TALLINN UNIVERSITY OF TECHNOLOGY
SCHOOL OF ENGINEERING
Department of Civil Engineering and Architecture

PHOTOCHEMICAL OXIDATION OF VANCOMYCIN IN AQUEOUS SOLUTION

VANKOMÜTSIINI FOTOKEEMILINE OKSÜDATSIOON VESILAHUSES

MASTER THESIS

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Tallinn 2021

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THESIS TASK

Student: Glory Adedotun Oladele, 195274EABM

Study programme, EABM03/18 Environmental Engineering and Management

Supervisor(s): Senior Researcher, Niina Dulova, 620 2854

Thesis topic:

(in English) *Photochemical oxidation of vancomycin in aqueous solution*

(in Estonian) Vankomütsiini fotokeemiline oksüdatsioon vesilahuses

Thesis main objectives:

1. To provide an overview of the properties of vancomycin, its effects, toxicity and occurrence in the environment, as well as advanced oxidation processes and their applications
2. To study photochemical oxidation of antibiotic vancomycin by UV-C photolysis, UV-C/H_2O_2, UV-C/PMS and UV-C/PDS systems in water
3. To compare the efficacy of vancomycin degradation and mineralization in selected advanced oxidation processes under different treatment conditions

Thesis tasks and time schedule:

No	Task description	Deadline
1.	Familiarization with the scientific literature: antibiotics/vancomycin and their/its occurrence in the environment, vancomycin removal processes, advanced oxidation processes, etc.	10.2020
2.	Experiments on the oxidation of vancomycin by selected oxidative processes	12.2020
3.	Writing a master's thesis: literature review, experimental part, analysis of the results, etc.	05.2021

Language: English **Deadline for submission of thesis:** 26 May 2021

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PREFACE

I would like to express my profound gratitude to my supervisor, Dr. Niina Dulova for her unwavering guidance and assistance in understanding the theory, conducting experiments and for her detailed comments and advice.

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Glory A. Oladele

LIST OF ABBREVIATIONS AND SYMBOLS

$HO^{\bullet}$	Hydroxyl radical
ARB	Antibiotic Resistant Bacteria
ARG	Antibiotic Resistance Genes
AUC	Area Under Concentration-time curve
COD	Chemical Oxygen Demand
DWTP	Drinking Water Treatment Plant
EC	Emerging Contaminant
E_g	wide band gap energy
HPLC	High Performance Liquid Chromatography
$I.C_{VAN}$	Inhibition Coefficient of vancomycin
MIC	Minimum Inhibitory Concentration
PDS	Peroxydisulfate
PMS	Peroxymonosulfate
ppb	parts per billion
PPCPs	Pharmaceuticals and Personal Care Products
ppm	parts per million
rpm	revolution per minute
TOC	Total Organic Carbon
VMN	Vancomycin
WWTP	Wastewater Treatment Plant

INTRODUCTION

Antibiotics, an important type of environmental pollutant under pharmaceuticals and personal care products (PPCPs) are recently named among pollutants of emerging concern (EC) as a result of their increasing impact on human, animal and environmental health (Kasprzyk-Hordern et al., 2009). Despite the numerous advantages of antibiotics to humans, the adverse impact of their occurrence in the environment are quickly outweighing their main purpose of treating or preventing infections (Wang& Zhuan 2019). Before the mass consumption of antibiotics as medicines, antibiotic resistance in human and animal pathogens were not common. However, the abuse of antibiotics have led to unplanned consequences (resistant genes in bacteria mainly developed overtime through exposure to unprecedented antibiotic selection pressures), which in turn require administering even more potent antibiotics (Larsson, 2014). Accumulation of antibiotic residues overtime and biotransformation of antibiotic drugs give rise to antibiotic multi-resistant bacteria genes incidence in the environment that is of increasing concern especially due to their ecotoxicological effect (Carvalho & Santos, 2016; Cycoń et al., 2016; Kümmerer, 2009).

As a consequence, antibiotics can end up in the environment via several means affecting water quality at varying quantity posing as threat to human health and ecosystem (Sires & Brillas, 2012; Tamtam et al., 2011; Zhang, 2016). The main entry routes into the environment for most antibiotics include domestic, industrial, hospital wastewater as well as effluents from wastewater treatment plants (WWTPs), aquaculture, livestock farming and improper discarding of unused medicines (Bottoni et al., 2010). PPCPs have been found in surface water, groundwater, raw sewage and soil (Charuaud et al., 2019).

Wastewater contaminated with high concentration of biodegradable pollutants could be treated using biological treatment. However, wastewaters from industries such as pharmaceuticals, textile, and agriculture contain toxic pollutants with low biodegradability (Olama et al., 2018, Touati et al., 2016, Kushniarou et al., 2019).
Antibiotics-contaminated industrial and municipal wastewaters are usually treated at WWTPs. It is almost impossible to achieve 100% contaminant removal with the conventional primary, secondary and tertiary treatment, therefore, WWTPs effluents commonly contain a certain concentration of antibiotics, which are subsequently discharged into receiving water bodies (Jones et al., 2005; Homem & Santos, 2011). An example of this situation was presented in a research conducted by Rosi et al. (2018); it was concluded that urban river water in Baltimore contained more pharmaceuticals

(including antibiotics) than its sub-urban counterpart and this greatly affected the rivers' microbial communities.

Depending on type and class of medicine, antibiotics may be released back either as parent compound in the active form, unaltered or converted into metabolites and degradation products (Yang et al., 2017). Some specific antibiotics easily degrade, such as ibuprofen and bezafibrate, whereas some are considerably more persistent, such as tetracyclines and fluoroquinolones, which enable them to spend longer time in the environment spreading further and accumulating overtime to higher concentrations (Larsen et al., 2004).

