (254/185 nm) p, pH 10, 25 °C | k = 0.8 min⁻¹ (ultrapure water), k = 0.9 min⁻¹ (synthetic effluent) | The formed degradation products are not toxic (Vibrio fischeri) | |
|                | Dexamethasone (Ghenaatgar et al. 2019) | Dexamethasone (Ghenaatgar et al. 2019) | 180 min UV light, 81.16% UV/ZrO₂, 75.64% BLB/ZrO₂, 69.36% halogen/ZrO₂, 47% UV/VO, 100% BLB/WO₃ (120 min), 100% halogen/WO₃ (120 min) | 100% halogen/WO₃ (120 min) | |
|                | Azithromycin (Čizmić et al. 2019) | Nanostructured TiO₂ film deposited on a borosilicate glass substrate, UV-C lamp (254/185 nm) p, pH 10, 25 °C | k = 0.8 min⁻¹ (ultrapure water), k = 0.9 min⁻¹ (synthetic effluent) | The formed degradation products are not toxic (Vibrio fischeri) | |
| AOP                          | Pharmaceutical drug                      | Conditions                                                                 | Efficiency/toxicity                  | By-product | Advantages and disadvantages |
|------------------------------|------------------------------------------|----------------------------------------------------------------------------|-------------------------------------|------------|------------------------------|
| Azithromycin (Kumar et al. 2021) | Ag@BiO$_2$I$_2$/SPION/Calg hybrid material 90 min under direct visible light (Xe lamp 300 W) | Ag@BiO$_2$I$_2$/SPION/Calg: 98.4%; Bi$_4$O$_5$I$_2$: 51.5% | P1 (via O-demethylation) P2 ($m/z$ = 720) P4 ($m/z$ = 593) L-cladinose ring P5 ($m/z$ = 433) D-desosamine P8 ($m/z$ = 177) loss of desosamine ring | Cleavage of C-O bond further in P8 leads to ring opening of cladinose to form P9 ($m/z$ = 121) and P10 ($m/z$ = 85) |
| Azithromycin (Naraginti et al. 2019) | ZrO$_2$/Ag@TiO$_2$ nanocomposite Visible light (250 W xenon lamp adjusted to 100 mW/cm$^2$), 8 h 100 mg/50 mL (2 mg/mL) of catalyst | 92% (20 mg/L) 52% (10 mg/L) 44% (5 mg/L) 18% (2.5 mg/L) Based on the E. coli growth, the effluent increased to 90.93 of detoxification efficiency, Using Vigna radiata, the germination index increased to 81.05% in effluent | TP-A and TP-B m/z 734.8 corresponds to O-demethylation or N-demethylation TP-C m/z 704.8 TP-D m/z 692.4 TP-E m/z 720.9 (simultaneous O-demethylation and N-demethylation) TP-K m/z 156.2 (dehydrated product of D-desosamine) TP-L m/z 114.2 (loss of N-methylenemethanamine fragment) TP-M m/z 121.1 TP-N m/z 85.3 |
| Azithromycin (Sayadi et al. 2019) | GO@Fe$_3$O$_4$/ZnO/SnO$_2$ Batch system: pH = 3, 120 min, azithromycin: 30 mg/L and 1 g/L of catalyst, UV-C lamp Continuous system: bed height (6.8 and 10 cm), flow rate (6 mL/min) and 30 mg/L | 90.06% (batch) Column breakthrough point 5 min (6 cm) 8 min (8 cm) 14 min (10 cm) | | |
### Table 3 (continued)

| AOP                        | Pharmaceutical drug | Conditions                                                                 | Efficiency/toxicity                                                                 | By-product                                                                                           | Advantages and disadvantages                        |
|----------------------------|---------------------|----------------------------------------------------------------------------|----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|---------------------------------------------------|
| Ciprofloxacin (Alhokbany et al. 2020) | Chitosan based nanocomposite (g-\(\text{C}_3\text{N}_4/\text{Ag}_{2}\text{PO}_4/\text{CS}\)) 60 min, room temperature, neutral medium, 2 mg of catalyst, ciprofloxacin = 20 mg/L | 90.43% 79.43% after six cycles                                                   | Decarboxylation of intermediate (I) produced intermediate (II) m/z 306.1 Then, intermediate (III) m/z 262.1 are produced. The cyclopropyl group form the quinolone ring produced intermediate (IV) with m/z 222.1, which was converted in to intermediate (V) with m/z 243.1 which are converted after decarboxylation and ring closing in to five member ring intermediate (VI), this produce the intermediate (VII) which are destroyed and produced the intermediate (V) |                                                   |
| Acyclovir (An et al. 2015)  | 25 °C, \(pH = 6.37\), 2.0 mW/cm² light intensity light source, Acyclovir = 50 \(\mu\)M, 0.5 g/L \(\text{TiO}_2\) | Degradation 100% Mineralization 80% More toxic products were produced during the photocatalytic degradation of acyclovir | Acyclovir m/z 226 m/z = 242 (monohydroxylated acyclovir) m/z = 258 (dihydroxylated acyclovir) m/z = 186 m/z = 204 m/z = 158 m/z = 152 (guanine) |                                                   |
| Tinidazole (Acosta-Rangel et al. 2018) | Iron-doped silica xerogels (1 g/L), Tinidazole = 25 mg/L, \(pH 7\), 25 °C, 1 h, solar irradiation | 98.38% HEK-293 cell viability was > 75%, indicating that neither tinidazole nor its byproducts have toxic effects on this type of cell | P1 178 g/mol P2 140 g/mol P3 137 g/mol P4 236.28 g/mol |                                                   |
| Sertraline (Rejek and Grzeguliska-Damszel 2018) | \(\text{TiO}_2\) (1.15 g/L), sertraline = 0.1 g/L, mercury lamp | 91%                                                                   |                                                   |                                                   |
| Hydroxychloroquine (Da Silva et al. 2021) | Hydroxychloroquine = 10 mM; catalyst dose: 2 g/L, \(pH = 7.5\); UV-A radiation (0.061 W/m²) | 96% Lactuca sativa and Artemia salina confirmed the reduction of effluent toxicity after treatment |                                                   |                                                   |
| AOP          | Pharmaceutical drug    | Conditions                                                                 | Efficiency/toxicity | By-product                                                                 | Advantages and disadvantages                                                                 |
|-------------|------------------------|-----------------------------------------------------------------------------|---------------------|----------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| Fenton      | Citralopram (Hörsing et al. 2012) | Molar ratio Fe²⁺/H₂O₂ 1/10, the concentrations of Fe²⁺ varied from 0.0003 to 12.5 mM, pH 3, initial concentration 100 µg/L | 90%                 | Citralopram is demethylated into Di-desmethylcitalopram. The second breakdown pathway also mimics the human metabolism and gives rise to formation of citalopram-N-oxide | Advantages: Highly oxidative capacity Disadvantages: Narrow working pH range, High costs Risks associated with handling, transportation and storage of reagents (H₂O₂ and homogeneous solution of iron ions) Significant iron sludge related second pollution |
| Electro-Fenton | Sertraline (Rachidi et al. 2021) | Sertraline = 0.01 mM, 4 h, carbon-carbon-lorraine felt as cathode and Pt foil as anode, 0.05 M of Na₂SO₄, 0.1 mM Fe²⁺, pH 3, 400 mA | 99% COD BOD₅/COD ratio increased from 0.47 to 3 | Electro-Fenton BDD 92% TOC Electro-Fenton Pt 84% TOC Electrolysis BDD 68% TOC Electrolysis Pt 17% TOC | Advantages: The on-site production of H₂O₂ avoid the risks related to its transport, storage, and handling The continuous regeneration of Fe²⁺ on the cathode minimize the iron sludge production and improve the degradation efficiency Disadvantages: Low H₂O₂ yield Low unit cell body throughput Low current density and low conductivity EF-Feox: High consumption of anode and large amount of iron sludge production |
| Chloroquine (Midassi et al. 2020) | Current density up to 60 mA/cm², O₂ flow rate up to 80 mL/min, pH 3.0 Electro-Fenton BDD or Pt systems | Electro-Fenton BDD 76% TOC Electro-Fenton Pt 73% TOC Electrolysis BDD 68% TOC Electrolysis Pt 17% TOC | 7-chloro-4-quinolinamine Oxalic acid | |
### Table 3 (continued)

