TALLINNA TEHNIKAÜLIKOOL

PHOTOCHEMICAL OXIDATION OF LOSARTAN IN AQUEOUS SOLUTION

LOSARTAANI FOTOKEEMILINE OKSÜDATSIOON VESILAHUSES

MASTER THESIS

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AUTHOR'S DECLARATION

Hereby I declare, that I have written this thesis independently.
No academic degree has been applied for based on this material. All works, major viewpoints and data of the other authors used in this thesis have been referenced.

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Thesis is in accordance with terms and requirements

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THESIS TASK

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Thesis topic:

Photochemical oxidation of losartan in aqueous solution

Losartaani fotokeemiline oksüdatsioon vesilahuses

Thesis main objectives:

1. To provide an overview of the properties of losartan, its occurrence and impact in the environment along with its removal processes
2. To study and compare the efficacy of losartan degradation and mineralization by UV/H_2O_2, UV/PDS, $UV/H_2O_2/Fe^{2+}$ and $UV/PDS/Fe^{2+}$ systems in water matrices
3. To study the effect of H_2O_2, PDS, and Fe^{2+} concentrations as well as the effect of the groundwater matrix composition on the oxidation efficiency of the target compound by the studied UV-induced systems

Thesis tasks and time schedule:

No	Task description	Deadline
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3.	Writing a master's thesis: literature review, experimental part, analysis of the results, etc.	05.2020

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CONTENTS

List of abbreviations and symbols

AOP	Advanced Oxidation Process
API	Active Pharmaceutical Ingredient
ARB	Angiotensin Receptor Blocker
AT1R	Type 1 Angiotensin II Receptors
CAS	Conventional activated sludge process
CEO	Concentration Effect Observed
DOC	Dissolved Organic Carbon
HELCOM	Helsinki Commission, The Baltic Marine Environment Protection Commission
LOR	Losartan
MWWTP	Municipal Wastewater Treatment Plant
NOEC	No Observed Effect Concentration
PDS	Peroxydisulfate
PMS	Peroxymonosulfate
TOC	Total Organic Carbon
US	Ultrasound
UV	Ultraviolet
WWTP	Wastewater Treatment Plant

INTRODUCTION

Water is continuously contaminated by anthropogenic pollutants through wastewater discharges and direct pollution. Although wastewater is typically treated at wastewater treatment plants (WWTPs), this treatment scheme has proved to be inefficient measure to avoid the entry of micropollutants and recalcitrant substances, such as active pharmaceutical ingredients (API), into receiving waterbodies (Deegan et al., 2011). There is a global concern about the presence of emerging contaminants and their potential hazardous effect in the aquatic environment (Botero-Coy et al., 2018). Pharmaceuticals have been considered emerging contaminants for decades (Miller et al.,2018; Quesada et al., 2019) and are among the most frequently detected contaminants in water (Botero-Coy et al., 2018). They are discharged into surface waterbodies through WWTPs, commonly in municipal wastewater and hospital wastewater, and concentrations range from ng L^{-1} to µg L^{-1} (Quesada et al., 2019; aus der Beek et al., 2016). The occurrence of these substances in the environment has been observed since 1960s in both Europe and the United States (Jjemba, 2018). The first concerns arose in the late 1990s, when the presence of pharmaceuticals in the river was associated with the feminization of fish. Then, it was found that the presence of diclofenac in water is linked with renal failure of vultures. In 2002, a study showed that about 80% of 139 streams in the United States were polluted with organic substances, including pharmaceuticals and personal care products (Deegan et al., 2011). HELCOM has estimated that every year about 1800 tons of pharmaceuticals enter the Baltic Sea via the discharges from municipal WWTPs. (Baltic Marine Environment Protection Commission, 2017). The CWPharma project study of Estonian surface waters funded by INTERREG Baltic Sea Region programme indicated that 89% of the analyzed samples contained at least two medicines. It is estimated, that majority of substances end up in environment after intended use via secretion into sewage (Eesti Vee-ettevõtete Liit, 2019).

Traditional WWTPs commonly use mechanical and biological treatment for removing excess nutrients, organic compounds and suspended solids from wastewater. This wastewater treatment scheme works efficiently if the substances to be removed are biologically degradable, hydrophobic, can be well absorbed in suspension and have a low polarity. In general, hydrophobic substances are easily removed via different separation processes. However, these properties do not apply to APIs, which are mostly hydrophilic, have a low adsorption rate and high biological activity, which makes them very stable and persistent to biological degradation (Martz, 2012). Removal of pharmaceuticals has therefore been shown to be ineffective in

conventional WWTPs and the release of pharmaceuticals poses detrimental effects on receiving ecosystem. The removal efficacy of pharmaceuticals varies greatly for different substances and treatment processes, for instance, carbamazepine, clarithromycin, cyclophosphamide and lidocaine are not removed in conventional WWTPs (Igos et al., 2013). Only about 8% of pharmaceuticals are removed efficiently (>95%) from wastewater and almost half of the compounds are removed under 50% efficiency (Baltic Marine Environment Protection Commission, 2017). In turn, advanced oxidation processes (AOPs), including the formation of highly reactive oxygen species, such as hydroxyl ($HO^{\bullet}$) and sulfate ($SO_4^{\bullet-}$) radicals, have received more attention and are considered as promising alternatives to traditional wastewater treatment methods, since they are not only effective in API decomposition, but also prone to reduce the toxicity of transformation products (Sbardella et al., 2020)

According to the HELCOM report, the most frequently detected APIs in Baltic Sea marine environment are anti-inflammatory and analgesic drugs, cardiovascular and central nervous system agents. Losartan (LOR), an angiotensin receptor blocker (ARB), is in top 20 pharmaceuticals measured in the highest concentrations in river water samples (average concentration ~100 µg L^{-1}) and WWTPs effluent (average concentration >0.1 mg L^{-1}). In this regard as well as due to its widespread use, LOR is proposed to be added to the "watch list" for monitoring (Baltic Marine Environment Protection Commission, 2017).

To date, a limited number of studies have been conducted on the use of $HO^{\bullet}$-based AOPs, and there is no data on the use of $SO_4^{\bullet-}$-AOPs to remove LOR from water. Therefore, the purpose of this study was to assess and compare the efficacy of LOR degradation and mineralization by UVC- and UVC/Fe^{2+}-activated peroxydisulfate (PDS) and hydrogen peroxide systems in different water matrices.

1.   LITERATURE OVERVIEW

1.1 Losartan

Losartan (LOR) is one of the hypertension medicines for lowering blood pressure (Shimizu et al., 2012). Medicines in ARB group are the most widely used antihypertensive drugs because of their good tolerability and fewer side effects. Approximately 25% of hypertensive patients worldwide are taking ARBs and they are also used for stable coronary heart disease, heart failure and the state after acute myocardial infarction (Dézsi, 2014).

LOR is a synthetic orally active, selective non-peptide antagonist against type 1 angiotensin II receptors (AT1R), and has been applied in medical treatments of a variety of cardiovascular diseases, including essential hypertension (European Medicines Agency, 2012; Xu et al., 2009). Angiotensin II is a potent vasoconstrictor and an important determinant of the pathophysiology of hypertension, which binds to the AT1 receptor. LOR selectively blocks AT1 receptor and does not have an agonist effect, nor does it block other ion channels or hormone receptors (European Medicines Agency, 2012). After oral intake LOR undergoes either conjugative or oxidative metabolism in liver after which it is transformed into hydroxylated and carboxylic acid (Xu et al., 2009).

1.1.1 Physical properties of Losartan

Losartan (2-Butyl-4-chloro-1-((2'-(1H-etrazol-5-yl)(1,1'-biphenyl)-4-yl)methyl)-1H-imidazole-5-methanol, Figure 1.1) is sold under the commercial name of Cozaar. Its molecular weight is 422.9 g mol^{-1} and it occurs in a powder (NIH U.S. National Library of Medicine). The melting point is 184 °C and the solubility in water at 25 °C is 8.22 mg L^{-1} (US EPA, 2012).
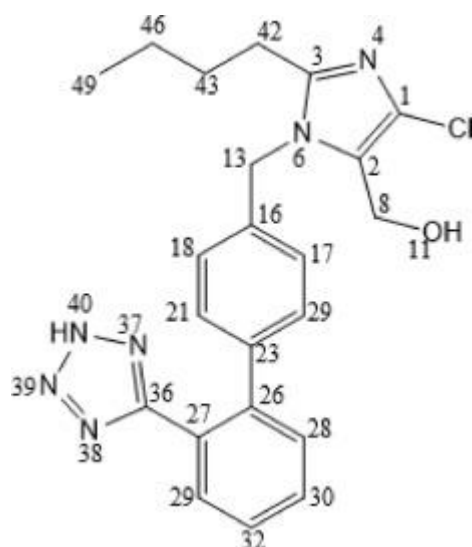
Figure 1.1 Losartan chemical structure (NIH U.S. National Library of Medicine)

LOR is considered stable under recommended storage conditions and hazardous decomposition products include carbon oxides, nitrogen oxides, hydrogen chloride gas and potassium oxides (Sigma-Aldrich, 2014). LOR is freely soluble in water, soluble in alcohol and slightly soluble in organic solvents such as acetonitrile, methyl ethyl ketone (O'Neal, 2013).

1.1.2 Medical properties of Losartan

LOR is well absorbed after oral administration and undergoes a first-pass metabolism, where an active carboxylic acid metabolite and other inactive metabolites are formed (European Medicines Agency, 2012). LOR is almost completely absorbed and undergoes substantial metabolism (Sica et al., 2005) The bioavailability of LOR is approximately 33% and the mean peak concentration is reached in 1 hour and in 3-4 hours for metabolites. Both LOR and its active metabolite are ≥99% bound to plasma proteins, primarily albumin (European Medicines Agency, 2012). The low bioavailability could be caused by a blend of incomplete absorption and variable first-pass metabolism (Sica et al., 2005). About 14% of the administered dose of LOR is converted to its active E 3174 metabolite, which is up to 40% more potent than its parent compound (Bolattin et al., 2015). In addition, inactive metabolites are formed. The plasma clearance of LOR and its active metabolite is about 600 mL min^{-1} and 50 mL min^{-1}, respectively (European Medicines Agency, 2012). In turn, the renal clearance of LOR and its active metabolite is about 74 mL min^{-1} and 26 mL min^{-1}, respectively. Both LOR and E 3174 are strongly bound to protein, mainly albumin,

namely 98.6–98.8% and 99.7% of the total concentration, respectively. As shown in Figure 1.2, LOR is first converted into E 3179 and then to E 3174, which is due to the cytochrome P450 (CYP) system (Sica et al., 2005).
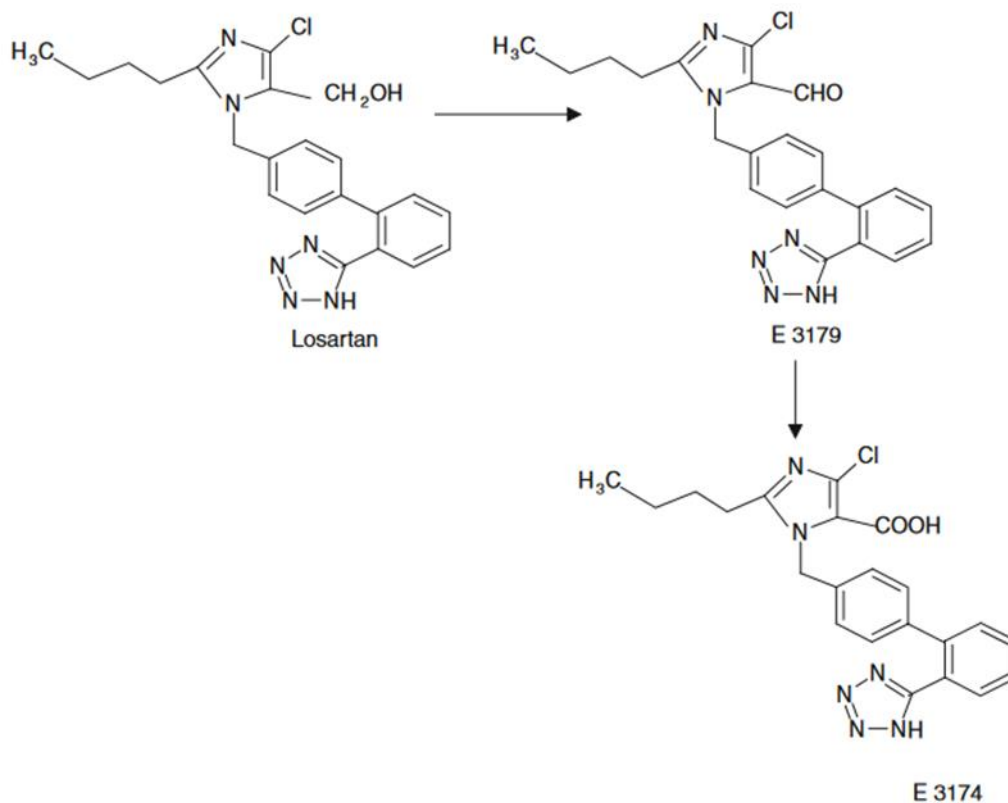

Figure 1.2 Losartan and its metabolites E 3179 and E 3174 (Sica et al., 2005)

During the oral administration of LOR, about 4% of the dose is excreted unchanged in the urine, and about 6% of the dose is excreted in the urine as an active metabolite. The pharmacokinetics of LOR and its active metabolite are linear with oral LOR potassium doses up to 200 mg (European Medicines Agency, 2012). Both LOR and metabolite E 3174 are not removed during haemodialysis (Sica et al., 2005).

1.1.3 Adverse properties of Losartan

The most common side effects associated with LOR administration include dizziness, low blood pressure, weakness, fatigue, hypoglycaemia, hyperkalaemia. More uncommon side effects include somnolence, headache, sleep disorders, palpitations, severe chest pain, low blood pressure and dose-related orthostatic effects, such as lowering of blood pressure appearing when rising from a lying or sitting position,

shortness of breath, abdominal pain, obstipation, diarrhea, nausea, vomiting, hives, itching, rash, localized swelling (European Medicines Agency, 2012).

Fetal toxicology studies suggested that LOR should be avoided during pregnancy (Sica et al., 2005). Use of LOR during the second and third trimesters of pregnancy reduces the renal function of the fetal and can cause morbidity and death of the fetal and newborn. This can be associated with fetal lung hypoplasia and skeletal deformations. It is therefore advised, that when pregnancy is detected, a patient should discontinue using LOR as soon as possible (NIH U.S. National Library of Medicine, 2018; Sica et al., 2005). It has not been determined whether LOR or its metabolites can be excreted in human milk, but both LOR and metabolite E 3174 have been detected in rat milk, which requires caution when used during lactation (Sica et al., 2005).