Owing to the high toxicity, polymeric structures, and non-biodegradable characteristics of some of these pollutants, traditional biological processes are not as effective to completely remove the pollutants (Homem & Santos, 2011) Therefore, efficient alternative technologies and analytical methods are required. Different biological, physical and chemical methods have been studied, however, the most applicable and effective have proved to be advanced oxidation processes (AOPs) due to their fast reaction time and oxidation efficacy (Wang & Zhuan, 2020).

AOPs such as Fenton and Fenton-like processes, ozonation, catalytic ozonation, activated peroxy-compounds oxidation, photocatalytic oxidation, electrochemical oxidation and ionizing radiation can be used for degradation and removal of recalcitrant pollutants (Cuerda-Correa et al., 2019; Gautam & Chattopadhyaya, 2016). Advanced oxidation processes can also be used as an effective pretreatment for conventional or biological treatment methods by converting or decomposing pollutants into shorter chain and more biodegradable compounds (Gogate & Pandit, 2004a, 2004b; Hernandez et al., 2002).

Therefore, this study focuses on the degradation and mineralization of the antibiotic compound vancomycin (VMN) by photochemical oxidation in water. The AOPs studied include UV-C-activated hydrogen peroxide (H_2O_2), peroxymonosulfate (PMS), and peroxydisulfate (PDS) systems. It should be noted that the efficiency of UV-C/H_2O_2, UV-C/PMS, and UV-C/PDS processes for vancomycin oxidation in water has not been previously evaluated. The results of this study can provide valuable information on the removal of VMN by UV-induced AOPs in water.

1. LITERATURE REVIEW

1.1 Antibiotics in the environment

The longstanding cornerstone of modern medicine has been the discovery of antibiotics to fight bacterial infections thereby increasing overall life expectancy, improving health status of human and animals (Catteau et al., 2018; Berkner et al., 2014; Stokes et al., 2020). Before the mass consumption of antibiotics as medicines, antibiotic resistance in human and animal pathogens were not common (Tacconelli et al., 2018; Nielsen et al., 2018). However, the overuse and misuse of antibiotics has led to unintended consequences (resistant genes in bacteria mainly developed overtime through exposure to unprecedented antibiotic selection pressures), which in turn require even more potent antibiotics (Larsson, 2014; Leung et al., 2012).

Antibiotics reach the environment through urine and excreta, which are sometimes unaltered from humans and animals that have undergone therapy, aquaculture, and wastewater from pharmaceutical companies producing antibiotics, hospitals, municipalities and more importantly through improper disposal of unused or expired drugs (Figure 1) (Bila & Dezotti, 2003; Ikehata et al., 2006; Homem & Santos, 2011).

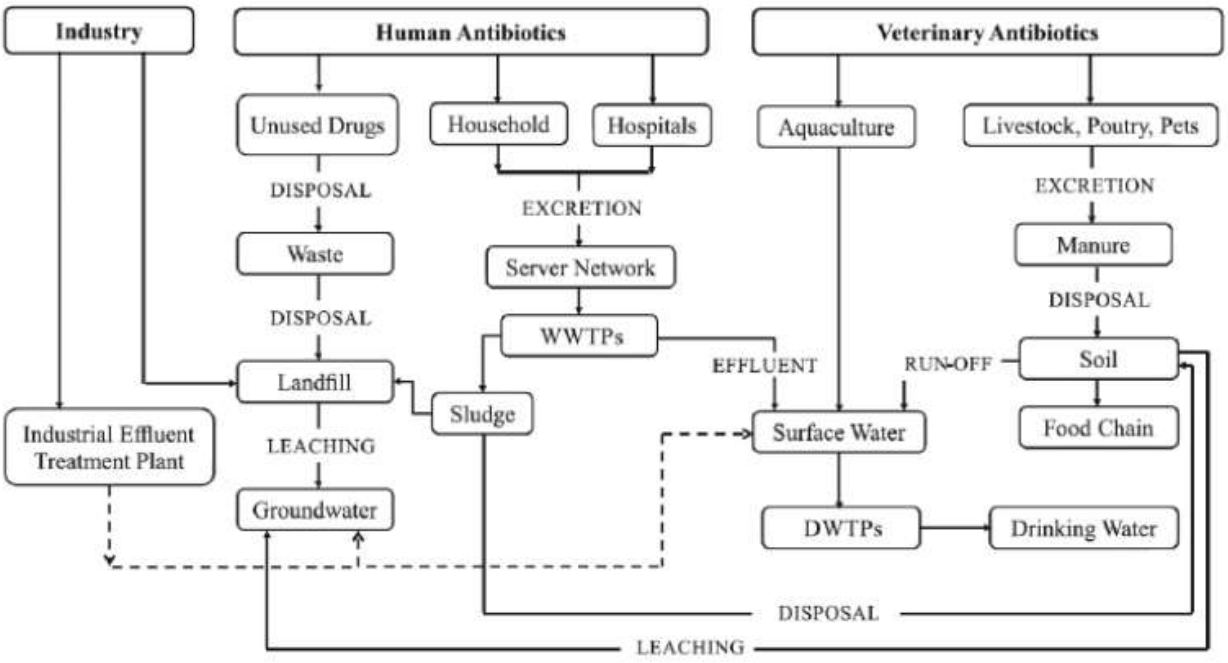

Figure 1. Schematic representation of major contributors to the spread of antibiotics into the environment and possible recontamination route for humans and animals (Frade et al., 2014)

Environmental vector balance especially of microbial ecosystem get largely affected overtime due to accumulation of antibiotics in sludge from wastewater treatment plants or manure from animal waste (Finley et al., 2013). Similarly, improper disposal of unused medicinal products, often into sewage system poses a valid route by which antibiotics are introduced into the environment (Barancheshme & Munir, 2018). Depending on the degradability rate of drugs, it is estimated that about 40-90% of administered antibiotic dose is released into the environment as a parent (active) compound (Polianciuc et al., 2020). The first reported case of water contamination by antibiotics was in England, thus, tetracyclines, macrolides and sulfonamides were detected in a river at a low concentration of 1 μg/L (Ikehata et al., 2006).