| AOP                  | Pharmaceutical drug                  | Conditions                                                                 | Efficiency/toxicity                                                                 | By-product                                      | Advantages and disadvantages                                                                 |
|----------------------|--------------------------------------|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------|------------------------------------------------|---------------------------------------------------------------------------------------------|
| Photo electro-Fenton | Fluoxetine (Manrique et al. 2019)    | 700 kJ/L m², IrO₂/RuO₂ as anode, 20-30A, 0.05 mol/L Na₂SO₄, 18 μM de Fe³⁺, fluoxetine = 40 mg/L, neutral pH | 70% 11% mineralization Degradation by-products do not increase or sustain toxicity |                                                 | Advantages: Higher degradation and mineralization rate Great UV input pH intervals between 2 and 4 Photolysis of by-products enhancing the mineralization processes Disadvantages: High cost related to electrodes and UV lamps Low energy consumption |
| Fenton-like          | Fluconazole (Zhang et al. 2020a, b)  | Cu-V bimetallic Catalyst, pH 6                                            | 15% H₂O₂ 82% CuOx/H₂O₂ 100% CuVOx/H₂O₂                                         |                                                 | Advantages: The metal-catalyst work over a broader pH The surface chemistry influences the H₂O₂ dissociation and HO● production The introduction of other transition metals improves the surface characteristics Metal ion doping improve the adsorption and catalytic performance Disadvantages Relative high cost (compared to conventional Fenton) Presence of transition metals on the effluent |
| Fluconazole (Zhang et al. 2020a, b) | Cu-Ce bimetallic catalysts, (0.1 g/L), fluconazole = 20 mg/L, H₂O₂ = 50 mM, pH = 5.0, at room temperature |                                                 | 94%                                                                              |                                                 |                                                                                             |
| Fenton-like combined with coagulation | Azithromycin (Yazdanbakhsh et al. 2014) | Coagulation process Poly aluminum chloride (PAX-18), 100 mg/L and pH 7.0 Fenton-like process: Fe⁰ = 0.36 mM/L H₂O₂ = 0.38 mM/L pH = 7.0 | Coagulation 82.14% COD Combined treatment: 96.89% COD |                                                 | Advantages: Combined processes enhance the COD removal                                         |
| AOP               | Pharmaceutical drug                        | Conditions                                                                 | Efficiency/toxicity | By-product | Advantages and disadvantages                                                                                                                                 |
|------------------|--------------------------------------------|----------------------------------------------------------------------------|---------------------|------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| Photo-Fenton     | Lamivudine (Lucena et al. 2020)            | Three UV-C lamps, 60 min, pH 5–6<br>Lamivudine: 30 mg/L<br>Fe = 120 mg/L<br>H₂O₂ = 600 mg/L (fractional addition at 0, 10 and 20 min) | 62.34%              |            | Advantages<br>Accelerate the reduction of Fe³⁺ to Fe²⁺<br>Reduce the iron sludge production and the initial Fe²⁺ concentration<br>Enhance the oxidation ability<br>Enhance the degradation efficiency of organic pollutants<br>Higher degradation rate<br>Decrease sludge volume generation<br>Disadvantages<br>Low utilization rate of light energy<br>High operation costs<br>Design of photoreactor<br>Short operating lifecycle of artificial UV sources<br>High energy consumption<br>Variability and limited availability of solar radiation<br>Wasting of oxidants (due to the radical-scavenging effect of H₂O₂ and its self decomposition)<br>Formation of solid sludge<br>Production of high amounts of anions in the effluent  |
|                  | Amoxicilin (Elmolla and Chaudhuri 2010)    | Amoxicilin = 104 mg/L, pH 3, UV-A (365 nm) = 6 W, H₂O₂/Fe²⁺ = 20, 50 min     | 100%                |            | 58.4% mineralization                                                                                                                                       |
|                  | Tinidazole (Velo-Gala et al. 2017)         | 120 min                                                                   | 45.20% (photolysis UVC) |            | 49.80% (photolysis solar) 100% H₂O₂/UVC 59.59% H₂O₂/solar 100% (photo-Fenton UVC) 100% (solar photo-Fenton) |
|                  | Fluoxetine (Manrique Losada, Quimbaya Nañez, and Torres Palma 2019) | 90 μM de Fe²⁺, 1000 μM de H₂O₂, 835 kJ/Lm² (acidic pH) 1.269 kJ/Lm² (neutral pH) | 80% acid pH 73% neutral pH 44% mineralization | Degradation by-products do not increase or sustain toxicity |
| AOP                         | Pharmaceutical drug                  | Conditions                                                                 | Efficiency/toxicity                                                                 | By-product | Advantages and disadvantages                                                                 |
|-----------------------------|--------------------------------------|-----------------------------------------------------------------------------|-------------------------------------------------------------------------------------|------------|-----------------------------------------------------------------------------------------------|
| Heterogeneous photo-Fenton  | Chloroquine phosphate (Wang et al. 2022) | pH 5, 2D micron-sized MOF (metal organic frameworks) sheet (BUC-21(Fe)),   | 21% under UV light 43.9% H₂O₂ + UV light 48.9% BUC-21(Fe) + H₂O₂ 100% BUC-21(Fe) + H₂O₂ + UV light (365 nm)  | B m/z = 322 C m/z = 340 D m/z = 114 E m/z = 159 | Advantages: Low iron ions leaching Efficient cycling of Fe³⁺ and Fe²⁺ Low iron sludge production Wide working pH range Reusability and long-term stability of catalysts Disadvantages Complicated synthesis routes High synthesis costs of catalysts Design of heterogeneous Fenton reactor |
| Sono-Fenton                 | Dexamethasone (Hasan Rahmani et al. 2015) | pH: 4, nano Fe⁰: 0.3 g/L, H₂O₂: 1.5 mmol, initial concentration: 15 mg/L and US: 140 kHz | 92%                                                                                   |             | Advantages: Enhances the HO● production Another reactive radical are produced Low Fe requirement |
| EO                          | Hydroxychloroquine (Ben-salah et al. 2020) | Electrochemical oxidation using BDD and its combination with UV irradiation and sonication 20 mA/cm², pH 7.1, 25 °C, | EO = 100% (300 min) PEO = 100% (180 min) SEO = 100% (60 min)  | EO: 7-chloro-4-quinolinamine (CQLA) Oxalic acid Oxamic acid Chloride, nitrate, and ammonium | Advantages: Avoid the sludge generation and the need for sludge final disposal methods and the involved environmental impact Good quality of the treated wastewater Sustainability (use of only electrons as reagents) no another chemical, high degradation and mineralization efficiency ease of automation for small-scale Disadvantages: High cost Potentiality to be scaled up for large applications The degradation efficiency is affected by the low rate of diffusion |
| AOP    | Pharmaceutical drug | Conditions                                                                 | Efficiency/toxicity                                                                 | By-product                                                                 | Advantages and disadvantages                                                                 |
|--------|---------------------|-----------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| EO     | Dexamethasone (Grilla et al. 2021) | BDD as anode and a stainless steel or carbon cloth cathode For simulated solar light experiments, a solar simulator equipped with a 100 W xenon, O2-free lamp was employed | 90% (45 min at 0.2 A/m², 5 mg/L) 92%± 2% (0.25–1 mg/L, 0.2 A/m²) 95% (electrochemical oxidation, persulfate addition and simulated solar light irradiation) | Dexamethasone C22H30O5F TP1 C22H30O6F TP2 C21H28O7F TP3 C21H28O6F TP4 C21H28O7F TP5 C20H28O6F TP6 C20H28O7F TP7 C16 H18O2F | **Advantages:** The process takes place at room temperature, without sludge generation, easy handling, high stability, and present high removal rates of chemical oxygen demand chemical-free treatment that requires relatively low maintenance and operational costs **Disadvantages:** The mineralization rate is affected if the H2O2 dosage in the solution is low |
| EO     | Abacavir (Zhou et al. 2019) | Penetration flux porous Ti/SnO2–Sb anode, 10 min at a j = 0.2 mA/cm²         | 97% 53.3% TOC (5 h, 5 mA/cm²) Abacavir showed chronic toxicity to fish, TP150 show the lowest toxicity | TP318 produced by the oxidation of the cyclopropylamine moiety TP246 formed from the cleavage of the cyclopropyl ring TP150 generated via the further degradation of the TP318 and TP246 |                                                                                             |
| EO     | Lamivudine (Y. Wang et al. 2019a, b) | Ti/SnO2–Sb/Ce–PbO2 anode, 20 mM Na2SO4, j ≥ 10 mA/cm² | 97.7% 14 mA/cm² 95.7% pH 5 98.3% 2.5 mg/L | Lamivudine (P229) Intermediates: P245, P111, S119, P135 |                                                                                             |
| UV/H2O2| Lamivudine (Lucena et al. 2020) | Three UV-C lamps (30 W and photons emissions of 1.98 × 10⁻³ W·cm⁻²) 180 min, pH 5–6 H₂O₂ = 600 mg/L [Lamivudine] = 5 mg/L | 97.33% The compounds formed after the treatment present toxicity to *Lactuca sativa* |                                                                                             | Advantages: The process takes place at room temperature, without sludge generation, easy handling, high stability, and present high removal rates of chemical oxygen demand chemical-free treatment that requires relatively low maintenance and operational costs **Disadvantages:** The mineralization rate is affected if the H2O2 dosage in the solution is low |
| AOP | Pharmaceutical drug | Conditions | Efficiency/toxicity | By-product | Advantages and disadvantages |
|-----|---------------------|------------|---------------------|------------|----------------------------|
|     | Ciprofloxacin (Guo et al. 2013) | pH 7, H₂O₂= 5 mM, 17-W low-pressure mercury lamp emitting at 254 nm, 25 °C, ciprofloxacin =10 mg/L | K=3.72 ± 0.24 x 10^{-2}/s | 17 by-products keto-derivative are transformed to produce two products through hydroxyl group addition or amidation. Desethylene ciprofloxacin reveals further oxidation at the piperazinyl ring Compound 7 loss of the cyclopropyl group (2C and 2H atoms) followed by introducing a hydroxyl group and CH₂ or losing a carboxyl group | Toxin of products assessed by Vibrio qinghaiensis demonstrated that UV/H₂O₂ process was more capable on controlling the toxicity of intermediates in CIP degradation than UV process. |    |
|     | Acyclovir (Russo et al. 2017) | UV₂₅₄ nm (4.7 mW/cm²), [H₂O₂]₀/[acyclovir]₀ = 20, pH = 6 | k = 2.30 ± 0.11 x 10⁹ l/M s | Formation of hydroxylated imidazole-based compounds or species formed by the fragmentation of the pyrimidine ring | The inhibition of Vibrio fischeri luminescence remained unchanged in the presence of UV₂₅₄/H₂O₂ irradiated solutions, in comparison to the untreated solution. |    |
| UV/H₂O₂ and moving-bed biofilm reactor | Azithromycin (Cano et al. 2020) | pH 9, 482 mg/L H₂O₂, 500 W/m² irradiance | 80.0% | Advantages: MBBR have the ability to accumulate biomass and biofilm allow a large number of microorganisms. |    |
| UV/chlorine | Azithromycin (Shokri et al. 2019) | Azithromycin = 2 mg/L, 254 nm: 12 h | 91.2% |    | Advantages: UV photolysis of HClO and ClO− generate HO● and Cl● degrade contaminants. Disadvantages: Possible harmful by-products. |    |
|     | Fluconazole (Cai et al. 2020) | λ=254 nm, pH 7, initial concentration of free available chlorine 100 μM, 25 ± 1 °C | 16.5% chlorine TP 305 | TP 301 |    |
|     |                           | 62.1% UV photolysis TP 287 | TP 285 | TP 287 |    |
|     |                           | 90.6% chlorine +UV TP 303 | TP 83 | TP 83 |    |
|     |                           | Most of transformation products had lower toxicity than fluconazole TP 151 | TP 151 | TP 151 |    |
| AOP                  | Pharmaceutical drug                  | Conditions                                                                 | Efficiency/toxicity | By-product | Advantages and disadvantages                                                                                                                                 |
|---------------------|--------------------------------------|-----------------------------------------------------------------------------|---------------------|------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Ultrasound          | Azithromycin (Muñoz-Calderón et al. 2020) | Ultrasound (40 kHz), 50 W, pH 9, 60 min, azithromycin = 1.0 mg/L            | 46.15%              |            | Safety, cleanliness, energy conservation, and no or minimal secondary pollution products not using chemicals to generate highly oxidizing species and not generating harmful products |
|                     | Azithromycin (Yazdani and Sayadi 2018) | ZnO nanoparticles, pH 3, 40 °C, 15 min, 1 g/L of catalyst, 50 mg/L of H₂O₂, azithromycin = 20 mg/L, 35 kHz | 98.4%               |            |                                                                                                                                                              |
|                     | Sulfamethoxazole (Al-Hamadani et al. 2016) | Glass beads and single-walled carbon nanotubes (45 mg/L) as catalyst      |                     |            |                                                                                                                                                              |
|                     | Tinidazole (Rahmani et al. 2014)      | pH 3, 120 kHz frequency, 333 mM/L of H₂O₂ and 150 min of operating time   |                     |            |                                                                                                                                                              |
| Ultrasound combined with biological treatment | Fluoxetine (Serna-Galvis et al. 2015) | 600 kHz, 20 °C                                                           |                     |            | Advantages                                                                                                                                                   |
| AOP            | Pharmaceutical drug         | Conditions                                                                 | Efficiency/toxicity       | By-product                                                                 | Advantages and disadvantages                      |
|----------------|-----------------------------|----------------------------------------------------------------------------|---------------------------|----------------------------------------------------------------------------|-----------------------------------------------------|