In patients treated with high doses of diuretics, symptomatic hypotension may occur after starting treatment with LOR (NIH U.S. National Library of Medicine, 2018). Patients with hepatic disease have shown a 50% reduction in plasma clearance of LOR and oral bioavailability about 2 times higher. This results in up to 5-fold increase in plasma LOR concentrations in this population (Sica et al., 2005).

Patients with renal artery stenosis, chronic kidney disease, severe congestive heart failure, or volume depletion may be at particular risk of developing acute renal failure on LOR. There have been observations about decreased plasma LOR concentrations when using an antibiotic rifampin (NIH U.S. National Library of Medicine, 2018). Furthermore, there is a clinically significant effect of rifampin as a potential inducer of LOR and E 3174 elimination (Williamson et al., 1998) and an increase in serum potassium concentrations while using potassium supplements or potassium-containing salt substitutes (NIH U.S. National Library of Medicine, 2018). There is also data suggesting an increase in relative risk for newly developed cancer, namely 9% for LOR, 11% for candesartan and 7% for telmisartan. The strongest implication of ARBs relative cancer risk was made for lung cancer (25% increase of relative risk, $p=0.01$) and prostate cancer (15% increase of relative risk, $p=0.076$) (Dézsi, 2014).

With a single daily dose of 100 mg, neither LOR nor its active metabolite accumulate significantly in plasma. Both biliary and urinary excretion contribute to the elimination of LOR and its metabolites (European Medicines Agency, 2012). The most likely outcome of an overdose would be tachycardia and hypotension (NIH U.S. National Library of Medicine, 2018).

There have not been reports of overdosing and toxicity with LOR, but side-effects and un-wanted health outcomes may happen in patients with renal dysfunction, diabetes mellitus, angioedema and hypothyroidism (NIH U.S. National Library of Medicine, n.d.-b). Over the time of commercial availability, 6 cases of liver damage due to LOR have been reported (Patti et al., 2019).

1.1.4 Toxicity and bioaccumulation of Losartan

Only limited data on toxicity and environmental effect is available for LOR, but since it has a logP value similar to other sartan group medicines, some of the effects are likely to be predicted. As the sartans are increasingly prescribed, they become more prevalent in the environment (Bayer et al., 2014). A risk assessment study in Norway evaluated over 1400 pharmaceutical compounds – drugs were screened against consumption, volume wastewater of influent, human metabolism, biodegradation and behavior in WWTP. Among the pharmaceuticals studied, fourteen compounds, including LOR, were selected for further study to assess potential risks to human health or the environment (Table 1.1) (Sanderson & Thomsen, 2009).

Table 1.1 Toxicity, consumption and occurrence of selected pharmaceuticals (Baltic Marine Environment Protection Commission, 2017; Sanderson & Thomsen, 2009; modified)

Name	Daphnid acute 48h LC50 (mg L^{-1})	Sales rank	MWWTP influents rank	River sample rank
Carbamazepine	13,8	14		8
Diclofenac	22,4	15	20	11
Ibuprofen	9,1	4	7	
Losartan potassium	**331**	**na**		**14**
Metformin	1345	3		
Paracetamol	9,2	1	1	18
Tramadol	73	19	12	6

* na – no answer

During the toxicity assessment of LOR to *Perna perna* in Brazil, all samples from rivers and Santos Bay contained LOR. The results of this assessment indicated adverse effects on the reproductive system at higher concentrations (Cortez et al., 2018). Another study of sea urchin *Lytechinus variegatus* found that LOR showed 50 mg L^{-1} and 70 mg L^{-1} of NOEC (No Observed Effect Concentration) and CEO (Concentration Effect Observed), respectively (Yamamoto et al., 2014). In comparison, for Valsartan, also sartan, the NOEC and CEO values were 12.5 mg L^{-1}

and 25 mg L^{-1}, respectively. These concentrations for both compounds are significantly higher than those detected in the environment.

Overall, the elimination efficacies for LOR vary in different WWTPs and laboratory studies, but the overall detection in the environment is at least a magnitude lower than any measured effect on living organisms. Even a mixture of five sartan group medicines and their degradation products caused no chronic toxicological effects to *Daphnia magna*. In addition the Ames fluctuation test did not demonstrate an increased frequency of mutations (Bayer et al., 2014)

1.1.5 Losartan in the environment

Due to new medical information and fewer side-effects medicines in the ARB group, they are becoming more and more prescribed all over the world (Imai et al., 2018). LOR is becoming increasingly popular within the hypertension prescription group and by 2016 it was the 9th most commonly prescribed medicine in the USA with over 49.2 million prescriptions per year (Figure 1.3) (*Losartan Potassium*, 2016).
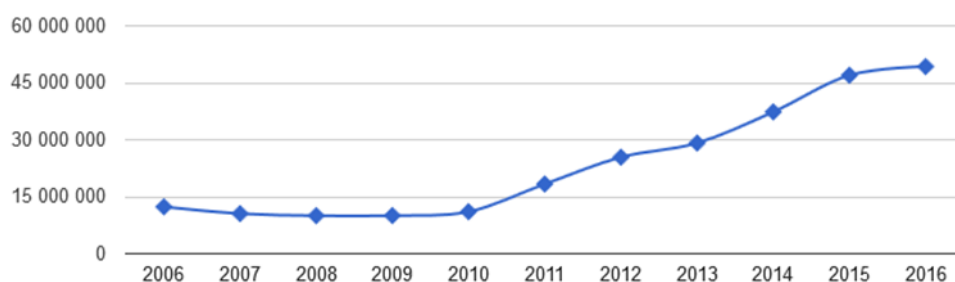

Figure 1.3 Losartan prescriptions 2006-2016 in USA (*Losartan Potassium*, 2016)

LOR oral bioavailability is about 33% and it is mainly eliminated from the body via urine and feces (Patti et al., 2019). This means it will end up in sewage and WWTPs, where it is not sufficiently removed via traditional biological treatment (Bayer et al., 2014).

According to the European Medicinal Agency, the threshold for ecotoxicological and fate tests for individual pharmaceuticals is 10 ng L^{-1} (Whomsley et al., 2019). During the study of pharmaceuticals in Tejo estuary (Portugal) LOR was present in 90% of the analyzed samples and found at maximum concentration of 64.7 ng L^{-1} (average 10.63 ng L^{-1}) (Reis-Santos et al., 2018). High levels of LOR, up to 2.4-2.5 mg L^{-1}, have been detected in the effluents samples of drug manufacturers WWTPs in

Patancheru, India. However, most studies have shown that the presence of LOR in the environment is at an acceptable level of risk (Godoy et al., 2015).

LOR belongs to the top 20 pharmaceuticals found in the highest concentrations in the Baltic Sea basin rivers (~0.5 mg L^{-1}) (Baltic Marine Environment Protection Commission, 2017). LOR was also detected in municipal waste water treatment plant (MWWTP) effluents in concentrations >0.1 mg L^{-1}. (Baltic Marine Environment Protection Commission, 2017). The main source of LOR aquatic contamination is inefficiently treated wastewater with reported removal rates of 50-80%. For example, in Portuguese hospital waste water effluents the concentration of LOR was found to be ranged between 59-910 ng L^{-1}; in Sweden the concentrations of LOR in medium scale WWTP effluents was between 705-980 ng L^{-1} (Cortez et al., 2018). ARB group medicines were also found in Vistula river (Poland) in concentrations over 1 µg L^{-1} and LOR was also found in tap water in trace levels (Giebułtowicz et al., 2016). In Colombia, LOR was detected in WWTP effluents at concentrations of 1-2 µg L^{-1} and is considered one of the most refractory compounds in wastewater (Botero-Coy et al., 2018).

Although the state of knowledge about individual pharmaceuticals and their ecotoxicity have improved, the effect of their mixtures on different organisms is still unknown. In general, there is much greater data available about API toxicity for freshwater organisms than for marine or brackish water organisms. These mentioned types of waterbodies are exposed to multi-component pharmaceutical mixtures from WWTP effluents and as a first step it is necessary to evaluate the risk of single components (Backhaus, 2014). It is also important to study toxicity of mixtures including metabolites and degradation products as these might pose even greater risk to aquatic organisms. Studies have shown that mixtures with a low concentration of different drugs can have an increased negative impact compared to the individual toxicity of the API, indicating a synergistic effect (Bayer et al., 2014)

1.2 Removal of Losartan from water

1.2.1 Removal of Losartan by biological processes

LOR is classified as an emerging contaminant (EC) (Baltic Marine Environment Protection Commission, 2017) and the occurrence of ECs in environment is often related to WWTPs discharges as a consequence of insufficient technologies for removing unwanted compounds (Ferreiro et al., 2020).

WWTPs often use conventional activated sludge (CAS) process (Figure 1.4), which is designed for continuous flow (Gusmaroli et al., 2020). The influent will go through preliminary treatment and primary clarification before entering a plug flow activated sludge reactor. This process uses an aeration tank, clarifier, and sludge return line. The process may have a large number of variations, such as a modified reactor layout, different aeration systems, influent patterns, extended aeration activated sludge (EAAS), membrane bioreactor (MBR) or other modifications. (Jafarinejad, 2017). Most traditional WWTPs are not designed to efficiently remove microcontaminants, and thus they partially removed and end up in receiving waterbodies. The continuous contamination of surface water may cause cumulative negative effects over generations of aquatic organisms (Barbosa et al., 2016).
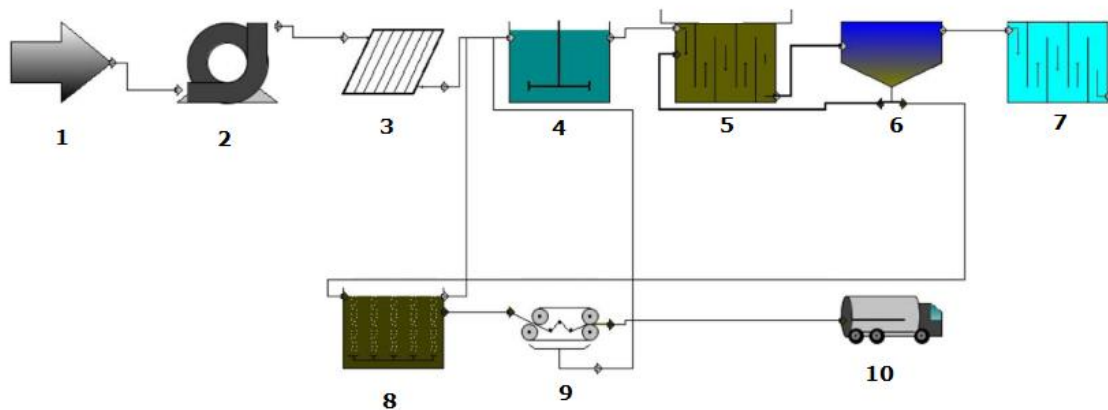

Figure 1.4 Layout of a WWTP using CAS: *1 – Influent Wastewater; 2 – Influent Pump Station; 3 – Preliminary Treatment; 4 – Equalization; 5 – Extended Aeration Activated Sludge; 6 – Secondary Clarifier; 7 – Chlorination; 8 – Aerobic Digestion; 9 – Belt-Filter Press; 10 – Hauling and Land Filling* (Jafarinejad, 2017)

For instance, LOR removal rates in the German WWTPs vary around 50-80% with the mean of 50% removal rate (Gurke et al., 2015). In the aforementioned WWTP, the wastewater is first mechanically treated with screens and a grit chamber, followed by biological removal of nitrogen and chemical precipitation of phosphorus. A Japanese WWTP in Kumamoto analyzed the fate of pharmaceuticals after activated sludge treatment (Matsuo et al., 2011). The removal efficiency of losartan was 33% and the effluent output of LOR was 5.17-18 g day^{-1}. It was found that LOR removal efficiency tends to increase when water temperature is higher and sludge retention time is longer.(Matsuo et al., 2011)

Membrane bioreactors (MBR) have shown higher efficiency than CAS, because they combine biological treatment with membrane filtration (Petrovic et al., 2013) In addition, the sludge retention time is usually longer and the diversity of microorganisms is higher in MBR. Therefore, the ability of adaption of specific microorganisms to degrade persistent microcontaminants in MBR is greater than in CAS (Das et al., 2012). In a comparative study of CAS and MBR processes efficacy, it was found that only one out of ten compounds had a higher removal rate in CAS process. MBRs have higher biomass concentration, which decreases the food to microorganisms ratio (F/M). This can help microorganisms to metabolize otherwise poorly degradable compounds and therefore explain why removal of some EC-s is more efficient in MBRs than in CAS processes (Verlicchi et al., 2012).

Different carriers for biofilm were tested for removal of pharmaceuticals from wastewater (Muter et al., 2017). Plastic units and three types of ceramic carriers were tested with and without biofilm as shown in Table 1.2. All the carriers demonstrated almost no effect on LOR removal and negative removal effect for 7-day experiment with carriers covered with biofilm. This could point to reversible adsorption and therefore indicate unsuitability of biological methods for LOR removal (Muter et al., 2017).

Table 1.2 Losartan removal efficacy with different type of carriers (Muter et al., 2017, modified)

	Without biofilm		With biofilm	
	2 h	7 d	2 h	7 d
Plastic	0.04±0.04	0.00±0.09	0.07±0.14	−0.06±0.04
Oxide ceramics	0.08±0.05	0.01±0.06	0.17±0.18	0.04±0.08
Ceramic beads	−0.05±n.d.	0.01±0.03	0.17±0.12	−0.01±0.14
Ceramic rods	0.00±0.02	−0.04±0.08	0.06±0.03	−0.07±0.07

*n.d. – no data

Collado et al. (2014) demonstrated variations in removal rates of LOR in different seasons, showing negative removal rates for winter months and efficient removal

rates for summer months (up to 80%). This uneven removal efficacy places LOR into low removal rate category substances and suggest the use of tertiary treatment to enhance the degradation. They tested UV as tertiary treatment and it proved not to be successful for LOR removal by itself resulting in additional removal of 15% (Collado et al., 2014).

1.2.2 Losartan removal by separation processes

During the biological treatment, LOR is adsorbed on different substrates during the process. This is well demonstrated by the fact that on-site sewage treatment facilities (OSSFs) at WWTPs have found LOR in 76% of samples taken from activated sludge (Wu et al., 2012). It was found that adsorptive removal by sand filtration has a low removal efficiency (<30%) for LOR (Wu et al., 2012). In a typical WWTP, the micropollutants can be adsorbed on suspended particles, activated sludge, dissolved humic substances and filtration membranes (Das et al., 2012). In a study comparing different sorbents, sand was the least effective sorbent for LOR, removing it with 10% efficacy (Zhang et al., 2019). Lignite and xylit had an efficiency <80%, while GAC and GAC/Polonite had an efficiency close to 100%.