In the environment, microbial antibiotics resistance are often favored, plants may absorb the residues via agro-ecosystem contamination (Jechalke et al., 2014). The risk of antibiotics pollution in the environment is fast spreading. Ye et al. (2007) carried out research on chlorinated drinking water and listed some persistent antibiotics found in the water at low levels. However, Rutgersson et al. (2013) emphasized that when the water was ingested orally, it did not pose any direct toxicity risk to human. The study of the negative impact of various antibiotic residue to physiological processes and ecotoxicological effects on plants showed that the residues depressed seed germination, overall crop growth and might be assimilated by crops (Malchi et al., 2014; Gros et al., 2019).

According to Gomes et al. (2020), emerging contaminants are chemicals or materials usually at trace concentrations found in the environment, which pose potential or real risk to the "One Health" trilogy (environment, human, and animal health). Pereira et al. (2015) and Richardson and Ternes (2018) listed some of these emerging contaminants: disinfectants, antibiotic resistant bacteria, antibiotic resistant genes, PPCPs, nanomaterials, fire retardants, pesticides, plasticizers, and surfactants. Pharmaceutical residues have been discovered in all environmental matrices: surface water (lakes, rivers, streams, estuaries, and seawater), groundwater (Lapworth et al., 2012; Fick, 2009), wastewater treatment plants effluents, influents, and sludge (Watkinson et al., 2009; Homem & Santos, 2011; Fent et al., 2006). Recently, drugs were discovered broadly in the geosphere and biosphere (Grenni et al., 2018; Riaz et al., 2018; Yang et al., 2011). Even the Earth's most pristine environment - Polar Regions, are reported to now harbor pharmaceutical contaminants (González-Alonso et al., 2017; Kallenborn et al., 2008). Thus, in Northern Antarctica, several endocrine disruptors together with antimicrobials and synthetic estrogens have been found (Esteban et al., 2016).

Therefore, PPCPs as well as their metabolites and degradation products pose a potential negative impact on the environment, living organisms and human health often either by means of migration or accumulation (Gracia-Lor et al., 2012; Sun et al., 2018).

1.2 Vancomycin

Vancomycin also called 'Mississippi mud' is an amphoteric glycopeptide antibiotic produced by soil bacteria *Amycolatopsis orientalis* (subsequently called *Streptomyces orientalis*) (Levine, 2006). VMN is one of the most administered antibiotics in medicine (Antunes et al., 2017). It is a complex, branched, tricyclic glycopeptide (Figure 2) often used to treat superbugs (Bruniera et al., 2015).

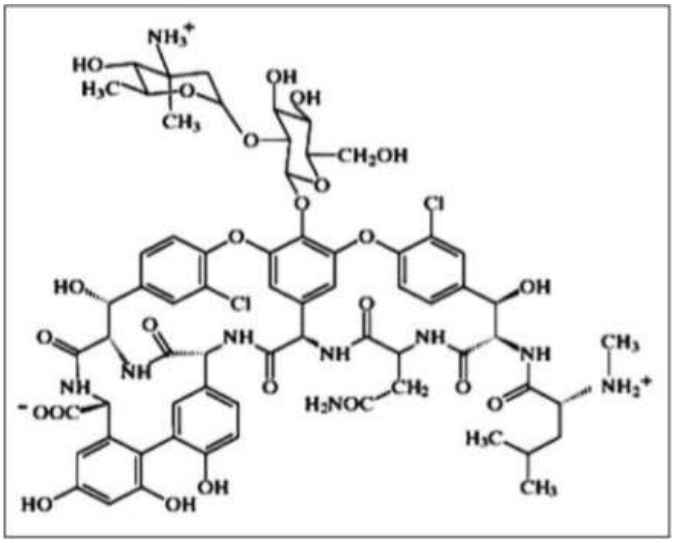

Figure 2. Structural formula of vancomycin (Vila et al., 2007)

Vancomycin was firstly isolated in 1952 by Dr. Kornfeld, an organic chemist at Eli Lily, which had a major program in discovering new antimicrobial agents with activity against gram-positive organisms and beta-lactam-resistant staphylococci (Moellering, 2006). It was gotten from a soil sample collected in the deep, interior jungle of Borneo (Griffith, 1981; Moellering, 2006) and was firstly introduced into medical clinic in year 1958 by the US Food and Drug Administration (Vila et al., 2007; Nolin, 2016).

Adequate VMN concentration level in blood serum is between 5 to 10 mg/L (Vila et al., 2007). It is used in the management of severe gram-positive bacterial infections (Gupta et al., 2011). The emergence of methicillin-resistant staphylococcal strains with reduced susceptibility to vancomycin has set the standard administration of high-dosage treatment to about 15 to 20 mg/L (Gupta et al., 2011). Vancomycin was previously discarded for over 50 years to favor other antibiotics because of its toxicity index

(ototoxic and nephrotoxic) but it reemerged due to the advent of pseudomembranous enterocolitis and the spread of methicillin-resistant *Staphylococcus aureus* (Levine, 2006). It was initially called "Compound 05865", but then given generic name Vancomycin from the term "Vanquish" and was firstly marketed under trade name, Vancocin (Moellering, 2006; Levine, 2006). VMN is administered to patients allergic to penicillin and cephalosporins. In general, VMN is considered a drug of last resort as it is the world's last line of defense against disease-causing bacteria and resistant bacteria infections (Robert, 2017).

The main physical and chemical properties of VMN are listed in Table 1 according to NCBI, 2021. Vancomycin is a white to tan lyophilized powder that is highly water-soluble (hydrophilic molecule). VMN is available in various forms: solution, powder for solution and capsule form. It is moderately soluble in methanol and insoluble in higher alcohols, acetone nor in ether (O'Neil, 2006).