| O₃/Fenton      | Amoxicilin (Li et al. 2015) | Amoxicilin = 100 mg/L, Fe²⁺ = 0.6 mM, 800 rpm, T = 25 °C, pH = 3, Oxygen flow = 150 L/h, 120 min | 100% degradation          | S1 C₉H₇N₃O₇S                                                             | Synergetic effect accelerate                       |
|                |                             |                                                                           | 65% mineralization         | S2 C₉H₈N₃O₈S                                                             | Fenton reagents to enhance                          |
|                |                             |                                                                           |                           | S3 C₇H₅N₂O₆                                                             | HO• generation which leads to higher oxidation rates |
|                |                             |                                                                           |                           | S4 C₇H₆N₂O₄S                                                             |                                                     |
|                |                             |                                                                           |                           | S5 C₉H₇N₂O₆                                                             |                                                     |
|                |                             |                                                                           |                           | S6 C₇H₅N₂O₆                                                             |                                                     |
|                |                             |                                                                           |                           | S7 C₇H₆O₉                                                                |                                                     |
|                |                             |                                                                           |                           | S8 C₇H₆NS                                                                |                                                     |
|                |                             |                                                                           |                           | S9 C₇H₆NS                                                                |                                                     |
|                |                             |                                                                           |                           | S10 C₇H₅N₂O₆                                                            |                                                     |
|                |                             |                                                                           |                           | S11 C₇H₅N₂O₆                                                            |                                                     |
|                |                             |                                                                           |                           | S12 C₇H₅N₂O₄                                                            |                                                     |
|                |                             |                                                                           |                           | S13 C₇H₅N₂O₄                                                            |                                                     |
|                |                             |                                                                           |                           | S14 C₇H₅N₂O₄                                                            |                                                     |
| Ozonation      | Acyclovir (Prasse et al. 2012) | O₃ generator 300, Fischer Technology, Germany | Using Vibrio fischeri, carboxyacyclovir revealed no toxic effects | m/z 274                                                                   | The volume of effluent remains constant along the process and sludge is not formed |
|                |                             |                                                                           |                           | m/z 198                                                                   | Installations require only a little space, O₃ is generated in situ, so that no stock chemical solutions are needed |
|                |                             |                                                                           |                           | m/z 170                                                                   | Can be applied even if the effluent fluctuates both in terms of flow rate and/or composition |
|                |                             |                                                                           |                           | m/z 153                                                                   | O₃ remnants can be eliminated as ozone tends to decompose into oxygen |
|                |                             |                                                                           |                           |                                                                           | Disadvantages:                                      |
|                |                             |                                                                           |                           |                                                                           | is unstable and can quickly decompose into molecular oxygen |
|                |                             |                                                                           |                           |                                                                           | alone does not cause complete oxidation of some refractory organic compounds, low reaction rate |
| Oseltamivir acid (Mestankova et al. 2012) | [Oseltamivir] = 25 mM (buffered to pH 7) and 10 mM t-butanol (HO• scavenger) | K = 1.7 105 M⁻¹ s⁻¹      |                                                                           | High cost of equipment and maintenance              |
|                |                             |                                                                           |                           |                                                                           | High requirements of energy                         |
| AOP                  | Pharmaceutical drug                        | Conditions                        | Efficiency/toxicity | By-product | Advantages and disadvantages                                                                 |
|---------------------|--------------------------------------------|-----------------------------------|---------------------|------------|----------------------------------------------------------------------------------------------|
| O$_3$/H$_2$O$_2$    | Sulfamethoxazole (Gomes et al. 2018)       | $O_3 = 0.42$ mM, $H_2O_2 = 5$ mM | ~100%               | by-products formed have a higher acute toxicity than the Sulfamethoxazole                      |
|                     |                                            | 45 min                            |                     |            |                                                                                              |
|                     |                                            |                                   |                     |            |                                                                                              |
| Photocatalytic ozonation O$_3$/UVA/TiO$_2$ | Ciprofloxacin (Asgari et al. 2021)       | $O_3 = 0.34$ g/h and catalyst doses of 1.0 g/L during 15 min reaction time at pH 9.0, $\lambda = 365$ nm | 98.5% (15 min, first cycle) 81.1% of TOC (60 min) 93.4% (in the sixth cycle)                   | By-products not inhibit the growth of S. aureus and E. coli | Advantages: Free electrons of the semiconductor can interact with ozone molecules forming ozonide radicals |
| Photocatalytic ozonation | Amoxicilin (Moreira et al. 2015)           | Amoxicilin = 0.1 mM, TiO$_2$ (0.5 g/L), natural pH, $O_3$ Flow 150 Ncm$^{-3}$/min, UV-Vis $>300$ nm | 100% TOC in 30 min | By-products not inhibit the growth of S. aureus and E. coli | Advantages: Catalytic ozonation process Dexamethasone (G. Asgari et al. 2020) | Catalyst promote the ozonation of organics by oxidation-reduction reaction |
| Catalytic ozonation process | Dexamethasone (G. Asgari et al. 2020)     | $Al_2O_3$ nanoparticles (0.5 g/L, pH 10, dexamethasone = 10 mg/L, 12 min) | 100%               |            | Advantages: Catalytic ozonation process Dexamethasone (G. Asgari et al. 2020) | Catalyst promote the ozonation of organics by oxidation-reduction reaction |
| Biological treatment coupled with ozonation | Sulfamethoxazole (Knopp et al. 2016)       | $0.87 \pm 0.29$ g $O_3$ at hydraulic retention time: 17 $\pm$ 3 min | 98%                |            | Advantages: Biological treatment coupled with ozonation | Sludge reduction and removal of recalcitrant organic contaminants from wastewater | Oxidation avoiding the harmful by-products |
| Biological treatment, sand filtration and ozonation | Carbamazepine Azithromycin Sulfamethoxazole (Nakada et al. 2007) | Activated sludge 9 h of retention time $O_3 = 3$ mg/L during 27 min | Carbamazepine 43.3% via activated sludge, 22.4% via sand filtration 8.25% via ozonation, azithromycin 92.6% via ozonation, sul- famethoxazole 61.5% via activated sludge, 26.9% via sand filtration 92.6% via ozonation |            | Advantages: Biological treatment, sand filtration and ozonation | Carbamazepine 43.3% via activated sludge, 22.4% via sand filtration 8.25% via ozonation, azithromycin 92.6% via ozonation, sul- famethoxazole 61.5% via activated sludge, 26.9% via sand filtration 92.6% via ozonation |
| O$_3$/PMS           | Rivabirin (Liu et al. 2021a, b)            | 10 $\mu$M ribavirin solution under ambient temperature (25 °C), and the pH of solution was buffered with 5 mM phosphate | 5% PMS $K = 3.84 \times 10^{-2}$ $O_3$ $K = 4.32 \times 10^{-1}$ O$_3$/PMS | Rivabirin m/z 245 | Advantages: O$_3$/PMS | The system simultaneously produce HO$^*$ and SO$_4^{2-}$ | PMS enhance ozonation | Disadvantages: Toxic by-products |
| AOP                                | Pharmaceutical drug                        | Conditions                                                                 | Efficiency/toxicity                                                                 | By-product  | Advantages and disadvantages                                                                 |
|-----------------------------------|--------------------------------------------|---------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-------------|------------------------------------------------------------------------------------------------|
| Photocatalysis-activated sulfate radical | Chloroquine phosphate (Yi et al. 2021)     | Catalyst: 34,910-pyrenetetracarboxydiimine (PDINH)/ MIL-88A composite     | Chloroquine (A) m/z = 320                                                          |             | Advantages: The active species are HO•, SO4•−, •O2•− and h+. High degradation rate of organic pollutants. |
|                                  |                                            | 30 min, irradiation of 300 ± 50 mW LED visible light, PDS, Chloroquine = 10 mg/L | 94.6% Toxicity Estimation Software (T.E.S.T.)                                       |             | By-products: B m/z = 292 C m/z = 264 D m/z = 247 E m/z = 159 F m/z = 179 G m/z = 164 H m/z = 142 I m/z = 114 J m/z = 158 K m/z = 102 L m/z = 159 M m/z = 118 |
|                                  |                                            |                                                                           | The LD50 was 3.07 mg/L for chloroquine, by-products D and C showed lower LC50 value, even the product D was “very toxic” By-products B, C, E, J, K, L, M and Q were even considered as “developmental non-toxicant” |             | Disadvantages: High activity and selectivity for removing organic pollutants Higher pH favors the non-radical activation |
|                                  |                                            |                                                                           | Advantages: The active species are HO•, SO4•−, •O2•− and h+. High degradation rate of organic pollutants. |
| Dexamethasone (Shookohi et al. 2019) | Persulfate dose = 0.1 mM, Dexamethasone = 20 mg/L and Al2O3 dose = 0.05 g/L | 88% pH 3 52% pH 11 94% (0.5 mM persulfate) 66% (without Al2O3) |                                                                                     |             |                                                                                               |
| Ciprofloxacin (Zhang et al. 2021) | CuO-LDH composite (0.25 g/L) 30 min, pH 4–10, Ciprofloxacin = 10 mg/L, oxidant = 1 mM | 14.4% (LDH) 94.4% (Cu4-LDH) |                                                                                     | P1 m/z = 334 P2 m/z = 306 P3 m/z = 300 P4 m/z = 263 P5 m/z = 205 |
| Ciprofloxacin (Zou et al. 2019) | Magnetic nitrogen-doped microalgae-derived carbon (Fe–N@MC) (0.2 g/L), ciprofloxacin = 10 mg/L, oxidant = 1 mM PMS, 120 min | 92.6% |                                                                                     | Ciprofloxacin m/z = 330 Pathway 1: m/z = 362, m/z = 334, m/z = 316, m/z = 306, m/z = 291, m/z = 263, m/z = 245 Pathway 2: m/z = 330, m/z = 286 Pathway 3: m/z = 348, m/z = 362, m/z = 334 |
| Ciprofloxacin (Shah et al. 2019) | Ciprofloxacin = 10 mg/L, Mn0 = 1.0 g/L, and S2O82− = 50 mg/L, 80 min | 95% |                                                                                     | NH4+, F−, NO2−, NO3−, and CH3COO− |
|                                  |                                            | The ecotoxicity were estimated from the acute and chronic toxicities towards aquatic organisms, the final product to be nontoxic |                                                                                     |             |                                                                                               |
azithromycin, ciprofloxacin, acyclovir, tinidazole, sertraline, and hydroxychloroquine. Photocatalysis is the main AOP used to treat SARS-CoV-2 pharmaceuticals according to Fig. 3 where the Pareto line is shown, the pharmaceuticals drugs below this line are those with few studies in this AOP and on which new research should focus, and the removal efficiency in all cases is higher than 84%. In the photocatalysis process, pH influences the surface charge of catalysts through the point of zero charge (Pzc), which is positive at \( \text{pH} < \text{Pzc} \), negative at \( \text{pH} > \text{Pzc} \), and neutral at \( \text{pH} = \text{Pzc} \). pH also affects the structure and properties of pharmaceuticals due to the pKa value, which indicates the chemical form of the molecule. At the working pH, the catalyst should be charged negatively, and the pharmaceutical drugs should be in ionic form (positively charged) to improve the electrostatic attraction. Moreover, as the pH increases, the oxidation potential of HO• decreases; as a consequence, more HO• is generated at low pH (Castañeda-Juárez et al. 2019).