To evaluate the efficacy of filter beds for removing pharmaceuticals from the sewage, a study was conducted with three different set-ups (Blum et al., 2019). Accordingly, the filter bed was filled with sand, with sand and crushed and washed hardwood-derived biochar or with gas concrete and the abovementioned biochar. The removal efficiency for LOR was 64±14%, 77±10% and 49±21%, respectively. The removal rate for LOR carboxylic acid, which is a physiologically active metabolite of LOR, was 35±9%, 37±11% and 16±12%.

1.2.3 Losartan degradation in chemical oxidation processes

Chemical oxidation is a potent way to degrade organic compounds into less toxic and more biodegradable products. There is a wide range of oxidation technologies using chemical oxidants for water and wastewater treatment; the most common are ozone, hydrogen peroxide, chlorines and permanganate (Tünay, 2010). Many AOPs combine strong oxidant with a catalyst and/or radiation to produce sufficient amount of hydroxyl radicals (HO$^\bullet$) (Table 1.3) (Cuerda-Correa et al., 2020).

Table 1.3 Classification of AOPs (Cuerda-Correa et al., 2020, modified)

AOP	Source of radicals
O_3 based processes	O_3 O_3/UV O_3/H_2O_2 O_3/H_2O_2/UV
H_2O_2 based processes	H_2O_2/UV H_2O_2/Fe^{2+} (Fenton) H_2O_2/Fe^{3+} (Fenton-like) H_2O_2/Fe^{2+}/UV (Photo-Fenton)
Photocatalysis	TiO_2/UV TiO_2/UV/H_2O_2
Sonochemical oxidation	Ultrasounds 20kHz–2MHz
Electrochemical oxidation	Electricity, 2-20A

Advanced oxidation processes such as ozonation, use of transitional metal catalyst, electrochemical degradation and photo-electro-Fenton processes have been tested for LOR degradation.

Bolattin et al (2015) used Cu(III) complex due to the involvement of Cu(III) in many biological electron transfer reactions. It is also used in oxidation-kinetics studies of various inorganic and organic substrates. The specific complex used was diperiodatocuprate(III) (DPC). The addition of Ru(III) catalyst in trace amounts improved the reaction efficacy by a factor of seven compared to the uncatalyzed reaction. Thus, the slow reaction between DPC and LOR was effectively catalyzed by Ru(III) in aqueous alkaline medium at room temperature (Figure 1.5). The main active species of DPC proved to be monoperiodatocuprate(III), while $[Ru(H_2O)_5OH]^{2+}$ was likely the active species of catalyst. The stoichometry for the reaction was 1:2 – one mole of LOR needs two moles of DPC.
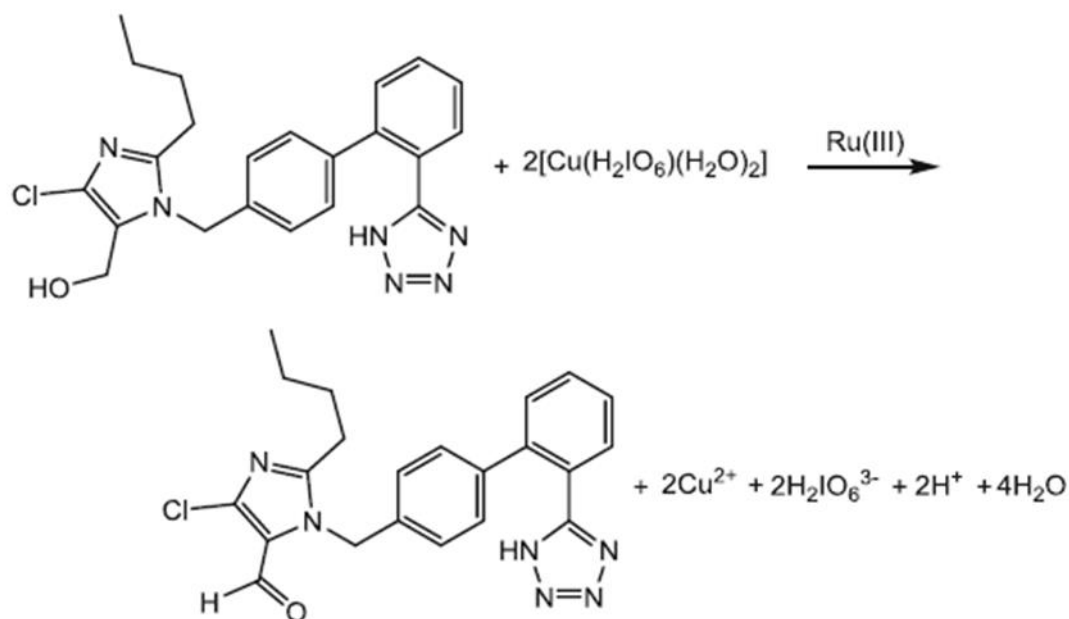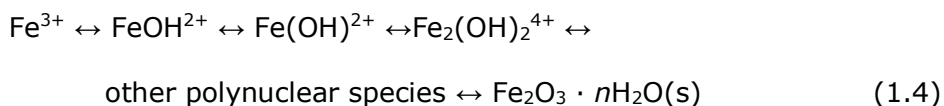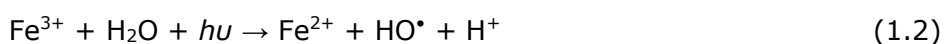
Figure 1.5. Reaction of losartan and Cu(III) complex over Ru(III) catalyst (Bolattin et al., 2015)

The Fenton process uses H_2O_2 decomposition with Fe^{2+} as catalyst to enhance production of $HO^\bullet$ radicals in acidic conditions (Eq. 1.1). The addition of ultraviolet (UV) radiation to the Fenton system, the so-called photo-Fenton process, increases the overall oxidation efficiency, since it produces additional $HO^\bullet$ radicals (Eq. 1.2) (Tünay, 2010). The formed Fe^{2+} reacts with H_2O_2 and produces more $HO^\bullet$ radicals via the Fenton reaction. If UVC light is used, the photolysis of H_2O_2 also contributes to $HO^\bullet$ production (Eq. 1.3). The main limitation for the Fenton process is the necessity for acidic pH (3-5) values and the remaining iron mainly in the form of hydrous ferric oxyhydroxides has to be removed from the solution (Eq. 1.4) (Sylva, 1972).

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + HO^\bullet + OH^- \tag{1.1}$$

$$Fe^{3+} + H_2O + hu \rightarrow Fe^{2+} + HO^\bullet + H^+ \tag{1.2}$$

$$H_2O_2 + hu \rightarrow HO^\bullet + HO^\bullet \tag{1.3}$$

$$Fe^{3+} \leftrightarrow FeOH^{2+} \leftrightarrow Fe(OH)^{2+} \leftrightarrow Fe_2(OH)_2^{4+} \leftrightarrow$$

$$\text{other polynuclear species} \leftrightarrow Fe_2O_3 \cdot nH_2O(s) \tag{1.4}$$

The oxidation of LOR aqueous solution by photo-electro-Fenton processes employing a dimensionally stable anode-gas diffusion electrode system with LED-type radiation was also studied (Martínez-Pachón et al., 2019). The system was used in the presence of NaCl. To maintain the performance of the Fenton reaction at a near-

neutral pH value, organic acids were used as complexing agents of iron ions. The results indicated that LOR was completely degraded after 90 min treatment at 3.42 mA cm^{-2} with addition of organic acid at unmodified pH or at pH 3.0 (Figure 1.6). Comparison of light sources indicated that the white-LED proved to be very efficient, and thus 100% LOR decomposed after 20 min of treatment (Figure 1.7).
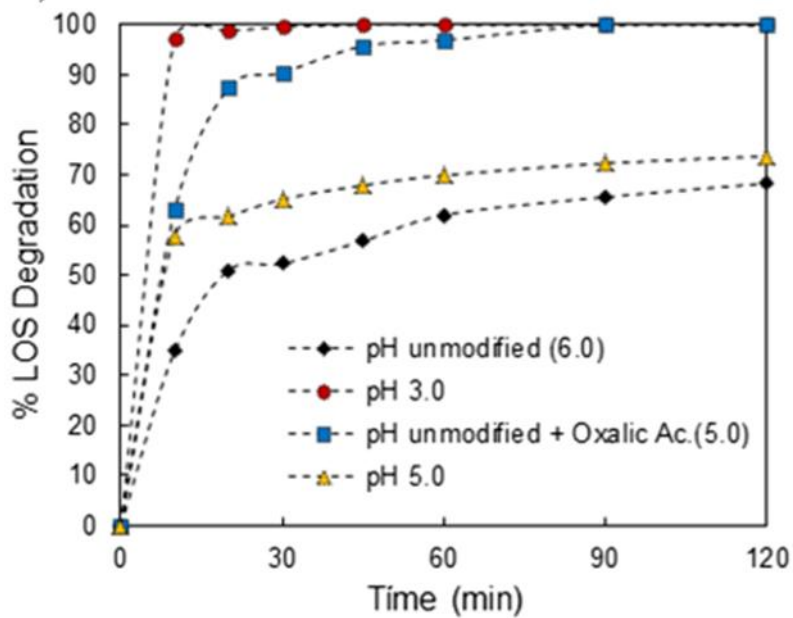

Figure 1.6 Effect of pH and organic acid on degradation of losartan (Martínez-Pachón et al., 2019)
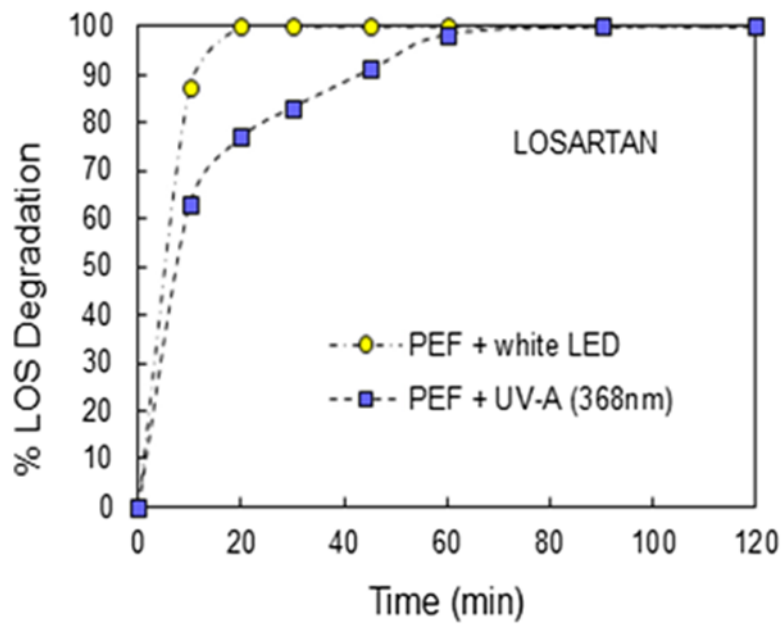

Figure 1.7 Effect of type of lamp on the degradation of losartan (Martínez-Pachón et al., 2019)

TOC removal by biological degradation test of LOR was conducted for treated and untreated solutions. Thus, by day eight the untreated solution showed 11% of TOC removal, whereas 60 min photo-electro-Fenton treatment had 61% removal by day six and complete removal by day eight. For LOR solution pre-treated with 300 min photo-electro-Fenton system the removal by day four was 36% and 100% by day six (Martínez-Pachón et al., 2019)

Guateque-Londoño et al (2020) investigated the mechanisms involved in LOR degradation by UVC-activated persulfate process in distilled water, including the evaluation of the target compound decomposition and mineralization, the evolution of toxicity, and the impact of the matrix, namely synthetic fresh urine, (Figure 1.8). The efficacy of UV/PS systems was compared with the results of TiO_2 photocatalysis. In addition, LOR degradation with UVC photolysis and PS oxidation were compared with the efficacy of UVC/PS and UVC/PS/isopropanol (IPA) systems (Figure 1.9). The initial LOR concentration was 43.38 µM. The results indicated that the UVC/PS system proved the most effective process among the studied for the target compound decomposition (Guateque-Londoño et al., 2020).

The application of ozonation proved effective in decolorization, deodorization, disinfection and removal of pharmaceuticals and other persistent organic (micro)pollutants (Paucar et al., 2019; Shriram & Kanmani, 2014). The removal efficiency is even higher when ozone is combined with H_2O_2 and/or UV (Tünay, 2010). The reaction mechanism for the O_3/H_2O_2 system is described by Eqs. (1.5-1.9) (Hernandez et al., 2002).