Table 1. Typical physical and chemical properties of vancomycin

Property	**Value**	**Reference**
CAS-Number	1404-90-6	ChemIDplus; DrugBank; EPA DSSTox; European Chemicals Agency (ECHA); Hazardous Substances Data Bank (HSDB); Human Metabolome Database (HMDB)
IUPAC Name	(1*S*,2*R*,18*R*,19*R*,22*S*,25*R*,28*R*,40*S*)-48-[(2*S*,3*R*,4*S*,5*S*,6*R*)-3-[(2*S*,4*S*,5*S*,6*S*)-4-amino-5-hydroxy-4,6-dimethyloxan-2-yl]oxy-4,5-dihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy-22-(2-amino-2-oxoethyl)-5,15-dichloro-2,18,32,35,37-pentahydroxy-19-[[(2*R*)-4-methyl-2-(methylamino)pentanoyl]amino]-20,23,26,42,44-pentaoxo-7,13-dioxa-21,24,27,41,43-pentazaoctacyclo[26.14.2.2^{3,6}.2^{14,17}.1^{8,12}.1^{29,33}.0^{10,25}.0^{34,39}]pentaconta-3,5,8(48),9,11,14,16,29(45),30,32,34(39),35,37,46,49-pentadecaene-40-carboxylic acid	PubChem URL:https://pubchem.ncbi.nlm.nih.gov

Synonyms	VANCOMYCIN COVANC Vancocin Vancoled Vancomicina Vancomycin HCl Vancomycine Vancomycinum	PubChem https://pubchem.ncbi.nlm.nih.gov SwissProt http://www.uniprot.org/
Molecular Formula	$C_{66}H_{75}Cl_2N_9O_{24}$	PubChem https://pubchem.ncbi.nlm.nih.gov
Compound Type	• Amine • Anti-Bacterial Agent • Drug • Ether • Glycopeptide Antibacterial • Metabolite • Organic Compound • Organochloride • Synthetic Compound	T3DB http://www.t3db.ca/toxins/T3D3543#toxicity_profile
European Community (EC) Number	215-772-6	European Chemicals Agency (ECHA)
Monoisotopic mass	1447.43 g/mol	PubChem https://pubchem.ncbi.nlm.nih.gov
Average Molecular Weight	1449.2 g/mol	PubChem https://pubchem.ncbi.nlm.nih.gov
Solubility in Water	0.22 g/L	Human Metabolome Database (HMDB)
LogP (Octanol-Water)	-3.1	Human Metabolome Database (HMDB), DrugBank
pKa (Strongest Acidic)	2.6	PubChem https://pubchem.ncbi.nlm.nih.gov
pKa (Strongest Basic)	11.7	PubChem https://pubchem.ncbi.nlm.nih.gov
Physical Description	Solid, powder	Human Metabolome Database (HMDB)
Decomposition	Emit nitric oxide and Chlorine which are hazardous and toxic	PubChem https://pubchem.ncbi.nlm.nih.gov
Potency	97-106%	Divya (2015)

Vancomycin is excreted unchanged in urine like most antibiotics. The mean half-life elimination of VMN in human plasma is about 4-6 hours with normal renal functioning while in anephric patients might take up to 7.5 days (HSDB). The degree of adsorption is slowed down by magnesium, manganese, calcium, and ferrous ions (AHFS, 2009).

1.2.1 Concentration of vancomycin in the environment

It has been noted that wastewater treatment processes are not entirely effective in removing pharmaceuticals and personal care products such as antibiotics (Liu & Wong, 2013). The PPCPs are deposited in the aquatic environment and may retain their original concentration and structures or become metabolized into other active or inactive compounds (Gracia-Lor et al., 2012; Yang et al., 2017). Thus, VMN was detected in French rivers at concentrations reaching up to 90 ng/L (Dinh et al., 2011). Similarly, Zuccato et al. (2010) assessed Italian aqueous environment by analyzing WWTPs influents, effluents and receiving rivers. The research confirmed that treated urban discharges serves as entry route of vancomycin and other antibiotic residues into surface water, even contaminating groundwater though at lower concentrations. The results were consistent with the findings in Germany when similar research was conducted by Rossmann et al. (2014). Complete removal of antibiotics in WWTPs effluent play an important role in the control of antibiotic pollution and occurrence in the environment especially in water matrices. The emergence of antibiotic resistance genes is now regarded as a more pressing concern due to the effect of antibiotics presence in the environment as in the case of bacteria which react to frequent use of vancomycin by developing resistance (Chang et al., 2017; Gousia et al., 2015; Rashidi et al., 2019). Frequent use of VMN in some hospitals has resulted in the emergence of resistance genes. Most commonly encountered VMN resistance genes are VanA and VanB (Flipse et al., 2019).

In Estonia, as of 2017 had 5.8% vancomycin antimicrobial resistance in clinical outpatient settings, which reduced to 4.1% in 2019 according to surveillance report of the European Centre for Disease Prevention and Control. EU/EEA generally had increased trend to *Enterococcus faecium*, which is resistant to VMN from 10.4% in 2014 to 14.9% in 2017 (ECDC, 2017).

1.2.2 Vancomycin mode of action and use

In terms of VMN pharmacology, the antibiotic works by preventing cross-linking and growth of the peptidoglycan strands of the cell wall (the defense cell wall of bacteria)

(Eric, 2007). Under standard condition, VMN forms hydrogen bond with D-alanyl-D-alanine moieties of peptidoglycan bacteria cell wall (Wang et al., 2018). This inhibit transglycosylase and transpeptidase activities during peptidoglycan growth preventing the binding of the expanding matrix with the new peptidoglycan thereby resulting in osmotic shock and cell lysis. VMN specifically targets gram-positive organisms and may be inactive again gram-negative bacteria as their cell wall contains lipopolysaccharides. Vancomycin affects the second stage of cell wall synthesis in susceptible bacteria (Watanakunakorn, 1984). Oral absorption of VMN is minimal; therefore, it is usually given intravenously (I.V) (Eric, 2007). The vast majority of consumed VMN is excreted in urine via glomerular filtration and active tubular secretion and require about 4-8 hours for half-life elimination in adults with normal renal function (Burgess & Drew, 2014; Vora, 2016). When taken orally, VMN works by killing the bacteria in the intestines only without killing any other bacteria or treat infections in other parts of the body and is excreted through feces. Intravenously administered VMN treats serious infections that other medicines may not treat. There is currently a debate on whether VMN should be given via central or peripheral line as midline catheters proffers a safe option for administering the compound (Moureau, 2021). In 2018, Cao et al. (2018) studied the metabolism and degradation of vancomycin in rat liver microsomes system. The study revealed that VMN is not metabolized in the liver and that organics and mineral salt may be favorable to the degradation of VMN in aquatic environment.