Table 2 shows the pKa value of the pharmaceutical drugs to provide guidance on the selection of the working pH. We also highlight the importance of determining the point of zero charge of the materials.

The catalyst activation depends on the material; for example, for ZrO\(_3\) and WO\(_3\) used to remove dexamethasone, the highest activation occurred by halogen lamps (more than 380 nm) (Gehenaatgar et al. 2019). Finally, \( \text{TiO}_2 \) is extensively used due to its availability, low cost, and high efficiency, and the use of doped/supported materials increases the cost for the preparation and characterization. Initial concentration, catalyst dose, pKa value, Pzc, catalyst, and illumination intensity are the most important factors, and the main radiation source used is lamps. The objective of this technology is to use solar radiation to decrease costs; however, their use is actually limited.

Fenton reaction

The Fenton process was discovered in 1894 by Henry John H. Fenton and is the reaction between ferrous ions and hydrogen peroxide to generate HO• under acidic conditions (Eq. 4) (Wang et al. 2021), which is a non-expensive and environmentally friendly oxidation method. The Fenton process follows complex mechanisms and includes more than 20 chemical reactions (Santos et al. 2011) that must be considered to understand the whole process.

\[
\text{Fe}^{2+} + \text{H}_2\text{O}_2 + \text{H}^+ \rightarrow \text{Fe}^{3+} + \text{H}_2\text{O} + \text{HO}^* \tag{4}
\]

The Fenton reaction efficiency depends on operation parameters such as pH, concentration of Fenton reagent, and initial organic pollutant concentration; pH is the main parameter, and the optimum is 2.0 to 3.5 (Zhang et al. 2019). The process involves the oxidation of \( \text{Fe}^{2+} \) to \( \text{Fe}^{3+} \), which
begins to precipitate above pH 3 in the form of oxyhydroxide (Aramyan 2017), and less HO• is generated. The oxidation potential for the redox couple \( \text{HO•}/\text{H}_2\text{O} \) is 2.59 V vs. NHE at pH 0 and 1.64 V vs. NHE at pH 14; in addition, the autodecomposition of \( \text{H}_2\text{O}_2 \) is accelerated at high pH. On the other hand, at pH values below 3, the iron complex \([\text{Fe(H}_2\text{O})_6]^{2+}\) forms and reacts more slowly, and \( \text{H}_2\text{O}_2 \) is solvated to form the stable hydroxidanium ion \([\text{H}_3\text{O}_2]^+\), which reduces its reactivity (Babuponnusami and Muthukumar 2014). Thus, pH control could be maintained using buffer solution; in this case, acetic acid/acetate buffer gives maximum oxidation efficiency compared with phosphate and sulfate buffers (Benitez et al. 2001) due to the formation of stable \( \text{Fe}^{3+} \) complexes. However, storage of buffers will increase the operating costs.
The Fenton reaction has been applied to remove citalopram. The optimum molar ratio Fe²⁺/H₂O₂ was 1/10 (14 mg/L Fe²⁺), and the efficiency was 90%. This AOP enhances the removal efficiency compared to ozonation and photolysis (Hörsing et al. 2012). Usually, the rate of degradation increases with an increase in the concentration of ferrous ions but can influence the content of total dissolved solids in the effluent (Babuponnusami and Muthukumar 2014). In the case of H₂O₂, currently, the literature indicates that the removal percentage increases with an increase in the dosage; in contrast, based on our experiences, H₂O₂ contributes to COD, and scavenging of HO• is generated through Eq. 5. For this reason, the dosage should be adjusted to ensure its complete consumption. Traditionally, the Fenton reaction is used since iron is nontoxic and H₂O₂ is relatively safe to use and is considered environmentally benign; however, some reports confirm that H₂O₂ is harmful to some organisms. The Fenton reaction reduces toxicity, COD, and BOD₅ and eliminates odor and color (Cuerda-Correa, Alexandre-Franco, and Fernández-González 2020).

\[ \text{HO}^* + \text{H}_2\text{O}_2 \rightarrow \text{HO}_2^- + \text{H}_2\text{O} \]  

The Fenton reaction is more effective at low initial concentrations of pollutants. In the case of SARS-CoV-2 pharmaceutical drugs, there is an advantage because according to Table 3, the initial concentration is in the range of µg/L to mg/L, similar to that found in wastewater.