$$H_2O_2 + H_2O \leftrightarrow H_3O^+ + HO_2^- \tag{1.5}$$

$$O_3 + HO^- \rightarrow HO_2^- + O_2 \tag{1.6}$$

$$O_3 + HO_2^- \rightarrow HO^\bullet + O_2^{\bullet-} + O_2 \tag{1.7}$$

$$O_3 + O_2^{\bullet-} \rightarrow O_3^{\bullet-} + O_2 \tag{1.8}$$

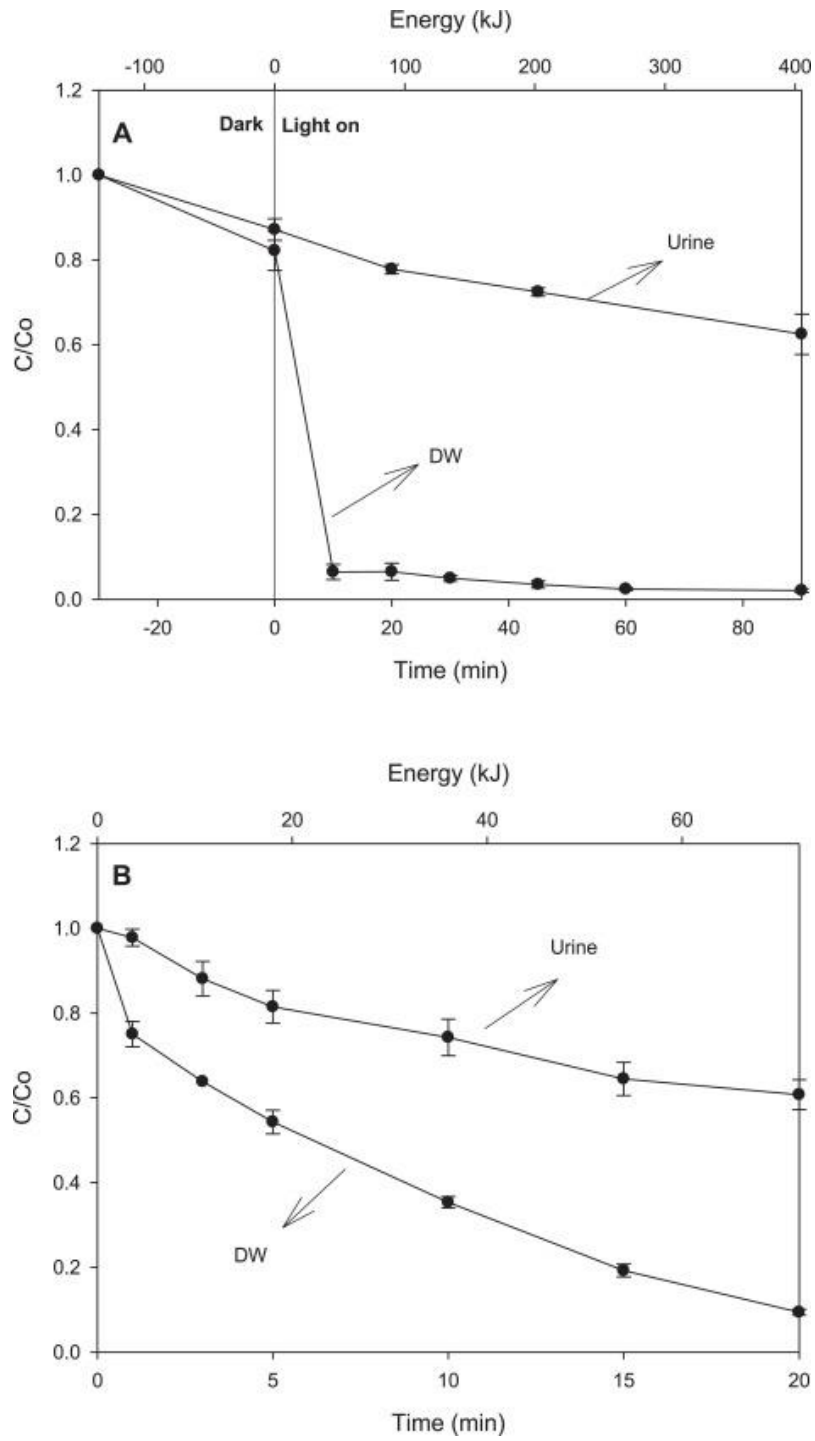$$O_3^{\bullet-} + H_2O_2 \rightarrow HO^\bullet + OH^- + O_2 \tag{1.9}$$

Figure 1.8 Comparison of LOR degradation in distilled water (DW) and simulated fresh urine: A: TiO2 photocatalysis; B: UVC/PS process. (Guateque-Londoño et al., 2020)
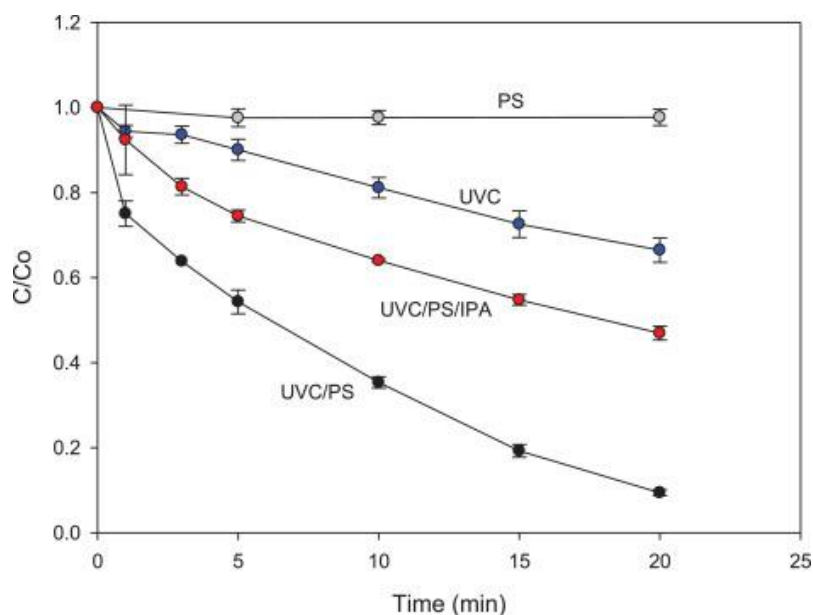
Figure 1.9 Degradation of LOR by the UVC/PS process (Guateque-Londoño et al., 2020)

In the case of UV/O_3 process, the main reactions can be described by Eqs. (1.10, 1.3, 1.11). Accordingly, the photolysis of O_3 generates H_2O_2 and, as a result, the O_3/UV process involves all mechanisms present in the O_3/H_2O_2 and UV/H_2O_2 system (Homem et al., 2010).

$$O_3 + H_2O + hv \rightarrow H_2O_2 \qquad (1.10)$$

$$2O_3 + H_2O_2 \rightarrow 2HO^{\bullet} + 3O_2 \qquad (1.11)$$

The application of ozonation and different combined ozone-based processes, such as O_3/UV, O_3/H_2O_2, O_3/UV/H_2O_2 for LOR decomposition in aqueous solution resulted in complete target compound degradation during a 5-minute treatment (Azuma et al., 2019). However, no LOR mineralization was observed during oxidation experiments, indicating the presence of stable by-products most likely in the form of organic acids.

Also, electrochemical degradation of LOR by electro-oxidation with boron-doped diamond electrode was studied (Salazar et al., 2016). The results demonstrated that at least 50% LOR mineralization was attained in 360 minutes. Four intermediates were detected during the oxidation, but they also degraded during the reaction period.

1.3 Sulfate radical-based oxidation processes

Persulfates are relatively new oxidants in comparison with previously listed, but gaining more interest, especially in the Fenton-like processes (Lee et al., 2018). Activated persulfate systems have been used for *in-situ* soil remediation to degrade pollutants such as diesel, polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), and total petroleum hydrocarbons (TPH) (Zhou et al., 2019). Pharmaceuticals and emerging pollutants have been gradually added to the list of potential targets for degradation with activated persulfate processes mainly in water matrices. Peroxydisulfate (PDS) has become widely used as oxidant in water and soil remediation due to its aqueous stability, efficacy and moderate cost (Zhou et al., 2019).

Peroxydisulfuric acid ($H_2S_2O_8$) can be formed in electrolysis of sulfate salt. The resulting persulfate salt is almost nonhygroscopic (Wacławek et al., 2017). Persulfate ($S_2O_8^{2-}$) is a powerful oxidant (E^0=2.01 V) with molecular weight 192.13 g mol^{-1} (NIH U.S. National Library of Medicine). Persulfates are usually applied in the form of sodium peroxydisulfate (PDS) salt, and triple potassium peroxymonosulfate (PMS) salt (Moreno-Andrés et al., 2019). Persulfate occurs also as ammonium salt, but is not used for *in-situ* chemical oxidation due to its low solubility and residual ammonium generation (Wacławek et al., 2017).

Sodium PDS salt ($Na_2S_2O_8$) is the first choice for *in-situ* chemical oxidation due to its high solubility and safe reaction products (Wacławek et al., 2017). PDS is stable at room temperature and has a low efficacy for water treatment on its own, therefore it needs activation for generating sulfate radicals ($SO_4^{\bullet-}$) (van Eldik & Hubbard, 2017). The activation of PDS could be done by different techniques, e.g. heat, UV radiation, transition metals or strong oxidants addition (Figure 1.10). The most important aspect of activation is to generate highly reactive species, which can then effectively degrade (micro)pollutants (Wacławek et al., 2017). Sulfate radicals can possess higher redox potential, higher selectivity and longer half-life in comparison with hydroxyl radicals based on activation methods. (Sbardella et al., 2020).
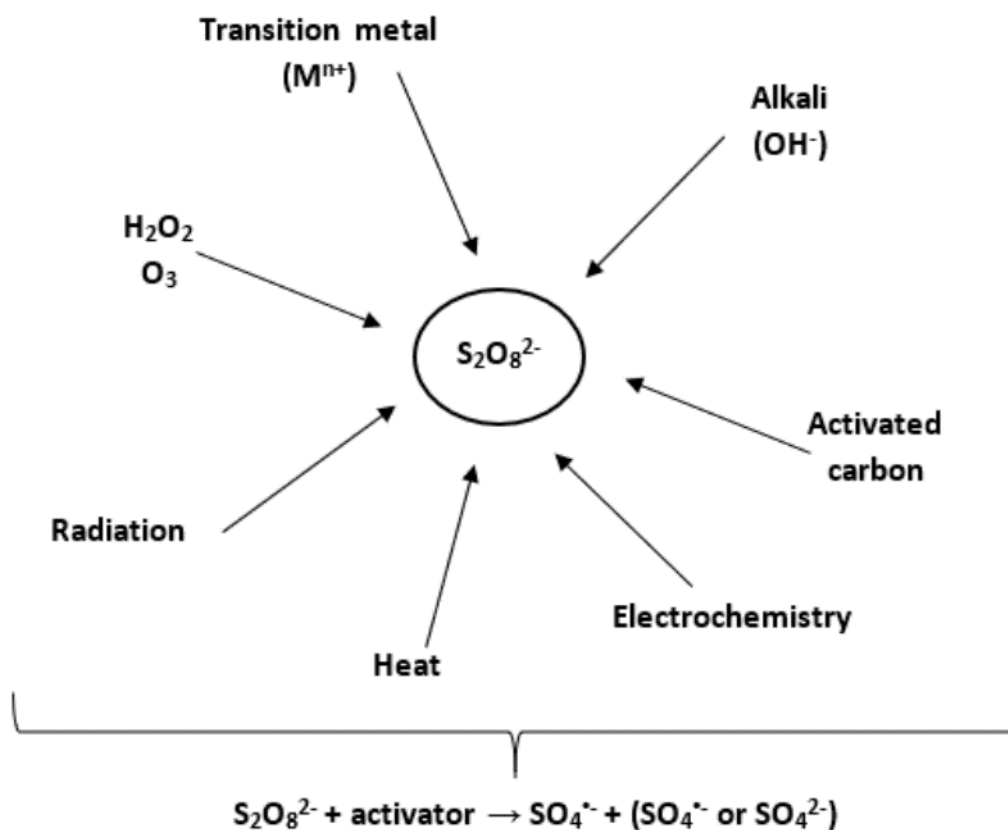
Figure 1.10 Activation methods of persulfate (Kattel, 2018)

$SO_4^{\bullet-}$ are formed during the activation of PDS, but $HO^\bullet$ radicals are also present in the system due to reactions with water, and the prevalence of any of them depends on the pH of the solution (Sun & Wang, 2015). Sulfate radicals have higher redox potential (E^0=2.60 V) at neutral pH whereas $HO^\bullet$ radicals (E^0=1.80-2.70 V) (Han et al., 2019). $SO_4^{\bullet-}$ are more selective and stable and have a longer half-life in comparison to $HO^\bullet$ radicals, and therefore sulfate radicals are more appropriate for *in-situ* chemical oxidation (Moreno-Andrés et al., 2019). To achieve the formation of $SO_4^{\bullet-}$ as the main oxidizing species the reaction can be performed through transition-metal catalysis. For instance, divalent cobalt was the most effective catalyst for PMS and Fe^{2+} is most commonly used for PDS, similarly to the Fenton reaction (Wacławek et al., 2017).

Hydrogen peroxide (H_2O_2) is a powerful oxidant used in the treatment for reduced sulfur species, cyanides, and organic compounds. H_2O_2 is a direct source for $HO^\bullet$ radicals (Figure 1.11). Hydrogen radicals are considered optimal for degradation, because they do not produce additional waste, they have a short half-life and are non-toxic and they are not corrosive to equipment. (Cuerda-Correa et al., 2020) The $HO^\bullet$ radicals are nonselective and react rapidly with many different substances. They

degrade organic pollutants through four basic pathways: addition of radical, abstraction of hydrogen, transfer of electron, and combination of radicals (Deng & Zhao, 2015).
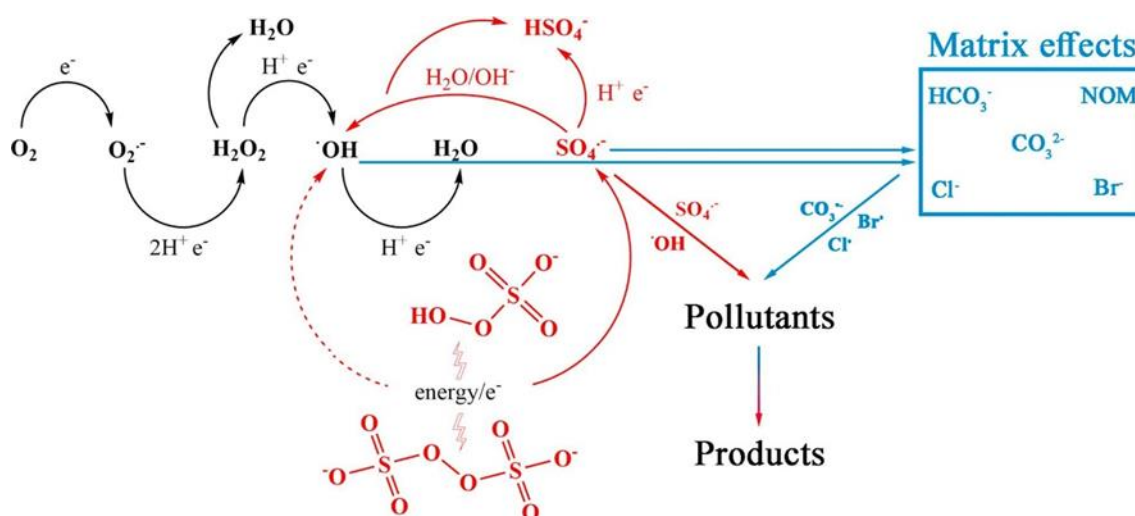

Figure 1.11 Activation of persulfate and electron transfers (Wacławek et al., 2017)

Combination H_2O_2 with PDS and iron together with UV radiation effectively produces radicals necessary for degradation of pollutants (Tünay, 2010). The activation of dual PDS/H_2O_2 system with a transitional metal such as iron (Fe^{+2}) will in addition to generating $SO_4^{\bullet-}$ radicals (Eq. 1.12) also produce $HO^{\bullet}$ radicals (Eqs. 1.13 and 1.1). Overall, the application of this system increases the extend of organic pollutants mineralization (Monteagudo et al., 2015).

$$S_2O_8^{2-} + Fe^{2+} \rightarrow Fe^{3+} + SO_4^{\bullet-} + SO_4^{2-} \qquad (1.12)$$

$$S_2O_8^{2-} + 2H_2O \rightarrow 2HSO_4^- + H_2O_2 \qquad (1.13)$$

In general, the efficiency of pollutants degradation by AOPs depends on the scavenging rate of the water matrix and the kinetics of the radical reaction with the target compound. The composition of the water matrix is especially important when it contains chlorine ions and therefore form chlorinated products in the reaction (Wacławek et al., 2017).