According to Kirst et al. (1998) the data for years 1975 to 1983 were compiled by the sole supplier of vancomycin, Eli Lilly database for years 1984 to 1996 by IMS international. As presented in Figure 3, the overall usage of VMN gained publicity again in the 1980s especially due to the emergence of methicillin-resistant *Staphylococcus aureus* in late 1970s. New VMN products with improved purity were developed and this stimulated an over 100-fold increase in its usage for about 20 years (Kirst et al., 1998; Levine, 2006).

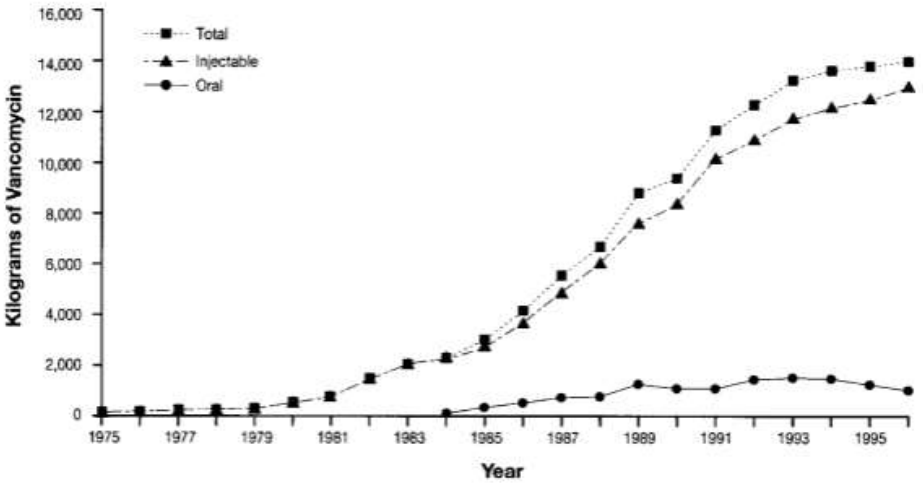

Figure 3. Historical yearly usage of vancomycin (kilograms) in the United States, France, Italy, Germany, United Kingdom, and the Netherlands (Kirst et al., 1998)

Vancomycin was among the most frequently used antibiotics in United States from 2006 until 2012 (Baggs et al., 2016). Some of the main uses of vancomycin are listed as follows:

- Vancomycin is prescribed as a broad-spectrum antibiotic used to treat infections caused by methicillin-resistant *Staphylococcus aureus*, methicillin-resistant *Staphylococcus epidermis* and amoxicillin-resistant enterococci (Rubinstein, 2014; Tookhi et al., 2021);
- To treat antibiotic-associated pseudomembranous enterocolitis - watery or bloody diarrhea caused by *Clostridium difficile* (Eric, 2007; Baines et al., 2009);
- To treat prophylaxis in endocarditis patients at risk who cannot tolerate penicillin, cephalosporin, ampicillin, or erythromycin (AHFS, 2009);
- To treat infections, including those relating to use of prosthetic devices such as braces, caused by gram-positive organisms with multiple antibiotic resistance (AHFS, 2009);
- Early treatment of possible methicillin-resistant *Staphylococcus aureus* infection as a first empiric antibiotic administered based on educated guess until the culture identification of infecting organism.

1.2.3 Impacts of vancomycin

Ecological risk of antibiotics in general is becoming a thing of utmost concern. Thenceforward, most acute and/or chronic ecotoxicity cases on bacteria, algae, fish and other invertebrates in aquatic environment has been traced to be caused by PPCPs like VMN (Carvalho & Santos, 2016). VMN may degrade to produce related degradation products through different means further explained in this study (USP, 2008). Such

degradation products, together with vancomycin and its metabolites may result in detrimental ecological effects. Vancomycin has a relatively low-level toxicity to plants (Pazuki et al., 2014). In plant tissue culture, VMN is one of the few antibiotics used to eliminate gram-positive bacterial infection (Carey et al., 2015). It has phytotoxic effect on root development of plant such as tomato, which accumulates antibiotics, but VMN does not pose a threat or effect on seed germination (Bellino et al., 2018).

Cycoń et al. (2016) demonstrated that extensive use of VMN, like other antibiotics leads to soil pollution, which alters the biodiversity of soil microbial communities and may exert selective pressure leaving antibiotic-resistant bacteria. Later it was suggested that the soil microorganisms had low initial resistance to VMN but proved to be resilient in the long-term.

Cao et al. (2018) confirmed that VMN is not metabolized in the liver but in the kidney. Accordingly, exposure to VMN has bloomed opportunistic pathogens such as *Achromobacter, klebsiella* and *Pseudomonas* thereby increasing human disease-related pathway and fecal microbiota transplantation as well as antibiotic resistance genes in the gut (Liu et al., 2020). After Fecal microbiota transplantation which is transfer of healthy bacteria though a processed mixture of liquid stool into a patient's intestine in order to balance bacteria in the recipient's intestine to fight infection, a remarkable return back to baseline was observed in the restoration of intestinal microbiome (Liu et al., 2020). When VMN is given for systemic infection, it is given intravenously preferably via infusion which can cause abscess, pain after extravasation because it is highly irritating (USP, 2006). Damage to kidney and hearing were believed to be side-effects of the early impure vancomycin (Moellering, 2006; Rybak, 2006).