Several modifications to the Fenton reagent have been made to overcome these limitations, such as integration with external energy, the addition of electricity or ultrasound, and the development of heterogeneous processes to improve the efficiency (Nasir et al. 2021).

**Heterogeneous Fenton process (HF)**

According to the literature, in the HF process, iron salts are replaced by solid catalysts containing Fe, and the reactions take place at the active site on the catalyst surface, avoiding iron leaching. The authors should develop long-term stable catalysts for use during various cycles that are easily separated without extra processes. The catalyst materials include supported catalysts that immobilize iron species on the surface of materials and nonsupported catalysts (natural iron-containing minerals). The structure and composition of the catalyst improve the electron transfer accelerating the reduction of Fe³⁺ to Fe²⁺ (Zhang et al. 2019). The main advantages include a lower and controllable rate of sludge production, reduced Fe release, a surface contribution to reactive radical generation, and a wider pH range (Moradi et al. 2020), as shown in Table 3.
Photo-Fenton (PF)

The essence of the photo-Fenton (PF) process is to accelerate the reduction of Fe$^{3+}$ to Fe$^{2+}$ by using the energy provided by light (290–400 nm) (Albornoz et al. 2021) (Eq. 6), the combination of UV or visible light with a conventional Fenton reaction can enhance the catalytic capacity of the catalyst and promote the direct photolysis of H$_2$O$_2$ to HO$^*$ (Eq. 7) (Ribeiro and Nunes 2021) to increase the degradation efficiency and reduce the iron sludge production. Moreover, the generation of ferrous ions from iron complexes in the presence of UV light also enhances the efficiency of the PF process (Eq. 8) compared to the conventional Fenton process (Nidheesh 2015; Aramyan 2017) improving the working pH. To overcome the disadvantages of using external lamps, the alternative use of solar energy as an economic and renewable energy source has gained attention in the photo-Fenton process. The yield for Fe(II) is wavelength dependent, and some chelating agents (L), such as EDTA, NTA, citrate, oxalate, and EDDS, can be added to improve complex formation (Clarizia et al. 2017).

$$\text{Fe}^{3+} + \text{hv} + \text{H}_2\text{O} \rightarrow \text{Fe}^{2+} + \text{HO}^* + \text{H}^+ \quad (6)$$

$$\text{H}_2\text{O}_2 + \text{hv} \rightarrow 2\text{HO}^* \quad (7)$$

$$\text{Fe}^{3+} + \text{hv} \rightarrow \left[\text{Fe}^{3+}L\right]^* \rightarrow \text{Fe}^{2+} + L^* \quad (8)$$

As shown in Table 3, PF was used to remove lamivudine, amoxicillin, tinidazole, and fluoxetine, and a removal efficiency of 100% was achieved by using a UV-A lamp and simulated solar irradiation (xenon lamp). In the last case, the authors indicated an increase in pharmaceutical degradation because Fe$^{3+}$ complexes can absorb radiation with wavelengths in the range of the solar spectrum, generating a greater concentration of HO$^*$. The photo-Fenton in heterogeneous mode was applied using a metal organic framework (MOF) microsized sheet (BUC-21(Fe)) synthesized by a hydrothermal method process and was used to treat chloroquine phosphate at pH 5. The major irradiation source was 365 nm (UV light), and the H$_2$O$_2$ consumption efficiency was 83.2% (Wang et al. 2022).

In conclusion, in the PF process, the authors must consider the H$_2$O$_2$ dosage, nature of radiation, temperature, Fe concentration, and working pH. Solar irradiation could be used as the irradiation source because it is ecologically clean and is not considered harmful; on the other hand, the main disadvantages have been identified, such as weather dependence and efficiency in the rainy season or on cloudy days, and in continuous systems, the solution can be heated during the treatment, favoring H$_2$O$_2$ decomposition. For this reason, the reactor design is important, and only 5% of solar irradiation is made up of UV radiation (Albornoz et al. 2021).

Electro-Fenton process (EF)

EF is classified into 4 categories depending on the Fenton reagent formation or addition: the cathode electro-Fenton process (EF-H$_2$O$_2$), sacrificial anode electro-Fenton process (EF-Fe$_{ox}$), Fe$^{2+}$ cycling electro-Fenton process (EF-Fere), and cathode and Fe$^{2+}$ cycling electro-Fenton process (EF-H$_2$O$_2$-Fere).

In EF-H$_2$O$_2$, Fe$^{2+}$ is externally added, while H$_2$O$_2$ is generated in situ via the electrochemical reduction of O$_2$ on the cathode (Ribeiro and Nunes 2021) (Eq. 9), and electrogeneration results in control of the oxidation. In EF-Fe$_{ox}$ (electrochemical peroxidation), H$_2$O$_2$ is externally added while Fe$^{2+}$ is electrogenerated using a sacrificial anode (Eq. 10) (Altin et al. 2017). In the EF-Fere process, H$_2$O$_2$ and Fe$^{2+}$ are both externally added, but Fe$^{3+}$ generated by the Fenton reaction is reduced to Fe$^{2+}$ on the cathode (Eq. 11) (Moreira et al. 2017). Finally, in the EF-H$_2$O$_2$-Fere process, H$_2$O$_2$ is generated in situ via cathodic reduction of O$_2$, Fe$^{2+}$ is produced in situ through the oxidation of the sacrificial anode, and Fe$^{3+}$ is regenerated on the cathode (Zhang et al. 2019; Ghanbari and Moradi 2015).

$$\text{O}_2 + 2\text{H}^+ + 2e^- \rightarrow \text{H}_2\text{O}_2 \quad (9)$$

$$\text{Fe} \rightarrow \text{Fe}^{2+} + 2e^- \quad (10)$$

$$\text{Fe}^{3+} + e^- \rightarrow \text{Fe}^{2+} \quad (11)$$

In the EF process, the cathode has a significant influence on the performance for the mineralization of pharmaceutical compounds. The gas diffusion electrode improves the performance of H$_2$O$_2$ electrogeneration due to the porous structure. Other electrodes include activated carbon fiber, carbon felt (Klidi et al. 2019), graphite, carbon nanotubes, graphite felt, BDD, and platinum, all of which can reduce the O$_2$ and Fe$^{3+}$ ions in the cathode.

According to Mousset et al. (2021), EF is the most cost-effective (108–125 €/m$^3$) technology compared to ozonation, photolysis, Fenton, PF, and photoelectro-Fenton considering sludge management, chemical use, and electricity consumption (Mousset et al. 2021). EF is used in small- and large-scale applications (Midassi et al. 2020). In SARS-CoV-2 drugs, only sertraline and chloroquine have been removed by EF using carbon felt and BDD as cathodes. The EF type used was EF-H$_2$O$_2$ (chloroquine). The advantage of EF technology is the formation of another oxidant (due to the support electrolyte addition). In chloroquine oxidation, the addition of Na$_2$SO$_4$ leads to the electrogeneration of HO$^*$, SO$_4$$^-\bullet$,
and persulfates ($S_2O_8^{2−}$) at the surface BDD anode (Midassi et al. 2020).

The combination of electrochemical and photochemical processes with the Fenton process is called photoelectro-Fenton (PEF); this process allows faster regeneration of $Fe^{3+}$ by photolysis of $Fe^{3+}$ (Eq. 6) generates a greater quantity of free radicals due to the combination effect (Aramyan 2017) and has been used to treat fluoxetine. The anode was $IrO_2$/ $RuO_2$ with an air diffuser as the cathode and solar radiation as the irradiation source. This process was carried out in acidic (3.08) and natural pH conditions, and according to the results, the systems allowed $Fe^{3+}$ to $Fe^{2+}$ conversion, avoiding hydroxide formation and increasing the working pH (Manrique et al. 2019). The efficiency was similar to heterogeneous photocatalysis and higher than the EF process, but PEF increased mineralization. Table 3 shows the main advantages and disadvantages in the EF process.