PDS and PMS can also be activated with UV, which is practical due to the already existing use of ultraviolet radiation at MWWTPs (Han et al., 2019; Wang & Wang, 2018). Therefore, UV can be used for disinfection and sterilization in parallel with activation of PDS for effective removing of organic micropollutants (Han et al., 2019). Activation of PDS is usually carried out by UVC radiation (λ=254 nm) due to its high energy and PDS absorptivity (Eq. 1.14) (Monteagudo et al., 2015; Wang & Wang,

2017). UVC wavelengths are especially well absorbed by H_2O_2 resulting in effective $HO^\bullet$ generation (Eq. 1.3) (Matafonova & Batoev, 2018).

$$S_2O_8^{2-} + hu \rightarrow 2SO_4^{\bullet-} \qquad\qquad (1.14)$$

The addition of Fe^{2+} into AOP system can be beneficial in acidic conditions, where it has a catalytic effect on H_2O_2 decomposition and therefore activation of PDS. The synergistic effect of combined $PDS/Fe^{2+}/UV$ treatment may be much higher than the effectiveness of single treatment method (Table 1.4). Still the efficacy depends on the chemical structure and physical properties of the compound and treatment conditions (Monteagudo et al., 2015).

Table 1.4 Activated PDS-based processes with synergistic effect for carbamazepine removal (Monteagudo et al., 2015)

Single system	TOC removal, %	Combined system	TOC removal, %	Synergy
US*	15.3	PDS/US	26.4	36.74
UVC	15.7	PDS/UVC	21.4	20.09
Fe^{2+}	3.4	PDS/Fe^{2+}	16.0	70.00
H_2O_2	0.5	PDS/H_2O_2	17.5	89.14
PDS	1.4	PDS/Fe^{2+}/UV/US	76.4	54.31
		PDS/Fe^{2+}/UV/H_2O_2	82.9	74.66
		PDS/Fe^{2+}/UV/US/H_2O_2	87.7	58.60

US – ultrasound

Sonolysis is a relatively new method in the AOP family. The mechanism of sonolysis involves the generation of free radicals through cavitation generated by ultrasound. The application of combined persulfate-based systems for azorubine degradation has been studied (Chakma et al., 2017). The obtained results demonstrated that the addition of Fe^{2+} to the UVC/PDS system had an adverse effect on the target compound degradation efficacy mainly due to scavenging of sulfate radicals by ferrous ions. In turn, the combined UVC/PDS/US system proved the most effective technique for azorubine decomposition in water (Figure 1.12).
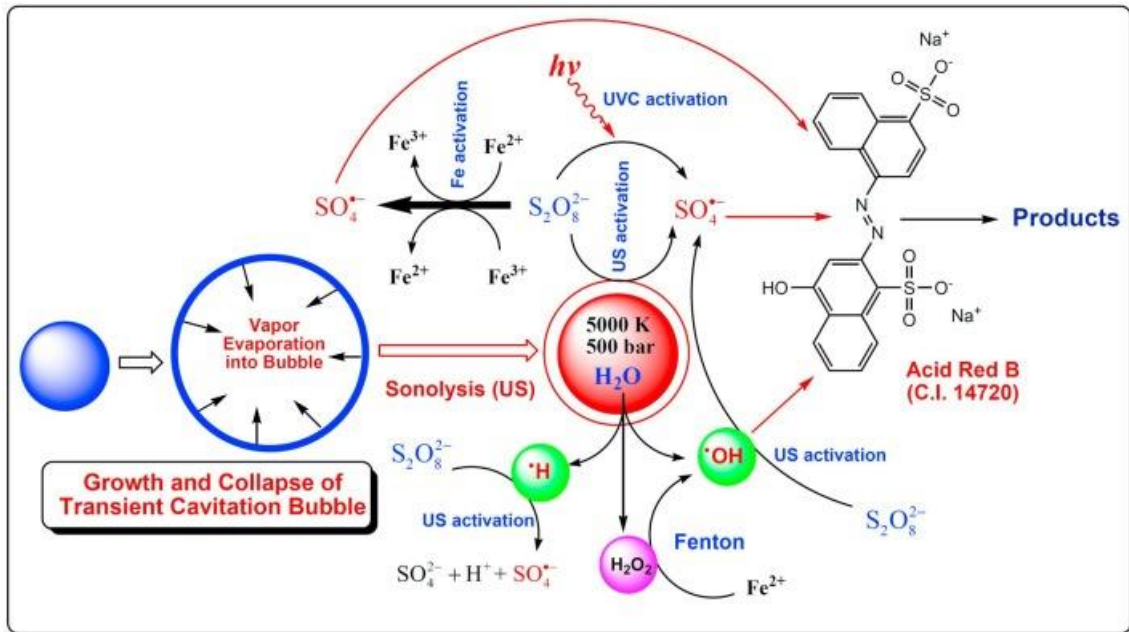
Figure 1.12 Mechanistic synergies in ultrasound-assisted persulfate based decolorization of azorubine dye (Chakma et al., 2017)

The application of UV/H_2O_2 and UV/PDS processes for sulfamethazine (SMT) degradation has been studied (P. Gao et al., 2012). The efficacy of SMT removal was low with only PDS oxidation or UV photolysis and resulted in 15.1% and 22.1%, respectively. In turn, the use of UV/H_2O_2 and UV/PDS oxidation allowed to achieve 87.5% and 96.5% LOR removal, respectively (Gao et al., 2012). Similarly, the photodegradation of piroxicam by UVC photolysis led to a 9% degraded in 30 min. The addition of PDS into the system resulted in complete removal of the target compound in less than min at optimized oxidant concentration (Frontistis, 2019).

1.4 Aim of the study

The current work provides an overview of the properties of losartan, its occurrence and impact in the environment along with its removal processes. The aim of the study was to examine and compare the efficacy of losartan degradation and mineralization by UV/H_2O_2, UV/PDS, UV/H_2O_2/Fe^{2+} and UV/PDS/Fe^{2+} systems in water matrices. In addition, the effect of H_2O_2, PDS, and Fe^{2+} concentrations on the oxidation efficiency of the target compound by the selected UV-induced systems was assessed. The impact of groundwater composition on the efficacy of LOR degradation was also evaluated.

2. MATERIAL AND METHODS

2.1. Chemicals

Losartan potassium salt ($C_{22}H_{22}ClKN_6O$, ≥99%) sodium persulfate ($Na_2S_2O_8$, ≥99%), sodium sulfite (Na_2SO_3, ≥98%), ferrous sulfate heptahydrate ($FeSO_4 \cdot 7H_2O$, ≥99%), potassium iodide (KI, ≥99%) and sodium hydrogen carbonate ($NaHCO_3$, 99%) were supplied by Sigma-Aldrich. Ethanol (C_2H_6O, EtOH, 99%) was obtained from Merck KGaA.

All the chemicals were of analytical grade used without further purification. All stock solutions were prepared in twice-distilled water (>18.2 MΩ cm) or in ultrapure water (UW) (Millipore Simplicity®UV System, Merck).

Groundwater (GW) sample was collected from a 19m deep borehole (Harjumaa, Estonia) and stored 4°C. The groundwater sample (real water matrix) was used without preceding purification for LOR degradation trials. The main parameters of groundwater samples are presented in Table 2.1.

Table 2.1 Chemical composition and main parameters of GW sample

Parameter	Unit	Value
pH		7.71
Alkalinity	$mgCaCO_3$ L^{-1}	350
Conductivity	µS cm^{-1}	820
Total organic carbon	mg L^{-1}	2.21
Fe^{2+}	mg L^{-1}	0.012
Total Fe	mg L^{-1}	0.175
Cl^-	mg L^{-1}	83.54
NO_3^-	mg L^{-1}	2.08
SO_4^{2-}	mg L^{-1}	33.95

2.2. Experiment procedure

The laboratory-scale experiments on LOR photochemical oxidation were performed in batch mode at ambient room temperature (22±1°C). LOR solutions (40 µM, 0.8 L) were treated in a 1.0-L cylindrical glass reactor for 2 h with a permanent agitation speed (~400 rpm). The agitation speed was selected to be sufficient for uniform distribution and complete dissolution of the Fe^{2+} activator. The treatment trials were carried out in

non-buffered solutions at pH 6.1±0.2 (in ultrapure water) and 7.7±0.2 (in groundwater). The ferrous ion activator, if necessary, was added first and, after its complete dissolution, the oxidation was initiated by adding oxidant (persulfate or hydrogen peroxide). Finally, the exposure to the UVC source, a low pressure mercury germicidal lamp (11 W, Philips TUV PL-S) located in a quartz tube inside the reactor, was provided. Notably, the UVC lamp was turned on at least 5 min prior the experiment to provide a constant output. The average irradiance entering the solution in the reactor measured by spectrometer (Ocean Optics USB2000+) equipped with SpectraSuite software was 2.7 mW cm^{-2}. A water cooling jacket was used to keep the constant temperature in the reactor (Figure 2.1).
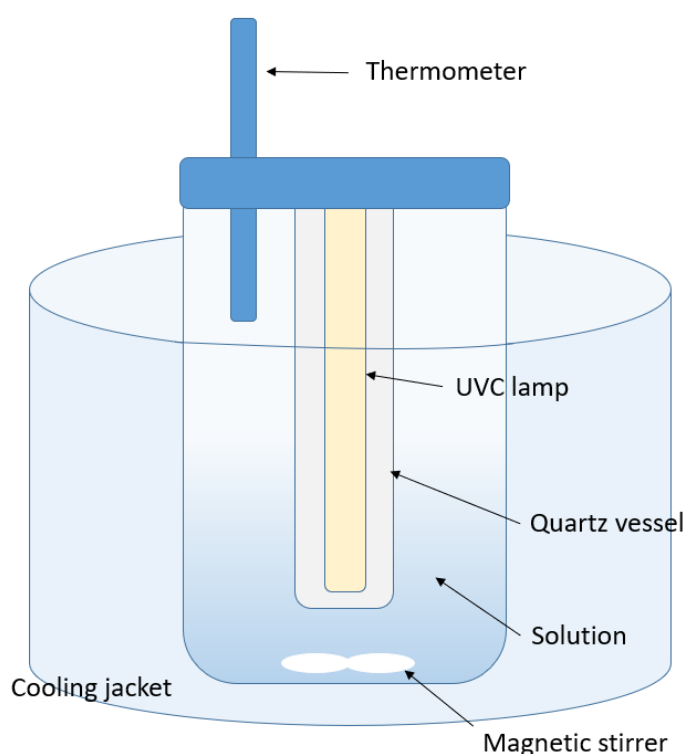

Figure 2.1. Laboratory-scale reactor for photochemical oxidation

The LOR/H_2O_2 and LOR/PDS molar ratios of 1/1, 1/5, 1/10, 1/20, corresponding to a molar concentration of oxidants 40, 200, 400 and 800 µM, respectively, were studied. The molar concentration of activator was in range of 20-80 µM in the UVC/H_2O_2/Fe^{2+} and UVC/PDS/Fe^{2+} systems. Samples for subsequent analyses were withdrawn at pre-determined time intervals. The oxidation quenching was done by the addition of ethanol (sample/ethanol volume ratio of 10/1) for high-performance liquid chromatography (HPLC) and by the addition of Na_2SO_3 ([oxidant]$_0$/[SO_3^{2-}] molar ratio of 1/10) for total organic carbon (TOC) analysis. All experiments were duplicated and the obtained results

are presented as the mean with a standard deviation of at least two parallel repeats less than 5%.

2.3. Analytical methods

The target compound concentration was quantified using a HPLC combined with diode array detector (HPLC-PDA, Shimadzu, Japan) equipped with a Phenomenex Gemini (150 x 2.0 mm, 1.7 mm) NX-C18 (110 Å, 5 µm) column. The analysis was performed using an isocratic method with a mobile phase mixture of 60% formic acid (0.3%) aqueous solution and 40% acetonitrile (with 0.3% formic acid). The flow rate was kept at 0.2 mL min^{-1}. Samples (75 µL) were analyzed at $\lambda=210$ nm.

The initial and final pH was measured using a digital pH/Ion meter (Mettler Toledo S220). The electrical conductivity of groundwater samples was measured using a digital EC meter (HQ 430d flexi, HACH Company).

The total organic carbon was measured by a TOC analyzer multi N/C® 3100 (Analytik Jena). The concentration of anions in groundwater was measured using ion chromatography (IC) with chemical suppression of the eluent conductivity (761 Compact IC, Metrohm Ltd.).

The residual H_2O_2 concentration in the treated samples (4.5 mL) was measured spectrophotometrically at $\lambda=410$ nm with titanium sulfate by a H_2O_2-Ti^{4+} complex formation (Eisenberg, 1943) (Genesys 10S, Thermo Scientific).

The measurement of residual PDS concentration in the treated samples (0.4 mL) was done spectrophotometrically (Genesys 10S, Thermo Scientific) at $\lambda=352$ nm by an excess KI reaction with PDS towards the formation of I_2 (Liang et al., 2008). The residual concentration of PDS was determined by using the standard multipoint calibration.