1.2.4 Vancomycin toxicity

Earlier, the best way to monitor VMN toxicity in human was to look at the trough values (Lodise et al., 2009). Recent studies has stated that ideal 24 hours area under consideration-time curve to minimum inhibitory concentration ratio dosing and monitoring which aim for a ratio of 400-600 is recommended for determining toxicity as well as dosage (Biagi et al., 2019). Traditionally, vancomycin has been considered to cause nephrotoxicity and, in some cases, ototoxicity especially in patients that have compromised renal function and the concentration becomes too high (Filippone et al., 2017; Mcgrady et al., 2020).

Some of the side effects of VMN include severe acute tubulointerstitial nephritis and exfoliative dermatitis (Hsu, 2001; Salazar et al., 2010), which could also arise when

VMN interacts with some toxic drugs such as aminoglycosides, aspirin, ceftriaxone, cyclosporine, furosemide (Plakogiannis & Nogid, 2007). Use of larger doses of vancomycin at curbing resistant strain of *Staphylococcus aureus* has reported led to acute kidney injury (AKI) (Bamgbola, 2016), neutropenia - low white blood cells (Farber & Moellering, 1983), thrombocytopenia (Marraffa et al., 2003). Other less frequent side effect includes allergic reactions, such as hives, wheezing, difficult breathing, abdominal pain, back pain, blood vessel inflammation (vasculitis or phlebitis), red man syndrome (Blumenthal et al., 2012). Due to concerns and reports of ototoxicity and nephrotoxicity, enthusiasm for VMN reduced and it became infrequently prescribed as it was considered a niche drug restricted only for use by patients with β-lactam allergies or patients infected with drug-resistant organisms (Levine, 2006; Nolin, 2016). Nephrotoxicity rate due to VMN varies between 5 to 43% in most studies (Carreno et al., 2014; Van Hal et al., 2013). The risk of nephrotoxicity increases with trough concentration and duration of therapy (Van Hal et al., 2013). A recent study argues that nephrotoxicity risk is increased when VMN is used concomitantly with aminoglycoside than when used alone (Jeffres et al., 2007; Lodise et al., 2008).

Ototoxicity caused by VMN is rare and might be irreversible as the risk factors have not been fully studied (Uda et al., 2019). Ototoxicity has also been linked to indiscriminate vancomycin dosage and use as well as administering of vancomycin with other ototoxic drugs like aminoglycosides, platinum-containing drugs, loop diuretics, and aspirin though it is unclear if the co-administration produces synergistic toxicity (Forouzesh et al., 2009; Uda et al., 2019).

According to Katikaneni et al. (2016) AKI surged with the administration of higher than the recommended trough level of VMN as a first-line antibiotic intravenously over a prolonged time period for treating methicillin-resistant *Staphylococcus aureus* infections. AKI was firstly attributed to impurities present in the early VMN formulations (Levine, 2006); this was buffed aside as it is believed that VMN is kidney-safe and any kidney injury could arise due to patient biological make-up, dosage among others (Filippone, 2017). However, recent analysis by Ray et al. (2016) and Gaggl et al. (2020) raised concern from VMN therapy as one-half of the AKI cases about 59% could be linked to VMN treatment.

Liu et al. (2020) further sinuated that even with therapeutic range and concomitant use of (flu)cloxacillin, increased exposure to VMN leads to AKI. It is also more likely to occur through the concurrent use of nephrotoxic agents (Knoderer et al., 2015) and in critically ill patients susceptible to renal perfusion (Bamgbola, 2016).

1.2.5 Vancomycin ecotoxicity

Ecotoxicology reflects the interaction between chemical, biological and physical stressors and organisms in the environment (Connon et al., 2012). The result of the process depends on the toxicological properties of the specific chemical and the degree of susceptibility shown by indicator organisms.

Ecotoxicity of VMN, penicillin and tetracycline were assessed by Havelkova et al. (2016) and Laquaz et al. (2018) on indicator representative organisms (biosensors) at all trophic levels of the aquatic ecosystem. The green freshwater algae *Pseudokirchneriella subcapitata* representing the producers, consumers (water fleas *Daphnia magna*) and decomposers (bacteria *Vibrio fischeri*) were all selected. The study revealed the high toxicity of VMN to all indicator organisms. VMN concentration of 546 mg/kg resulted in 50% reproduction inhibition of *F. candida* in 28 days and ultimately mortality. On the other hand, *Vibrio fischeri* proved insensitive to VMN and no inhibition of bioluminescence was reported (Brandt et al., 2015).

1.2.6 Vancomycin degradation in water

Most conventional WWTPs were not designed to handle wastewaters containing highly polar contaminants such as antibiotics (Xu et al., 2007). This can be partly attributed to the fact that antibiotics exist at low concentrations in the environment; however, they still remain high priority pollutants as their activities affect the environment (Mojica et al., 2011). Additionally, conventional end-of-pipe treatment technologies are more costly and might not be the best option as it is best to properly remove potentially hazardous pharmaceutical compounds as close as possible to their primary source (Jones et al., 2005).

Conventional WWTPs commonly use destructive methods: chemical oxidation and biodegradation, and non-destructive methods: adsorption, filtration and coagulation/flocculation/sedimentation, liquid extraction and membrane techniques.

Recently, oxidation process as well as photolysis (deterioration of compound by gaining light energy) has gained more recognition in antibiotic degradation with more emphasis on advanced oxidation processes (Ge et al., 2018). Advanced oxidation processes have proved to be the best option for antibiotics degradation and removal in water and wastewater (Zhang et al., 2006).