**Sono-Fenton (SF)**

In sonolysis, $HO^•$ is produced through transient cavitation, which is a phenomenon comprising essentially three phases: nucleation, growth, and an implosive collapse of a gas or vapor bubble. The main factors influencing the efficacy are sonication frequency, acoustic intensity, temperature, and static pressure (Moradi et al. 2020). In the SF process, $HO^•$ is produced in water via acoustic cavitation due to the presence of ultrasound irradiation (US) (Nidheesh 2015; Aramyan 2017), and the complex intermediate formed, $[FeOOH]^{2+}$, decomposes rapidly to form $HO^•$ ($E^° = 1.65$ V) and $Fe^{2+}$ according to Eqs. 12 and 13 (Tugrul Albayrak and Tavman 2021). If the initial concentration of pharmaceuticals is small, the probability of interaction between $HO^•$ and molecules is also small and recombines through Eq. 14. Moreover, ultrasound and cavitation also generate intense micromixing in the medium through microturbulence, which increases the probability of interaction. $HO^•$ production depends on the $H_2O_2$ concentration and temperature and pressure reached in the medium (Chakma and Moholkar 2013). This system requires a low amount of iron salt compared to the Fenton system; moreover, the amount of iron ions present in the treated water is low, which is of great economic importance (Moradi et al. 2020).

$$Fe^{3+} + H_2O_2 \rightarrow [Fe − OOH]^{2+} + H^+ \quad (12)$$

$$[Fe − OOH]^{2+} + Fe^{2+} + HO^• \quad (13)$$

$$HO^• + HO^• \leftrightarrow H_2O_2 \quad (14)$$

The combined treatment using ultrasound and ultraviolet radiation along with Fenton reagents is known as sono-photo-Fenton (SPF), which enhances the production of $HO^•$ due to the sonolysis of water, $H_2O_2$ production by recombination of $HO^•$ in the presence of UV radiation and the highest generation of reactive radicals such as $H^•$ and $HOO^•$.

These systems (SF and SPF) can be realized in homogeneous or heterogeneous mode; in heterogeneous mode, ultrasound not only generates reactive radicals but also cleans the catalyst surface to prevent the accumulation of pollutants and their byproducts generated in the degradation process (Moradi et al. 2020). Hence, when the process is carried out, the oxidation rate and the mass transfer are increased. In recent years, only dexamethasone has been treated by SF in heterogeneous mode at pH 4 using nanoscale zero valent iron and 140 kHz as the US frequency, and according to the advantages, recalcitrant organic pollutants are an efficient and environmentally friendly technique.

The critical revision of the SF indicates that effective parameters are pH, $H_2O_2$ dose, initial concentration of pollutant, $Fe^{2+}/Fe^{3+}$ concentration, irradiation intensity, ultrasonic power, and temperature (Moradi et al. 2020). Using solar radiation reduces the costs associated with high energy consumption; however, it cannot be effectively applied in countries with low solar irradiation (Asgharzadeh et al. 2019).

**Fenton-like (FL)**

Due to high reagent consumption and the production of iron sludge in Fenton oxidation systems, many researchers use other transition metal ions, such as $Fe^{3+}$, $Mn^{2+}$, $Cu^{2+}$, $Co^{2+}$, and zero valent iron to replace $Fe^{2+}$ to catalyze $H_2O_2$ to produce $HO^•$. This kind of system is called a Fenton-like oxidation system and can be realized in homogeneous or heterogeneous form. The main drawback in the homogeneous type is the high concentration of ferrous ions in the treated water, which produces a large amount of sludge and a narrow pH range. In contrast, heterogeneous Fenton-like reactions possess a wider effective pH window, and the catalyst is easier to separate from the solution (Liu et al. 2021a, b). Some materials are applied in this process, such as carbon aerogels (Wang et al. 2021), metal–organic frameworks (Du et al. 2021), and clays. Fluconazole has been treated using FL in heterogeneous mode; the advantage was the working pH (5–6), and the removal efficiencies were up to 94% using bimetallic catalysts.

Azithromycin was treated in simulated wastewater using poly aluminum chloride (PAX-18) as a coagulant at pH 7.0 in the first step, reaching 82.14% COD removal. Then, an FL oxidation process was performed using 0.36 mM/L $Fe^0$ and 0.38 mM/L $H_2O_2$, and the COD removal rose to 96.89%.

However, in recent years, the combination of Fenton oxidation and biological processes has been carried out because
Effluents show low biodegradability and high organic carbon content, and a good coupling strategy consists of a pre-oxidation step using AOPs (Silva et al. 2013). In pretreatment, pharmaceutical drugs are transformed into easily biodegradable intermediates, enabling the use of a biological process as a posttreatment to minimize the environmental impacts (Monsalvo et al. 2015). In these systems, the processing cost can be reduced, working at 40–60% of the stoichiometric H₂O₂ dose in the Fenton step (Su et al. 2016).

In Fenton processes, according to Fig. 4, the removal efficiencies are greater than 63%, and the best (> 99%) were achieved in EF, FL, PF, and heterogeneous PF, showing the poor applicability of conventional reactions. Additionally, Fig. 5 shows the scheme of Fenton reactions through the pH, which is the main reason for the use of modified systems.

**Photolysis**

Photodegradation of pharmaceutical drugs in the environment can occur directly or indirectly. Direct photodegradation occurs through the absorption of solar radiation energy or UV lamps by organic matter, allowing the formation of an excited state that leads to their degradation (Luo et al. 2018). Indirect photodegradation occurs when certain molecules absorb photons, which provides the energy required to excite specific electrons and form oxidizing species (called photosensitizers), such as HO• and peroxyl radicals (ROO•), by the action of solar radiation, mainly by UV-C radiation due to their capacity to promote the cleavage of chemical bonds (Albornoz et al. 2021). In real wastewater, the presence of inorganic ions (NO₃⁻, NO₂⁻, HCO₃⁻, CO₃²⁻, Cl⁻, Fe³⁺) can...
affect photodegradation because they act as photosensitizer scavengers of radicals and as irradiation filters (Oliveira et al. 2019), and the process is highly dependent on the pH of the solution due to the pKa value. In UV/H₂O₂ activation, UV radiation in aqueous media in the presence of H₂O₂ allows the generation of HO• through Eq. 7 and enhance H₂O₂ regeneration (Shokri et al. 2019). This system has been applied to remove lamivudine, ciprofloxacin, acyclovir, and azithromycin, as shown in Table 3. Based on this work, it concluded that using artificial lamps avoids the disadvantages of solar irradiation use, and the removal percentage is greater than 80%. As a result of the analysis, the more important parameters are the pKa value (chemistry form in solution), initial concentration (which is proportional to the removal percentage), H₂O₂ dosage, and intensity and wavelength of the radiation.

**Electrooxidation process (EO)**

In the EO process (anodic oxidation), pollutants must reach the electrode surface, and oxidation reactions take place once they are adsorbed onto this surface (Särkkä et al. 2015; Brillas and Martínez-Huitie 2015). As a consequence, the nature of the electrode materials influences the selectivity and efficiency; mass transfer is the most important process; anode materials recently used include dimensionally stable anode (DSA) electrodes, graphite, boron-doped diamond (BDD) electrodes, PbO₂, Pt, IrO₂, RuO₂, SnO₂, and Ti.

The electrodes are divided into active and nonactive electrodes. The active electrodes produce soft oxidation with the formation of polymers and many refractory species as final products of the electrolytic process. During the process, HO• interacts with the electrode surface, and oxidation is carried out by the direct transfer of electrons from the electrode surface and not by the action of HO•. The disadvantages are low efficiencies and oxide formation (Karacali et al. 2019).

Nonactive electrodes such as SnO₂, PbO₂, and BDD are very harsh, and organic compounds are easily mineralized, avoiding the production of polymers and low concentrations of refractory species (Barrera-Díaz et al. 2014). In the process, HO• directly attacks organic compounds, which is the main reason to consider this process as a “direct electrochemical process” (Barrera-Díaz et al. 2014). Figure 6 shows a scheme for the EO process at the laboratory scale.

In indirect oxidation, so-called mediated electro-oxidation, oxidants such as chlorine, hypochlorite (Kraft et al. 1999), hydrogen peroxide, peroxocompounds, and ozone (Chu et al. 2012) are formed at electrodes. Moreover, salt contained in solution can produce oxidants such as chlorine, sulfates, phosphates, and many other types of anions.

Finally, the pH, temperature, and presence of UV radiation influence the chemical activation of oxidants. Light irradiation enhances the effectiveness of oxidants produced on the electrode surface, producing the photo electro-oxidation (PEO) process. Photoactivation of electrochemically generated reactive species increases the efficiency of the process although homogeneous catalysis (Barrera-Díaz et al. 2014).

The combination of ultrasound, irradiation, and EO enhances mass transfer and produces new radical species due to the high pressure and temperature reached during the implosive collapse of bubbles; this process is called sono-electro-oxidation (SEO).

Electrochemical technologies such as EO, PEO, and SEO have been used to treat pharmaceuticals such as...
hydroxylchloroquine, dexamethasone, abacavir, and lamivudine using BDD, Ti/SnO2-Sb, and Ti/SnO2-Sb/Ce-PbO2 electrodes. Electrochemical technologies achieve a removal percentage of more than 90% in SARS-CoV-2 pharmaceuticals, as shown in Fig. 7. In conclusion, pH, current intensity, support electrolyte type, anode, temperature, agitation, and initial concentration.