3. RESULTS AND DISCUSSION

First, the efficiency of direct UVC photolysis for LOR decomposition was evaluated. The obtained results were compared with the efficacy of UVC-activated persulfate and hydrogen peroxide systems at a LOR/oxidant molar ratio of 1/5 in LOR decomposition in ultrapure water (Figure 3.1). Both the direct UV photolysis and studied UVC/PS and UVC/H_2O_2 systems proved to be effective and resulted in more than 95% of LOR degradation in 60 min.
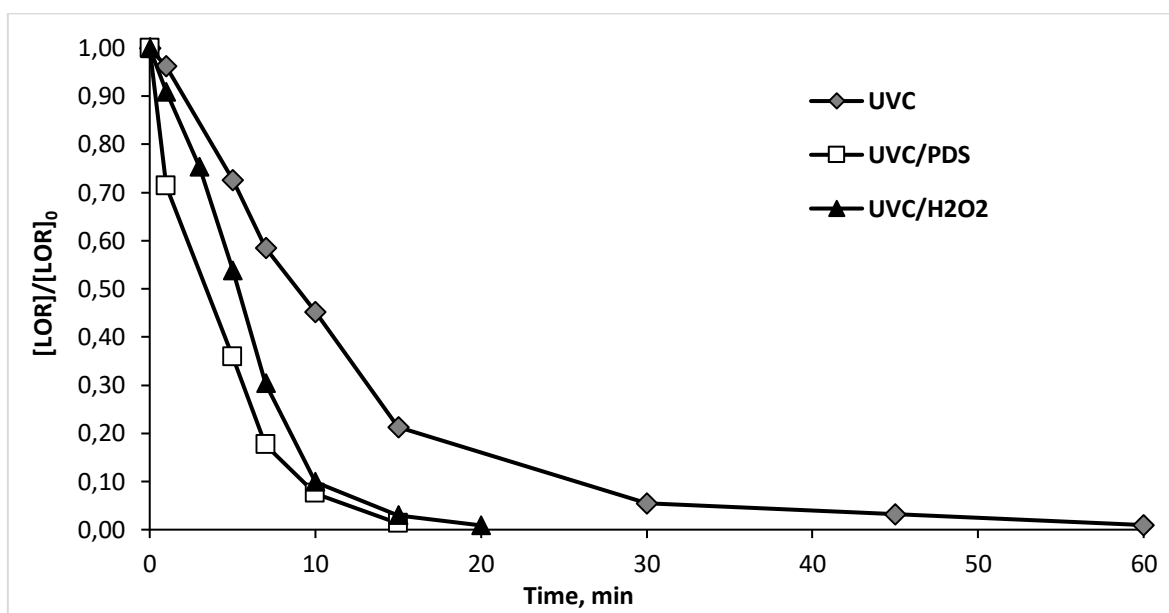

Figure 3.1 LOR degradation by the UVC photolysis, UVC/H_2O_2 and UVC/PDS systems: C_t/C_0 versus time ([LOR]$_0$ = 40 μM, [PDS]$_0$ = [H_2O_2] = 200 μM)

In addition, the obtained results clearly indicated that LOR degradation in the UV-activated systems followed a pseudo-first order kinetics law ($r^2 \geq 0.95$) and may be described with regard to the LOR concentration through Eq. (3.1).

$$\frac{dC_{LOR}}{dt} = -k_{abs} \times C_{LOR}$$ (3.1.)

where k_{obs} is the observed pseudo-first-order rate constant.

Blank PDS and H_2O_2 oxidation experiments were carried out without UVC radiation addition at a LOR/oxidant molar ratio of 1/10. The results showed negligible LOR degradation efficiency along with 99% residual oxidant concentration remaining in both systems after 2 hours of treatment. In contrast, the application of direct UVC photolysis indicated complete degradation of the target compound with k_{obs} of 0.081 min^{-1} (Figure 3.2). However, after UVC photolysis, a low LOR mineralization was observed (TOC

removal of 8%), which indicates the formation of stable by-products. This is consistent with the results of other studies where direct UV photolysis, as well as non-activated PDS and H_2O_2 systems, showed little or limited effect on the decomposition and/or mineralization of the target compounds (Guateque-Londoño et al., 2020; Martínez-Pachón et al., 2019).
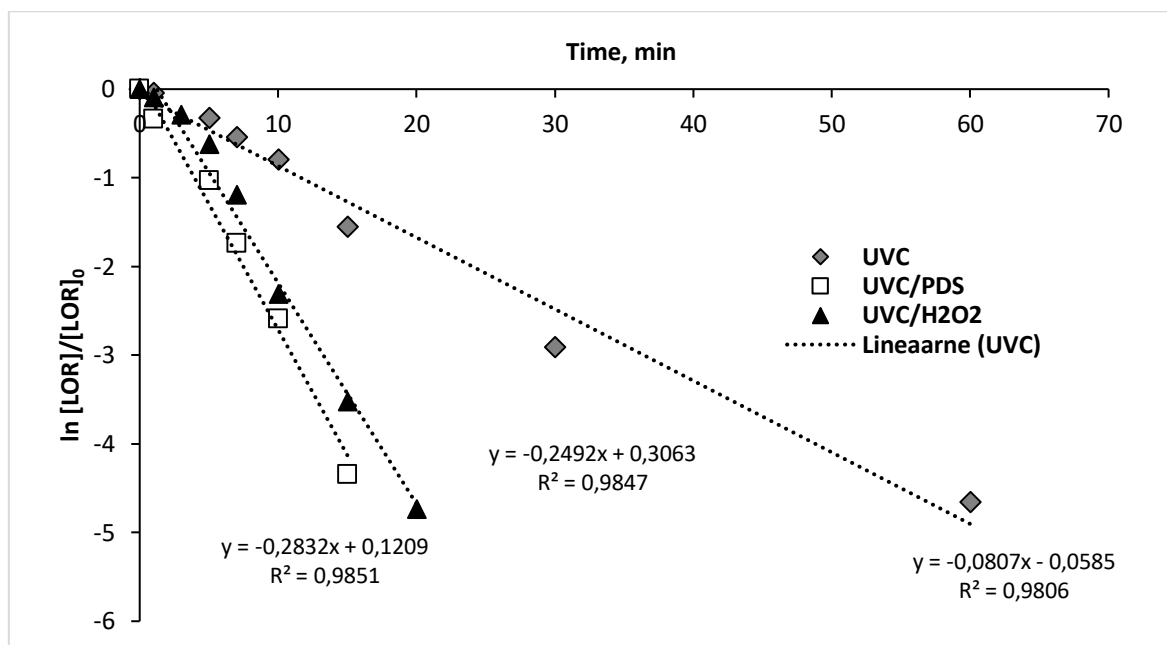

Figure 3.2 LOR degradation by the UVC photolysis, UVC/H_2O_2 and UVC/PDS and systems: plotting of function ln (C_t/C_0) for k_{obs} values calculation through linear regression ([LOR]$_0$ = 40 µM, [PDS]$_0$ = [H_2O_2] = 200 µM)

3.1. UVC photolysis, UVC/PDS and UVC/H_2O_2 systems for LOR decomposition

The effect of oxidant dosage on the performance of LOR decomposition in UVC/oxidant systems was studied at LOR/oxidant molar ratios of 1/1, 1/5, 1/10 and 1/20 (Figures 3.3 and 3.4). Regardless of the oxidant used, increasing the dose of the oxidizing agent used led to a more rapid decomposition of the target compound in the UVC/oxidant system. A similar tendency was observed in the case of LOR mineralization by UVC-activated H_2O_2 and PDS systems. This observation can be explained by the reactions presented in Eqs. (1.3) and (1.14), where UVC radiation activates hydrogen peroxide and persulfate to form hydroxyl and sulfate radicals, respectively. Thus, increasing the dosage of the oxidant used in the UVC/oxidant system improves the removal of the target compound due to the more abundant formation of free radicals.
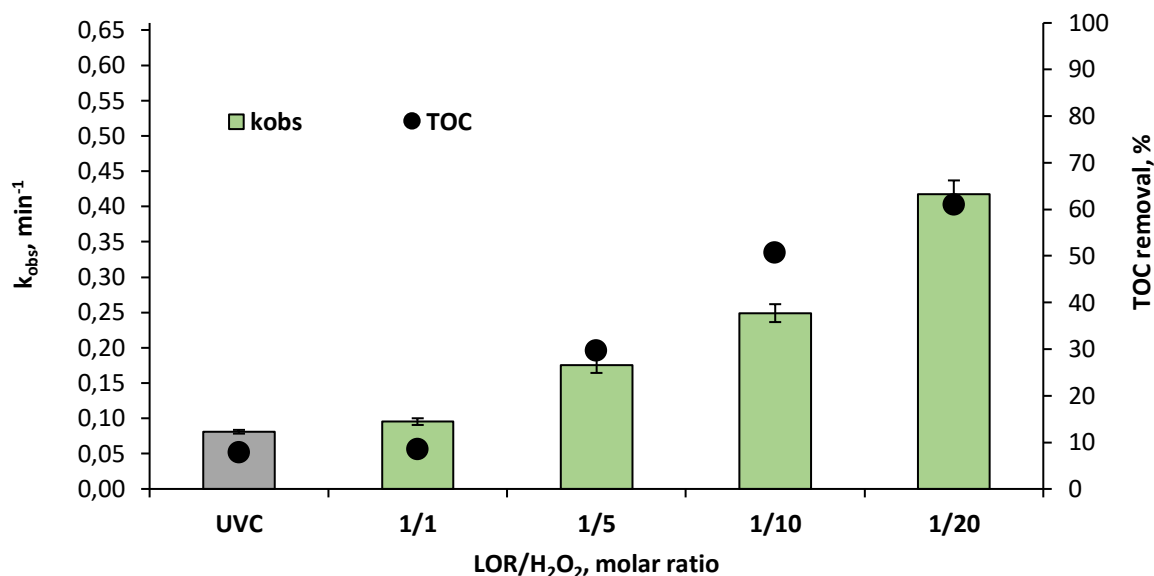
Figure 3.3 LOR degradation rate constants and TOC removal by the UVC photolysis and UVC/H_2O_2 system at different LOR/H_2O_2 molar ratios ([LOR]$_0$ = 40 μM, t = 2 h)
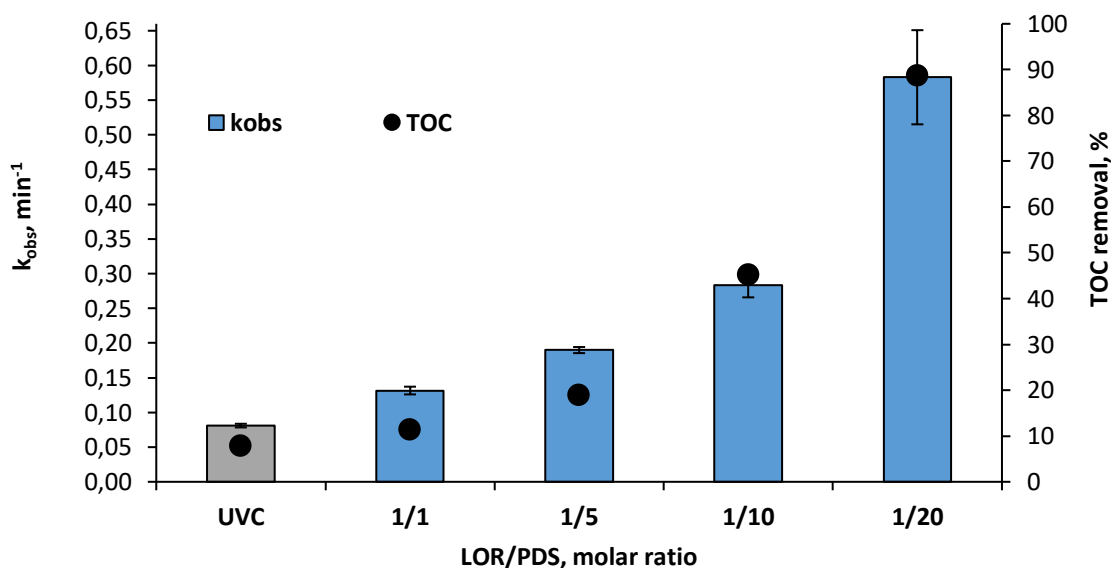
Figure 3.4 LOR degradation rate constants and TOC removal by the UVC photolysis and UVC/PDS system at different LOR/PDS molar ratios ([LOR]$_0$ = 40 μM, t = 2 h)

In the UVC/PDS systems, the degradation of LOR was in general faster than in the UV/H_2O_2 systems at the same oxidant concentration used. This indicates a higher efficiency of sulfate radicals in comparison with hydroxyl radicals for the degradation of LOR. Accordingly, the application of a LOR/oxidant molar ratio of 1/1 resulted in a k_{obs} value of 0.095 min^{-1} and 0.132 min^{-1} in the UVC/H_2O_2 and UVC/PDS systems, respectively. The five-fold higher concentration of oxidant used in the UV-activated H_2O_2

and PDS system led to a k_{obs} value of 0.175 min^{-1} and 0.19 min^{-1}, respectively. The highest observed rate constants were obtained at a LOR/oxidant molar ratio of 1/20 and were 0.418 min^{-1} and 0.583 min^{-1} for hydrogen peroxide and persulfate, respectively.

The LOR mineralization, determined by the TOC removal, increased faster with an increase in the dosage of oxidant in the UVC/H_2O_2 system compared to the UVC/PDS systems. However, at the highest oxidant concentration of 800 µM, the observed TOC removal was 61% and 89% in the UVC-activated H_2O_2 and PDS process, respectively, which indicates the inhibitory effect of excess hydrogen peroxide on the overall efficiency of LOR decomposition.

The efficacy of oxidant utilization in the studied UVC-activated hydrogen peroxide and persulfate systems was assessed as shown in Figure 3.5. In general, an increase in the used dosage of the oxidant has led to its more efficient utilization. For example, a 2-fold increase in the concentration of the oxidant from a LOR/oxidant molar ratio of 1/1 → 1/5 resulted in 10% → 20% of the consumed H_2O_2 and 28% → 49% of the consumed PDS in the UVC/H_2O_2 and UVC/PDS system, respectively. The differences between the oxidant utilization efficiency for H_2O_2 and PDS were smaller at higher molar ratios, namely, the oxidant utilization was 55% and 66% for the molar ratio of 1/10 and 81% and 93% for the molar ratio of 1/20 after a 2-h oxidation in the UVC/H_2O_2 and UVC/PDS systems, respectively. It is noteworthy that in the case of non-activated H_2O_2 and PDS oxidation of LOR in aqueous solution, the oxidants consumption was less than 2%.
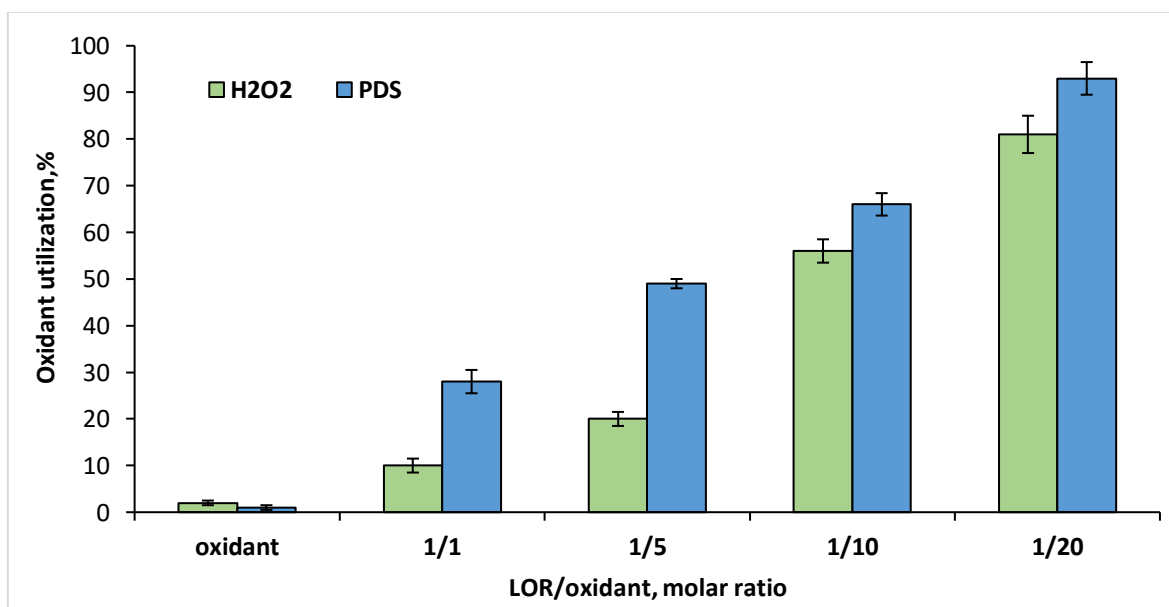

Figure 3.5 Oxidant utilization in the UVC/oxidant systems at different UVC/oxidant molar ratios ($[LOR]_0$ = 40 µM, t = 2 h)

To assess the changes in pH during LOR oxidation, the initial (pH_0) and final (pH_{120}) were measured for all systems studied, and the data obtained are presented in Table 3.1. The pH drop observed both in the UVC/H_2O_2 (pH_{120} = 4–4.7) and UVC/PDS (pH_{120} = 2.9–4.1) systems was mainly caused by the formation of acidic intermediates and acidity of the oxidants used.