1.3 Antibiotics in the environment

Advanced oxidation processes are set of chemical treatment processes characterized by the generation of highly reactive and non-selective hydroxyl radicals ($HO^{\bullet}$) from catalyzed ozone or peroxy-compounds to effectively remove organic and inorganic contaminants (Andreozzi et al., 1999; Homem & Santos, 2011; Oppenländer, 2003). These processes were firstly proposed for the purification of drinking water in the 1980s and were then studied for different wastewaters treatment (Deng et al., 2015; Glaze and Kang, 1989). The application of AOPs result in the efficient degradation of various organic pollutants, reduction of their toxicity while increasing biodegradability (Wang & Zhuan, 2020). Almost all types of organic contaminants can be turned into harmless and stable inorganic compounds, such as water, carbon dioxide and salts; hence, they are said to undergo mineralization (Pervez et al., 2019; Saleh et al., 2020). Hydroxyl radicals are generally produced from one or more primary oxidants (mainly ozone, oxygen, hydrogen peroxide) and/or energy source (ultraviolet light) and/or catalysts (Fe^{2+}, TiO_2).

The most common AOPs can be classified into two main groups: photochemical and non-photochemical processes. Photochemical AOPs include homogeneous and heterogeneous processes while non-photochemical AOPs include cavitation, ozonation, Fenton and Fenton-like processes, wet air oxidation, and peroxone process (Litter, 2005, Homem & Santos, 2011; Trovó et al., 2011).

Combining some of these processes, such as enhancement of photocatalysis with hydrogen peroxide addition, can degrade antibiotics and non-biodegradable compounds in effluents or convert them to smaller molecular substances, which could alleviate the inhibitive effect of antibiotics on microorganisms as well as enhance their removal rate (Hernandez et al., 2002; Safari et al., 2014). The organic compounds are oxidized to less refractory, less toxic and more biodegradable intermediate species or even mineralized (Huber et al., 2003). Occasionally, the formed metabolites are potentially more dangerous than the original parent compound (Dantas et al., 2008). Under standard conditions, AOPs can significantly reduce the concentration of pollutants from several hundreds' mg/L to less than 5 µg/L and as such significantly reduce chemical oxygen demand (COD) and total organic carbon (TOC) values (Munter, 2001).

The main advantage AOPs has over other chemical and biological processes is that these processes are environmentally friendly as pollutants are not transferred from one phase to the other unlike in chemical precipitation and adsorption and, additionally, massive amounts of hazardous sludge are not produced (Ayoub et al., 2010).

$HO^{\bullet}$ are highly reactive species that destroy pollutants and impurities by breaking them down first into simpler molecules and then decomposing or mineralizing such molecules (Andreozzi et al., 1999). $HO^{\bullet}$ has an oxidative potential between 2.8 V (pH 0) and 1.95 V (pH 14) (Pera-Titus et al., 2004). Hydroxyl radicals attack organic pollutants (R) through four main multi-step pathways: radical addition (Eq. 1), hydrogen abstraction (Eq. 2) in which hydrogen atom is taken from an organic compound (R-H) by the $HO^{\bullet}$ to form organic radical ($R^{\bullet}$), electron transfer (Eq. 3) and radical combination (Collin, 2019, Bokare & Choi, 2014).

$$R + HO^{\bullet} \rightarrow RHO \quad (1)$$

$$R\text{-}H + HO^{\bullet} \rightarrow H_2O + R^{\bullet} \quad (2)$$

$$HO^{\bullet} + RX \rightarrow RX^{\bullet+} + HO^{-} \quad (3)$$

$HO^{\bullet}$ perform optimally in groups of powerful oxidants that does not generate additional waste, are not toxic nor corrosive and have short lifetime (Cuerda-Correa et al., 2019). $HO^{\bullet}$ is an unselective strong chemical oxidant and it is highly suggested for the removal of problematic organic pollutants as it attacks nearly all organic complexes and diminishing the pollutant composition (Mohajerani et al., 2009).

For example, targeted micropollutants removal has been studied with UV photolysis and UV/H_2O_2 processes (Shu et al., 2013; Olmez-Hanci & Arslan-Alaton, 2013; Ghime & Ghosh, 2020). It was observed that the overall rate of oxidation and removal efficiency for the selected organic micropollutants in wastewater were enhanced in the presence of H_2O_2.

Recently, much attention has also been drawn to oxidation processes based on sulfate radicals (AOP-$SO_4^{\bullet-}$) (Deng & Ezyske, 2011).

1.3.1 Ozonation

Ozone is a powerful oxidant used for the treatment of water and wastewater especially those containing bio-refractory and/or toxic organic pollutants, such as pesticides (Gottschalk et al., 2009; Ikehata & Gamal El-Din, 2006), surfactants (Ikehata & Gamal El-Din, 2004), pharmaceuticals (Hansen et al., 2016). Ozonation is an environmentally friendly technique as it has no negative impact on the environment (Wang & Bai, 2017). Oxidation with ozone occurs through two main mechanisms: direct ozonation with dissolved molecular ozone (O_3) and indirect ozonation through the formation of $HO^{\bullet}$ via Eqs. (4-8) (Zaviska et al., 2009; Wang & Bai, 2017).

$$O_3 + HO^{-} \rightarrow HO_2^{\bullet} + O_2^{\bullet-} \quad (4)$$

$$HO_2^{\bullet} \leftrightarrow O_2^{\bullet-} + H^+ \quad (5)$$

$$O_3 + O_2^{\bullet-} \rightarrow O_3 + O_2 \quad (6)$$

$$O_3^{\bullet-} + H^+ \rightarrow HO_3^{\bullet} \quad (7)$$

$$HO_3^{\bullet} \rightarrow HO^{\bullet} + O_2 \quad (8)$$

The main limitations of ozonation are the low solubility of ozone in water, the cost of energy to produce ozone, and the formation of hazardous by-products such as bromate (Katsoyiannis et al., 2011). The treatment efficiency of ozonation depends on the pH of the medium, ozone dosage and the nature of the contaminant. It can be increased by combining ozone with hydrogen peroxide and/or UV radiation (Cuerda-Correa et al., 2019).