**Sonochemical technology**

As shown in the previous section, in ultrasound technology, HO• is generated during cavitation according to Eq. 15 (Muñoz-Calderón et al. 2020) in the range of 20 kHz to 10 MHz, and increased reaction time results in the production of HO• but increases energy consumption.

$$H_2O + \rightarrow H^+ + HO^\cdot$$  \hspace{1cm} (15)

When H2O2 is added, US breaks the H2O2 molecule, generating additional HO•, and excess H2O2 can trap HO• radicals, generating HO2• radicals (Eqs. 16 and 17).

$$H_2O_2 + \rightarrow \rightarrow 2HO^\cdot$$  \hspace{1cm} (16)

$$H_2O_2 + HO^\cdot \rightarrow HO_2^\cdot + H_2O$$  \hspace{1cm} (17)

The parallel reaction that occurs during US treatments is the recombination of HO• to produce H2O2. To enhance this process, some metals, semiconductor nanoparticles, or materials, such as TiO2, ZnO and Cu2O, carbon nanotubes, and glass beads, have been used to reduce the activation energy and accelerate the response due to an increase in the number of active bubbles and radicals; this process is called ultrasonically assisted catalysis (Yazdani and Sayadi 2018; Al-Hamadani et al. 2016). The pH of the solution plays an important role in ultrasonic removal due to its effects on the distribution of electric charge on the catalyst surface and oxidation potential. When using US, solutions tend to increase in temperature, significantly allowing H2O2 decomposition. In real wastewater, the presence of more hydrophobic or volatile compounds than pollutants diminishes the efficiency of the ultrasonic process (Yazdani and Sayadi 2018).

Azithromycin, sulfamethoxazole, and tinidazole have been treated by conventional ultrasound, and the frequency applied is in the range of 35 to 120 kHz. According to Table 3, the removal efficiencies are proportional to frequency, and the optimum working pH is above the pKa value (Table 2), guaranteeing the ionic form of the pharmaceuticals, and the efficiencies are between 46 and 72%. When H2O2 was added, the efficiency increased from 8.5 to 77% (Rahmani et al. 2014), demonstrating additional HO• production. In US-assisted catalysts, glass beads and single-walled carbon nanotubes have been added to treat sulfamethoxazole, and the maximum removal percentage was obtained in the presence of a combination of materials at 1000 kHz. The materials increased the number of HO• due to ultrasonic irradiation and the adsorption capacity, which was associated with an increase in the number of collapsing bubbles. Additionally, the size particles and the frequency of the ultrasound played major roles (Al-Hamadani et al. 2016). On the other hand, ZnO catalysts have been used to treat azithromycin and have some advantages, including high efficiency, short reaction time, and easy workup (Yazdani and Sayadi 2018).

Finally, when ultrasound was coupled with biological treatment, the sonochemical process transformed fluoxetine into biodegradable substances: the biodegradability index increased from 0.05 to 0.40, eliminating 70% of TOC, and this effluent was driven to a subsequent biological treatment (Serna-Galvis et al. 2015).

According to our experience, if the working pH is above the pKa value (mainly when the pKa value is high), researchers must add H2O2 or catalyst to improve HO• generation to enhance the oxidation of the molecular form. At acidic pH, catalyst particles favor the effective surface of materials and improve catalytic degradation. In conclusion, the most important parameters are the frequency, treatment time, pH, and temperature. If catalyst is added, the particle size and dose must be considered (as the amount of catalyst increases, HO• increases).

**Ozonation**

Ozone is an unstable gas compounded by three oxygen atoms (O3) and is one of the most potent oxidizing agents (2.07 V). The main drawback is the generation of O3 from oxygen, for which an electric discharge over a stream of air or pure oxygen is used (Eqs. 18 and 19), which consumes large amounts of energy, thus handicapping the scaling of the process (Cuerda-Correa et al. 2020). When O3 is dissolved in water, it produces a broad spectrum of reactive oxygen radicals (Rekhate and Srivastava 2020). Ozonation in water results in the formation of harmful byproducts such as aldehydes, carboxylic acids, and
bromates when reacting with dissolved organic matter (Nasir et al. 2021). Ozonation has deficient mineralization, and low molecular weight byproducts can exhibit more toxicity than primary pollutants.

\[ O_2 + \text{electric spark} \rightarrow 2O^* \]  
(18)

\[ O_2 + O^* \rightarrow O_3 \]  
(19)

The mechanism of oxidation by O₃ takes place in two ways: direct reaction with dissolved O₃ or indirect oxidation through the formation of HO*. The mechanisms depend on factors such as the nature of the contaminant, the dose of O₃, or the pH of the medium. Under acidic conditions (pH < 4), direct ozonation prevails, and at pH > 9, the indirect route is carried out (Cuérdia-Correa et al. 2020). In general, degradation rates increase as pH increases, and high pH favors O₃ decomposition into free radicals. According to Table 3, acyclovir and oseltamivir were eliminated through ozonation, and the results revealed no toxic effects in Vibrio fischeri after treatment.

The O₃ base process can be combined with H₂O₂, UV light, catalyst, photocatalyst, or ultrasound to enhance HO* production, which increases the treatment efficiency. O₉/UV promotes O₃ decomposition by direct and indirect production of HO*, improving mineralization processes. O₉ absorbs UV light at \( \lambda = 254 \text{ nm} \), generating HO* as a consequence of the reaction between atomic oxygen and water (Cuérdia-Correa et al. 2020), and UV light can excite organic molecules, increasing their susceptibility.

O₃/H₂O₂ (peroxone AOP) involves the formation of hydroperoxide anion (HO₂⁻), which reacts with O₃ and leads to HO* formation, and secondary reactions make the process continue (Eqs. 20–25). Ciprofloxacin was treated under this process, and the efficiency was > 95% using H₂O₂ in the range of 2 µM–20 mM and O₃ (0.1–0.23 mM) (De Witte et al. 2009; Rosal et al. 2008). According to Table 3, in recent years, sulfamethoxazole has been removed using 5 mM H₂O₂ and 0.42 mM O₃ (Gomes et al. 2018), and this process allows mineralization through direct and indirect oxidation. In this process, we recommended toxic analysis to evaluate the viability of the process; in some cases, the by-products are more toxic than the precursor; moreover, in order to apply in real matrices, inorganic ions can be monitored due to the scavenger effect.

\[ H_2O_2 \rightarrow HO_2^- + H^+ \]  
(20)

\[ HO_2^- + O_3 \rightarrow HO^* + O_2^- \]  
(21)

\[ HO^* \rightarrow O_2^* + H^+ \]  
(22)

\[ O_2^* + O_3 \rightarrow O_2 + O_5^- \]  
(23)

\[ O_3^- + H^+ \rightarrow HO^* + O_2 \]  
(24)

\[ HO^* + O_3 \rightarrow HO_2^* + O_2 \]  
(25)

The catalytic ozonation process can be done in two ways: homogeneous and heterogeneous. In the homogeneous catalysts, such as transition metals (Fe²⁺, Mn²⁺, Ni²⁺, Co²⁺, Cd²⁺, Ag⁺, and Zn²⁺) (Wu et al. 2008; Wang and Chen 2020) are used to influence the rate of reaction, the selectivity of O₃ oxidation, and the efficiency of O₃. In heterogeneous mode, a solid catalyst improves ozonation, and the materials used include metal oxides (MnO₂ (Shen et al. 2022; He et al. 2021), Fe₃O₄ (Kohantorabi et al. 2022), MgFe₂O₄, CuFe₂O₄, ZnFeO₄, MgO), supported metal oxides (Fe₃O₄/CdO, Fe₃O₄@Ce-Uio-66 (Mohebali et al. 2022), CuMn₂O₄ (A. Li et al. 2021), NiCo₂O₄ (Chen and Wang 2021), MgO/g-C₃N₄ (An et al. 2020)), and some porous materials (zeolites Su et al. 2022; Araújo et al. 2021), carbon nanotubes, activated carbon (ceramics) and modified materials (Faghhiinezhad et al. 2022). The materials enhance the probability of electron transfer, lowering the activation energy. Dexamethasone was removed using Al₂O₃ nanoparticles at pH > pKa until complete removal. In conclusion, the catalytic system is highly effective in achieving fast and complete mineralization, and the efficiency depends on the kinds of catalyst, the target pollutants, and the pH value.

Photocatalytic ozonation (POCz) is a less ozone-consuming and cost-effective technology. The positive synergistic effect of photocatalytic ozonation results in the generation of HO* which enhances the degradation of organic pollutants, controls the ozonation byproducts, and reduces electron–hole recombination (Moreira et al. 2015). The materials recently used in this technology include TiO₂ with graphene oxide (Beltrán and Checa 2020). Using lamps (300–365 nm) as an irradiation source, ciprofloxacin and amoxicillin were removed, reaching up to 85% TOC removal.