Table 3.1 Residual pH (pH_{120}) after a 2-h oxidation in the UVC/H_2O_2 and UVC/PDS system at different molar ratios ($[LOR]_0$=40 µM)

Process	LOR/oxidant, molar ratio	pH_0	pH_{120}
UVC/H_2O_2	1/1	6.24	4.61
	1/5	6.12	4.25
	1/10	6.01	3.79
	1/20	6.16	4.70
UVC/PDS	1/1	6.29	4.13
	1/5	6.11	3.62
	1/10	6.18	3.21
	1/20	6.11	2.92

Based on the results obtained, it can be assumed that the UVC/PDS system has the greatest potential for both the degradation of LOR and its mineralization in aqueous solution.

3.2. $UVC/PDS/Fe^{2+}$ and $UV/H_2O_2/Fe^{2+}$ systems for LOR decomposition

The literature review has suggested a synergistic effect of using multi-component systems. To examine the possible improvement in LOR decomposition, the dual UV/Fe^{2+} activation of oxidants, corresponding to $UVC/H_2O_2/Fe^{2+}$ and $UVC/PDS/Fe^{2+}$ and systems, was evaluated. Accordingly, the effect of a fixed concentration of oxidant and activator on the effectiveness of $UVC/oxidant/Fe^{2+}$ systems in the degradation and mineralization of LOR was studied (Figures 3.6 and 3.7).

The blank H_2O_2/Fe^{2+} and PDS/Fe^{2+} oxidation (without UV light source) at a $LOR/oxidant/Fe^{2+}$ molar ratio of 1/10/1 resulted in 51% and 28% of LOR degradation, respectively, after a 2-h treatment. This is in good agreement with the available literature, where it was found that the addition of UVC radiation significantly improved the rate of contaminants decomposition in Fe^{2+}-activated H_2O_2 and PDS systems

(Monteagudo et al., 2015). Notably, the oxidant utilization was 6 times higher in the PDS/Fe^{2+} system (~90%) compared with the H_2O_2/Fe^{2+} system (~15%). However, TOC removal measurements showed minor LOR mineralization in both systems studied.
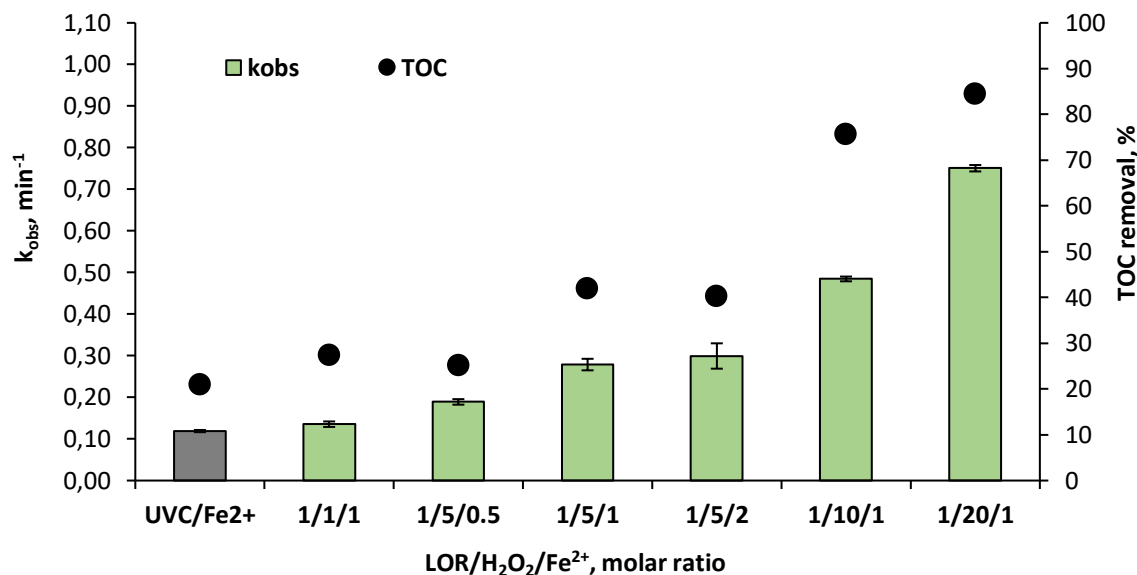
Figure 3.6 LOR degradation rate constants and TOC removal by the UVC/Fe^{2+} process ($[Fe^{2+}]_0$ = 40 µM) and UVC/H_2O_2/Fe^{2+} system at different LOR/oxidant/Fe^{2+} molar ratios ($[LOR]_0$ = 40 µM, t = 2 h).
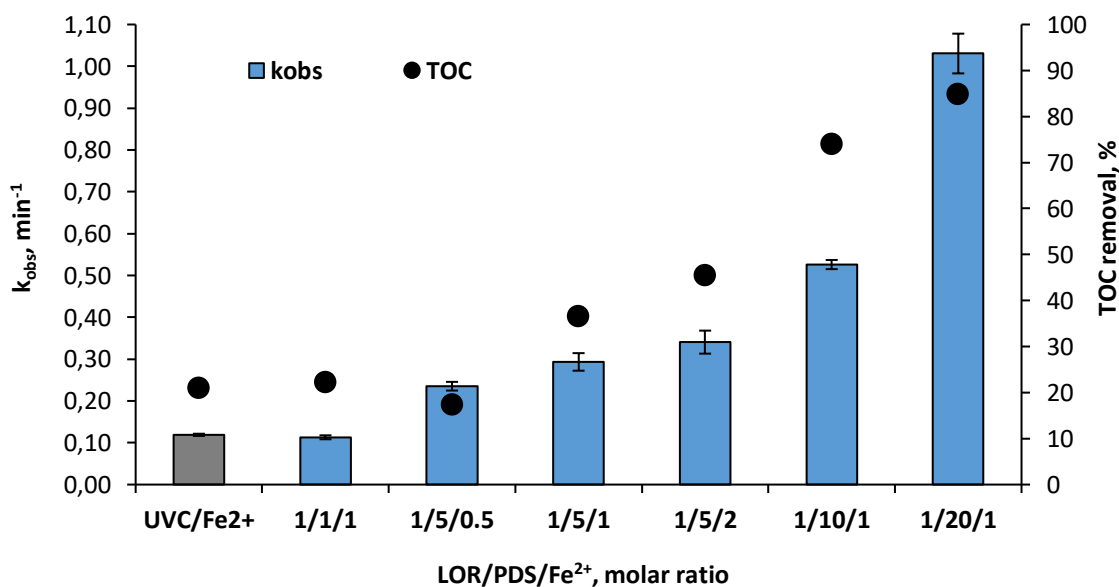
Figure 3.7 LOR degradation rate constants and TOC removal by the UVC/Fe^{2+} process ($[Fe^{2+}]_0$ = 40 µM) and UVC/PDS/Fe^{2+} system at different LOR/PDS/Fe^{2+} molar ratios ($[LOR]_0$ = 40 µM, t = 2 h).

The effectiveness of the UVC/Fe^{2+} system for the degradation of target compound at a LOR/Fe^{2+} molar ratio of 1/1 was also evaluated. Thus, a k$_{obs}$ value of 0.118 min^{-1} and 21% of TOC removal after a 2-h treatment was obtained. Comparison of the results of the UVC/Fe^{2+} system and direct UVC photolysis showed that the addition of Fe^{2+} into the system positively affected the efficiency of LOR oxidation. A further addition of oxidant (H$_2$O$_2$ or PDS) into the UVC/Fe^{2+} system led to a further enhancement in the decomposition and mineralization of LOR.

Similar to the results obtained in the UVC/oxidant systems, an increase in the dosage of oxidant at a fixed activator concentration led to higher k$_{obs}$ values and more effective TOC removal in the UVC/oxidant/Fe^{2+} systems (Figures 3.6 and 3.7). Accordingly, the use of the UVC/oxidant/Fe^{2+} system at the lowest studied concentration of H$_2$O$_2$ and PDS of 40 µM led to a k$_{obs}$ value of 0.135 min^{-1} and 0.113 min^{-1}, respectively. Likewise, the TOC removal in the UVC/PDS/Fe^{2+} system at a LOR/PDS/Fe^{2+} molar ratio of 1/1/1 was slightly lower (22%) compared with the UVC/H$_2$O$_2$/Fe^{2+} system (27%) at the same concentration of oxidant and activator. A further 5-fold increase in the oxidant concentration to 200 µM at a fixed activator concentration of 40 µM resulted in a k$_{obs}$ value of 0.279 min^{-1} and 0.293 min^{-1} in the UVC/H$_2$O$_2$/Fe^{2+} and UVC/PDS/Fe^{2+} system, respectively. The highest k$_{obs}$ values of 0.751 min^{-1} and 1.031 min^{-1} with around 85% of LOR mineralization were attained in the UVC/Fe^{2+}-activated H$_2$O$_2$ and PDS systems, respectively, at a LOR/oxidant/Fe^{2+} molar ratio of 1/20/1.

It is noteworthy that the amount of activator turned out to be important for the efficient optimization of the studied UVC/oxidant/Fe^{2+} systems. Thus, a decrease in the Fe^{2+} concentration form 80 µM → 20 µM at a fixed oxidant concentration of 200 µM resulted in a slower LOR degradation (k$_{obs}$ value of 0.295 min^{-1} → 0.189 min^{-1}, for H$_2$O$_2$-based systems; k$_{obs}$ value of 0.341 min^{-1} → 0.235 min^{-1}, for PDS-based systems) and less effective mineralization (TOC removal of 40% → 25% and 45% → 17%, respectively).

Overall, compared to the UVC/oxidant systems, faster LOR degradation and more complete mineralization were observed in the studied UVC/oxidant/Fe^{2+} systems at the same oxidant concentration used, except for the TOC removal at a PDS concentration of 800 µM. This observation can be explained by a more efficient and faster generation of hydroxyl and sulfate radicals in the dual activated UVC/oxidant/Fe^{2+} systems compared to the UVC/oxidant processes.

The efficacy of oxidant utilization in the studied UVC/Fe^{2+}-activated H$_2$O$_2$ and PSD systems was also evaluated as presented in Figure 3.8. Similar to the UVC/oxidant systems, an increase in the applied oxidant concentration has led to its more efficient utilization. The highest H$_2$O$_2$ and PSD utilization (more than 96%) among the studied

UVC/oxidant/Fe^{2+} systems was observed at a LOR/oxidant/Fe^{2+} molar ratio of 1/20/1. As a general rule, oxidants were consumed more completely in the UVC/oxidant/Fe^{2+} systems compared to the UVC/oxidant systems at the same concentration of H_2O_2 and PDS used (Figures 3.5 and 3.8).
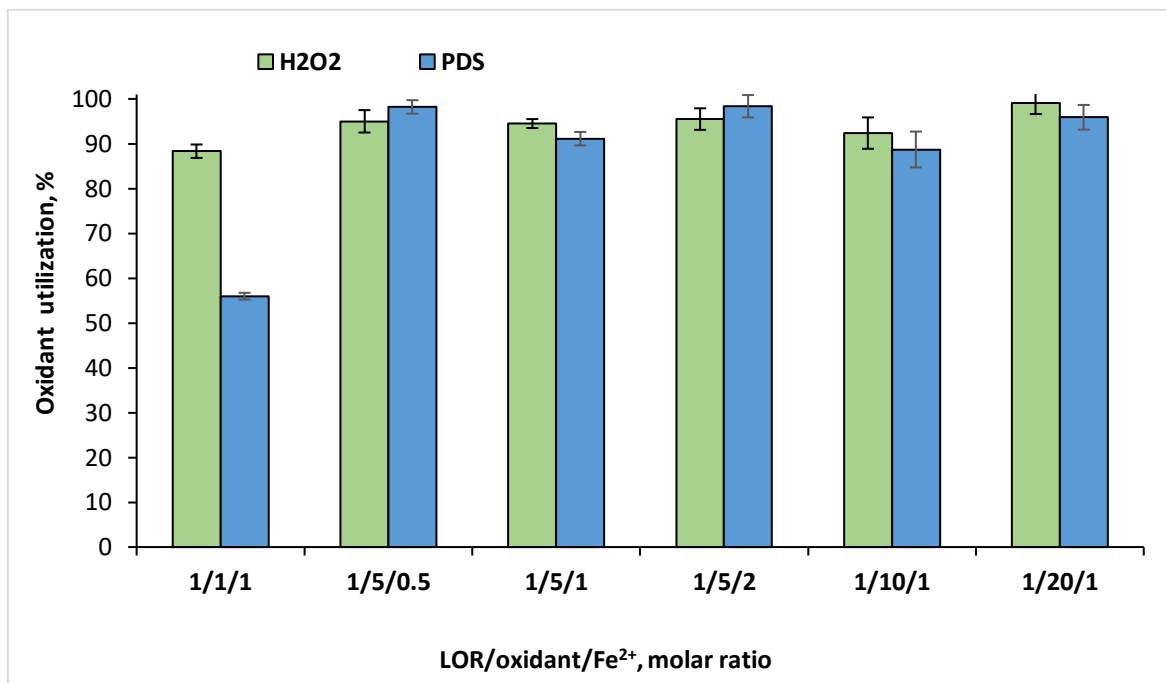
Figure 3.8 Oxidant utilization in the UVC/oxidant/Fe^{2+} systems at different UVC/oxidant/Fe^{2+} molar ratios ([LOR]$_0$ = 40 µM, t = 2 h)

The final pH_{120} values of the solutions treated by UVC/H_2O_2/Fe^{2+} and UVC/PDS/Fe^{2+} systems were in the range of 2.9-4.6, mainly due to the acidity of the activator and oxidants as well as the formation of acidic by-products during LOR oxidation (Table 3.2).