As a rule, in the ozonation process, the chemical structure, concentration of the pollutant, pH, and temperature are the main operational parameters. Finally, biological treatment coupled to ozone is capable of removing the byproducts generated by ozonation to minimize the risks that may arise due to the formation of toxic byproducts; moreover, this system can treat the metabolites present in wastewater. Sulfamethoxazole, carbamazepine, and azithromycin present in real wastewater were eliminated through ozonation/biological treatment using AOP as pretreatment, enhancing the removal percentage in the effluent (Table 3). This kind of system is rarely used due to the cost of pretreatment.
Sulfate radical-advanced oxidation processes (SR-AOPs)

SR-AOPs are processes in which the generation of \( \text{SO}_4^{2-} \) is promoted, alone or jointly with \( \text{HO}^+ \) (Giannakis et al. 2021). A proper oxidant should be activated, peroxymonosulfate (PMS) (redox potential 2.01 V vs. NHE) and peroxodisulfate (PDS) (1.82 V vs. NHE) are widely used oxidants. \( \text{SO}_4^{2-} \) can be produced from PDS or PMS via the following physical activation methods: heating, light radiation, ultrasonic waves, or chemical activation: transition metal ion activation, alkaline activation, strong oxidizers, photocatalytic and electrochemical activation (Xia et al. 2020) through the following reactions.

\[
S_2O_8^{2-} + 2e^- \rightarrow 2SO_4^{2-} \tag{26}
\]

\[
\text{HSO}_5^- + 2H^+ + 2e^- \rightarrow \text{HSO}_4^- + H_2O \tag{27}
\]

\( \text{SO}_4^{2-} \) has a higher redox potential \( E_0 = 2.5–3.1 \) V vs. NHE than \( \text{HO}^+ \) \( E_0 = 1.8–2.7 \) V vs. NHE); moderate conditions of \( pH \) reaction (2.0–8.0) and longer half-life \( (t_{1/2} = 30–40 \mu s) \) (Nfodzo and Choi 2011) and can generate highly reactive oxygen species (ROS) (Yang et al. 2015).

Photocatalysis can decompose PMS and PDS into free radicals (Eqs. 28, 29, 30), and depending on the catalyst, other radicals can be generated (\( \text{O}_2^{2-}, \text{HO}^+ \)).

\[
\text{HSO}_5^- + e_{CB}^- \rightarrow \text{SO}_4^{2-} + \text{HO}^+ \text{orSO}_4^{2-} + \text{HO}^+ \tag{28}
\]

\[
\text{HSO}_5^- + h_{VB}^+ \rightarrow \text{SO}_4^{2-} + H^+ \tag{29}
\]

\[
S_2O_8^{2-} + e_{CB}^- \rightarrow \text{SO}_4^{2-} + \text{SO}_4^{2-} \tag{30}
\]

This kind of photocatalysis can be carried out in homogeneous or heterogeneous mode; the homogeneous mode presents high efficiency at \( pH < 7 \), while in heterogeneous mode (HM), the catalyst has the potential to be reused (Giannakis et al. 2021). To treat SARS-CoV-2 pharmaceuticals, HM has been applied and the materials and precursors used are PDINH/MIL-88A(Fe) composites/PDS, Al\(_2\)O\(_3\) nanoparticles/persulfate, CuO supported on Mg Al layered double hydroxide (LDH) and CuO-LDH composite/persulfate, and magnetic nitrogen-doped microalgae derived carbon (Fe-N@MC)/PMS, and nano zerovalent manganese/persulfate according to Table 3 \( pH \) affects the catalytic activity of the materials, redox potential of \( \text{HO}^+ \) and \( \text{SO}_4^{2-} \), the activation, and chemistry form of pharmaceuticals.

Simultaneous generation of \( \text{HO}^+ \) and \( \text{SO}_4^{2-} \) by the reaction of \( \text{O}_3 \) with PMS (\( \text{HSO}_5^- \)) was applied to remove ribavirin. During the process, ribavirin was dehydrogenated and then lost the amide of the methanol group. Less than 5% ribavirin was degraded by PMS alone, and the higher removal efficiencies of the \( \text{O}_3/PMS \) process were attributed to the increased formation of free radicals and accelerated \( \text{O}_3 \) consumption (Liu et al. 2021a, b).

The Fenton process is capable of degrading pharmaceutical compounds; however, several disadvantages have been previously mentioned. Using this technology, photo-Fenton-like in HM was used by adding PMS combined with mesoporous manganese oxide (MnO\(_2\)) microspheres to produce \( \text{HO}^+ \) and \( \text{SO}_4^{2-} \) using simulated solar radiation to treat ciprofloxacin, and ROSs were produced from PMS by simulated sunlight irradiation. PMS-based Fenton-like reactions can produce many active substances and even directly degrade pollutants. A PMS activation system employing SA Co–N–C(30) as a high-efficiency catalyst was used to treat chloroquine. According to the results, the size of the catalyst plays an important role in the catalytic performance.

Future trends and discussion

According to this review, AOPs are a promising technology for treating SARS-CoV-2 pharmaceutical drugs, and the removal percentage is greater than 60%. In general, the available scientific literature is limited to lab-scale tests using aqueous solutions or simulated wastewater, and the industrial scale is limited to \( \text{O}_3 \), which appears to be more economically viable; however, the authors do not agree with this statement and conclude that this is due to the knowledge maturity in this technology. Articles focusing on full-scale operational conditions are scarce, and only in the last few years have they gained attention. To increase the feasibility of AOPs to be used at a large scale, several aspects should be improved, and research work should be performed on different topics, e.g., reactor design, costs, and toxicity (effluents and by-products). Moreover, emerging compound are not regulated, we recommend take into account the criteria established by WHO and EPA.

Additionally, AOP coupling as a pre- or posttreatment with conventional processes shows high removal efficiencies (>80%) and has been applied to remove only sulfamethoxazole, carbamazepine, and azithromycin. From the analysis, AOPs arise as beneficial technologies for the removal of SARS-CoV-2 pharmaceuticals that may be found in wastewaters derived from pandemic events. The main disadvantages of AOPs include their high cost (expensive reagents), energy consumption, and the lack of proper reactors hinder their wide applicability, and the literature only includes operational costs at the laboratory scale in aqueous solution.

Another important issue is that the variability in real matrices (presence of ions, dissolved organic matter, color, variable \( pH \), and turbidity), before the AOP selection, should be carried out a complementary characterization.
On the other hand, high removal efficiencies using UV radiation have been attained in concomitance with AOPs, although operational costs are higher due to the use of artificial lamps. Additionally, solar radiation use is commonly applied to enhance mineralization and decrease costs; in some cases, this kind of AOP has been successfully applied for the removal of these compounds, leading to their complete mineralization without the generation of any toxicity. Meanwhile, several disadvantages should be overcome, such as season dependence and efficiency on rainy or cloudy days. As a result of the literature review, photocatalysis is the most common AOP used to remove these compounds in aqueous solution due to its nonselective degradation ability; however, until today, most of the published results have focused on the use of UV irradiation (due to the bandgap value), and TiO₂ is the most commonly used metal oxide owing to its advantages: it is inexpensive, commercially available, nontoxic, and photochemically stable. Recently, different modifications enhanced their efficiency and reusability; these methods allow their immobilization and/or incorporated metallic ions, reducing the bandgap value and enabling the use of solar radiation as the activation energy. Additionally, darunavir, favipiravir, galidesivir, remdesivir, ritonavir, tenofovir, tocilizumab, arbidol, gimsilumab, and lenolinlab have not been treated by AOP, showing the gap in knowledge in this field.

In conclusion, it recommends choosing the proper working pH value, considering the pKa value to minimize reagents, time, and costs. Additionally, TOC analysis should be considered a priority in order to report pharmaceutical mineralization, not only their transformation but also toxicological analysis must be performed because oxidation leads to changes in the molecular structure, which may give rise to entirely byproducts that may have similar or even higher toxicity than the original molecule. Finally, in this article, researchers can find the main parameters involved in each AOP and the fundamentals to new researchers.

Conclusions

SARS-CoV-2 pharmaceutical drugs and metabolite derivatives have a significant rise in their presence in wastewater, water, and hospital effluents by novel SARS-CoV-2, generating environmental and human health impacts. Knowledge is limited, and the environmental effect of the pandemic will be felt for years to come. After decades of research on AOPs, these processes have proven their efficiency for the removal of a variety of organic pollutants; however, most studies are at the laboratory scale in aqueous solution. To avoid unnecessary reagents or time, it is necessary to chemically know the compound to be removed, and energy costs must be reduced. In this context, solar technologies show novel and affordable ways to remove these stable compounds, and the application of renewable energy sources in real matrices should be investigated in order to avoid the disadvantages. Some AOPs that generate sludge should be minimized, and possible alternatives for the valorization of such waste should be explored.

Author contribution All authors contributed to the study conception and design. The literature search and data analysis were performed by Monserrat Castañeda-Juárez, Luis Antonio Castillo-Suárez, Elia Alejandra Teutli-Sequeira, and Ana Gabriela Sierra-Sánchez. The first draft of the manuscript was written by Monserrat Castañeda-Juárez, Ivonne Linares-Hernández, and Verónica Martínez-Miranda. All authors commented on previous versions of the manuscript and approved the final version.

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Declarations

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