Table 3.2 Residual pH (pH_{120}) after a 2-h oxidation in the UVC/H_2O_2/Fe^{2+} and UVC/PDS/Fe^{2+} system at different molar ratios ([LOR]$_0$=40 µM, t=2 h)

Process	LOR/oxidant, molar ratio	pH_0	pH_{120}
UVC/H_2O_2/Fe^{2+}	1/1/1	6.12	4.26
	1/5/1	6.30	4.27
	1/10/1	6.10	4.36
	1/20/1	6.33	4.36
UVC/PDS/Fe^{2+}	1/1/1	6.24	3.85
	1/5/1	6.24	4.59
	1/10/1	6.10	3.23
	1/20/1	6.03	2.90

Overall, the UVC/Fe^{2+}-activated PDS system at elevated oxidant concentrations proved to be more effective than the UVC/H$_2$O$_2$/Fe^{2+} system for degradation and mineralization of the target compound. Nevertheless, both UVC/oxidant/Fe^{2+} systems can be considered promising methods for LOR decomposition in UW.

3.3. LOR decomposition by UVC- and UVC/Fe^{2+}-activated processes in groundwater

To evaluate the possible on-site application of the studied systems to remove LOR from real water matrices, experiments were conducted with groundwater samples artificially contaminated with LOR. Thus, the UVC/oxidant (LOR/oxidant molar ratio of 1/10) and the UVC/oxidant/Fe^{2+} (LOR/oxidant/Fe^{2+} molar ratio of 1/10/1) systems were studied in GW; the results obtained were compared with the corresponding UW trials (Figures 3.9 and 3.10).
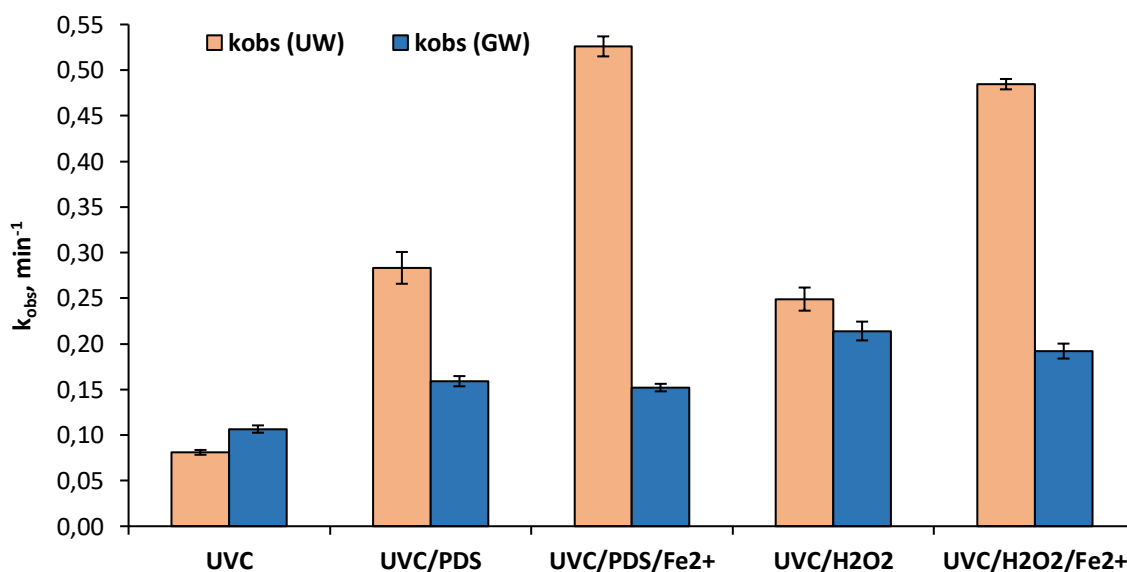
Figure 3.9 LOR degradation rate constants by the UVC photolysis, UVC/PDS, UVC/PDS/Fe^{2+}, UVC/H$_2$O$_2$ and UVC/H$_2$O$_2$/Fe^{2+} systems in different water matrices ([LOR]$_0$=[Fe^{2+}]$_0$=40 μM, [PDS]$_0$= [H$_2$O$_2$]$_0$= 400 μM)

The application direct UVC photolysis for LOR degradation in GW was more efficient than in UW (Figure 3.9) and resulted in a k$_{obs}$ value of 0.106 min^{-1} along with 25% of TOC removal. This observation can be explained by the presence of chloride anions in the groundwater matrix (Table 2.1), which are able to generate additional radicals by reacting with available hydroxyl radicals (Frontistis, 2019). The formation of chloride

radicals most likely contributes to a more efficient degradation of the target compound and intermediates. Moreover, other inorganic anions such as carbonate and bicarbonate present in GW may act as radical scavenger and generate less reactive carbonate radicals (Frontistis, 2019).
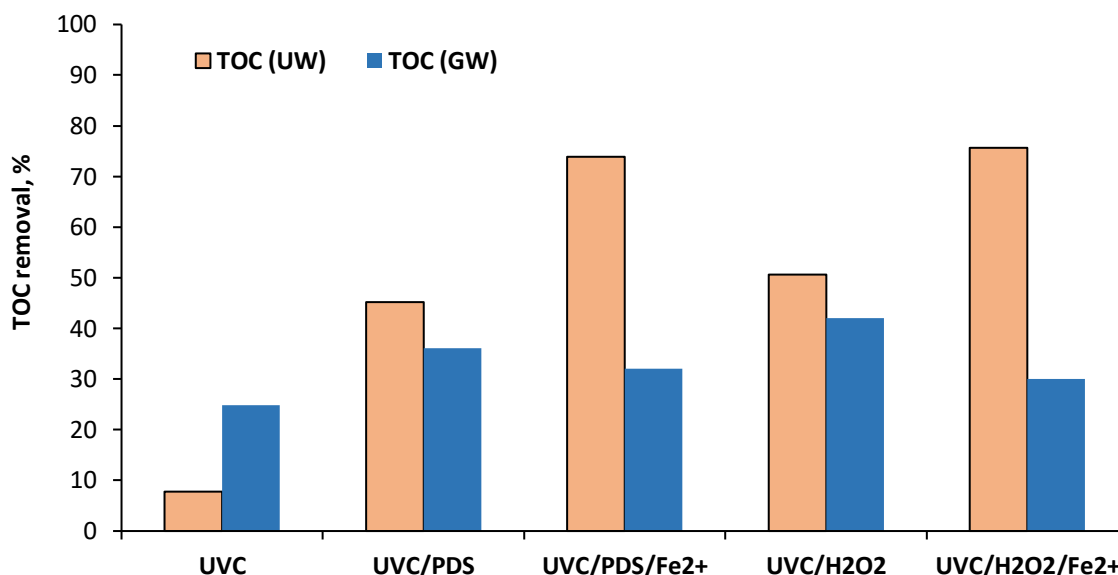

Figure 3.10 TOC removal during LOR oxidation by the UVC photolysis, UVC/PDS, UVC/PDS/Fe^{2+}, UVC/H_2O_2 and UVC/H_2O_2/Fe^{2+} systems in different water matrices ($[LOR]_0=[Fe^{2+}]_0=40$ µM, $[PDS]_0= [H_2O_2]_0= 400$ µM, t = 2 h)

The UVC/oxidant and UVC/oxidant/Fe^{2+} systems resulted in slower LOR degradation and lower TOC removal in GW compared to UW trials at the same oxidant and activator concentrations as compared with UW trials results. This suggests the inhibitory effect of water matrix of the studied processes efficacy, which coincides with the results of the experiment with synthetic fresh urine (Guateque-Londoño et al., 2020). Accordingly, k_{obs} values of 0.192 min^{-1} and 0.152 min^{-1} were obtained in GW in the UVC/H_2O_2/Fe^{2+} and UVC/PDS/Fe^{2+} system, respectively, which were almost 3 times lower compared to k_{obs} values of 0.485 min^{-1} and 0.526 min^{-1} obtained in UW. The TOC removal showed a similar tendency, as it was and 30/76% and 32/74% after a 2-h UVC/H_2O_2/Fe^{2+} and UVC/PDS/Fe^{2+} treatment, respectively, in GW/UW.

Unlike the UW test results, the addition of Fe^{2+} activator to the UVC/H_2O_2 and UVC/PDS systems in GW resulted in a decrease in LOR degradation and TOC removal. For example, the obtained k_{obs} values were 0.159 min^{-1} and 0.152 min^{-1} for the UVC/PDS and UVC/PDS/Fe^{2+} system, respectively. In the case of the UVC/H_2O_2 and UVC/H_2O_2/Fe^{2+} systems, a k_{obs} value decreased from 0.214 min^{-1} to 0.192 min^{-1}, respectively.

Overall, the results of the UVC/Fe^{2+}-activated oxidant systems indicate a strong impact of the buffered groundwater matrix on the efficiency of LOR decomposition. The main reason for this observation may be the fact that the iron activator was partially removed from the system by precipitation as a ferric hydroxide complex. This assumption is confirmed by the fact that in all GW trials only a slight change in pH$_{120}$ value was observed. For example, after direct UVC photolysis pH$_{120}$ was 7.7±0.1 and after the UVC/oxidant/Fe^{2+} treatment pH$_{120}$ was 7.1±0.2. In addition, moderate utilization of oxidants (in the range of 54-66 %) was observed after a 2-h oxidation of LOR by the studied systems in GW.

SUMMARY

This study examined the application of different oxidants in the UVC/oxidant and UVC/oxidant/Fe^{2+} systems for LOR degradation and mineralization in aqueous solution. The oxidants compared were persulfate (PDS) and hydrogen peroxide (H_2O_2). The UVC/PDS system proved to be more effective in the target compound decomposition compared to the UVC/H_2O_2 systems at the same oxidant concentrations used. The addition of Fe^{2+} considerably improved the LOR degradation and mineralization by the UVC/oxidant/Fe^{2+} systems compared to UVC/oxidant systems. The overall efficacy in the target compound decomposition and mineralization was as follows: UVD/PDS/Fe^{2+} system > UVC/H_2O_2/Fe^{2+} system > UVC/PDS system > UVC/H_2O_2 system. Regardless of the system used, LOR mineralization was incomplete. The highest k_{obs} values obtained in the UVC/oxidant/Fe^{2+} system at a LOR/oxidant/Fe^{2+} molar ratio of 1/20/1 were 0.751 min^{-1} and 1.031 min^{-1} along with 84% and 85% TOC removal for H_2O_2 and PDS, respectively. The oxidant utilization was the most effective at a LOR/oxidant molar ratio 1/20 for all the studied systems, ranging from 80% in the UVC/H_2O_2 system to almost 100% in the UVC/H_2O_2/Fe^{2+} system. The UVC/oxidant and UVC/oxidant/Fe^{2+} systems resulted in slower LOR degradation and lower TOC removal in GW compared to UW trials at the same oxidant and activator concentrations as compared with UW trials results.

The results of this study provide valuable information for the practical application of UVC-activated H_2O_2(/Fe^{2+}) and PDS(/Fe^{2+}) systems for the degradation of LOR in water matrices.

KOKKUVÕTE

Magistritöö raames uuriti erinevate oksüdantide efektiivsust losartaani (LOR) lagundamiseks ja mineraliseerimiseks vesilahuses. Võrreldi UVC(/Fe^{2+})-aktiveeritud persulfaadi (PDS) ja vesinikperoksiidi (H_2O_2) oksüdatsiooni efektiivsust. UVC/PDS kombinatsioon osutus UVC/H_2O_2 süsteemidest efektiivsemaks kõigil analüüsitud oksüdantide kontsentratsioonide juures. Fe^{2+} lisamine UVC/oksüdant süsteemi parandas LOR lagundamise efektiivsust võrrelduna UVC/oksüdandi süsteemidega. Oksüdeerimise süsteemid saab sihtaine lagundamise ja mineraliseerimise efektiivsuse alusel reastada järgnevalt: UVC/PDS/Fe^{2+} süsteem > UVC/H_2O_2/Fe^{2+} süsteem > UVC/PDS süsteem > UVC/H_2O_2 süsteem. LOR mineraliseerimine oli kõigi süsteemide puhul mittetäielik. Uuritud süsteemides toimus pseudo esimest järku reaktsioon, mille puhul määrati katseliselt reaktsiooni kiirus (k_{obs}). Kõrgeimad k_{obs} väärtused ja TOC (kogu orgaaniline süsinik) eemaldamised saavutati UVC/oksüdant/Fe^{2+} süsteemides, LOR/oksüdant/Fe^{2+} moolsuhte 1/20/1 korral. Seega, UVC/PDS/Fe^{2+} süsteemi puhul saavutati k_{obs} = 1.031 min^{-1} ja UVC/H_2O_2/Fe^{2+} süsteemis k_{obs} = 0.751 min^{-1}, vastavalt 85% ja 84% TOC eemaldamise efektiivsusega. Oksüdantide kasutus oli kõige efektiivsem LOR/oksüdant moolsuhte 1/20 puhul kõigis uuritud süsteemides, jäädes vahemikku 80%-st UVC/H_2O_2 süsteemis kuni ligi 100%-ni UVC/H_2O_2/Fe^{2+} süsteemis. UVC/oksüdant ja UVC/oksüdant/Fe^{2+} süsteemides toimus põhjavees LOR lagundamine aeglasemalt ning TOC eemaldamine ebaefektiivsemalt võrreldes samade oksüdantide ja aktivaatorite kontsentratsioonidega ülipuhta veega läbi viidud katsetes.

Magistritöö tulemuste põhjal saadi olulist informatsiooni UVC-aktiveeritud H_2O_2(/Fe^{2+}) ja PDS(/Fe^{2+}) süsteemide efektiivsuse ja rakendamise kohta LOR lagundamiseks erinevates vesikeskkondades.

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