1.3.2 Fenton and Fenton-like process

The Fenton reaction was invented in 1894 by Henry John Horstman Fenton (Koppenol, 1993; Hayyan et al., 2016). This reaction generates hydroxyl radicals from ferrous ions-activated hydrogen peroxide in an acidic medium. It is an oxidation method widely used in wastewater treatment for destroying refractory and toxic pollutants since late 1960s (Huang et al., 1993). In the reaction, ferric ion (Fe^{3+}) was oxidized from ferrous ion (Fe^{2+}) by hydrogen peroxide to produce $HO^{\bullet}$ via Eq. (9) (Barbusiński, 2009; Wang & Zhuan, 2020).

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + HO^- + HO^{\bullet} \quad (9)$$

The ferric ion produced could further react with hydrogen peroxide or superoxide radical anion ($O_2^{\bullet-}$) via Eqs. (10-11) (Hayyan et al., 2016; Ameta et al., 2018).

$$Fe^{3+} + H_2O_2 \rightarrow Fe^{2+} + O_2^{\bullet-} + 2H^+ \quad (10)$$

$$Fe^{3+} + O_2^{\bullet-} \rightarrow Fe^{2+} + O_2 \quad (11)$$

The amount of added chemicals must be carefully optimized as excess Fe^{2+} and H_2O_2 scavenge the produced $HO^{\bullet}$ (Eqs. 12-13) (Ameta et al., 2018; Barbusiński, 2009).

$$Fe^{2+} + HO^{\bullet} \rightarrow Fe^{3+} + HO^- \quad (12)$$

$$H_2O_2 + HO^{\bullet} \rightarrow HO_2^{\bullet} + H_2O \quad (13)$$

Some of the main advantages of the Fenton process include high degradation efficiency and easy operation, however, the efficiency of this process largely depends on pH value (optimal pH around 3) (Duesterberg et al., 2008). In addition, at the end of the process, large amount of iron-containing sludge (secondary pollutant) is formed, which might be difficult to handle and dispose. To tackle these disadvantages, heterogeneous catalysts

or chelated catalysts can be introduced to improve the degradation of organics at neutral pH values, reduce the amount of sludge produced and promote redox reaction cycle of Fe^{2+}/Fe^{3+}. Such modified Fenton processes are commonly referred to as Fenton-like processes. (Zhou et al, 2008). Some of such heterogeneous catalysts are iron minerals like magnetite, goethite, ferrite, schorl (Xu et al., 2013; Wang et al., 2015), zero-valent iron (Xu and Wang, 2011); single metal, metallic oxide like MnO_2 (Saputra et al., 2013).

In general, the Fenton process has been effectively used to decompose organic compounds, such as pharmaceuticals, phenols, etc. (Tsapovsky et al., 2020; Xu et al., 2020).

1.3.3 Photo-Fenton process

When Fenton oxidation is conducted under UV radiation (photo-Fenton process), ferric ions produced in Eq. (9), undergo photo-reduction and are converted to ferrous ions as shown in Eqs. (14-15) (Ameta et al., 2018; Tamimi et al., 2008). UV light is absorbed up to a range of 400 nm. The photo-Fenton process generates more $HO^{\bullet}$, which enhance the oxidation efficacy and increase the rate of degradation of organic pollutants (Arslan-Alaton et al., 2010).

$$Fe^{3+} + H_2O + hv \rightarrow Fe^{2+} + HO^{\bullet} + H^{+} \quad (14)$$

$$Fe^{3+} + H_2O_2 + hv \rightarrow Fe^{2+} + HO_2^{\bullet} + H^{+} \quad (15)$$

Some of the advantages over conventional treatment methods include less sensitivity to toxic chemicals, less harmful by-products, decomposition of unused hydrogen peroxide to oxygen, etc. However, the process only occur in acid medium and iron removal is required (Brienza and Katsoyiannis, 2017).

For example, Lofrano et al. (2009) did a comparison between efficacy of photocatalysis, Fenton and photo-Fenton processes for the treatment of catechol. The results indicated that the Fenton and photo-Fenton processes are highly efficient in the target compound mineralization as well as in the removal of aromaticity. In another study, the photo-Fenton process was employed for the removal of sodium dodecyl sulfate from synthetic solutions and soft drink wastewater (Malakootian et al., 2016). More than 71% of the surfactant was removed from the real sample in 30 min, indicating the effectiveness of this treatment method.

Other Fenton-type systems include electro-Fenton, sono-Fenton, sono-photo-Fenton and sono-electro Fenton processes (Ameta et al., 2018).

1.3.4 Photocatalytic oxidation

Photocatalysis is an ecofriendly technique that degrades organic pollutant by harnessing UV-A radiation and/or solar energy using a semiconductor/photocatalyst (Khalid et al., 2017). The technique is a sustainable and energy-saving technology applied to wastewater contaminated with pollutants of low biodegradability, high complexity, and high concentration (Guo et al., 2017). Due to some limitations, co-catalytic elements such as noble metals, transition metals, non-metalloids, and metalloids (carbon nanotube, carbon quantum dots, graphene) are doped into the process to enhance performance (Olama et al., 2018). The most used photocatalysts are TiO_2 and ZnO (Koe et al., 2019).

TiO_2 photocatalysts produce positive holes with oxidative capacity when excited, in the valence band (hv^+_{vb}), while negative electrons with reductive capacity are produced at the conduction band (e^-_{cb}) via Eqs (16-18) (Deng et al., 2015).

$$TiO_2 + hv \rightarrow e^-_{cb} + hv^+_{vb} \quad (16)$$

$$hv^+_{vb} + H_2O_{(absorbed)} \rightarrow HO^{\bullet}\cdot + H^+ \quad (17)$$

$$e^-_{cb} + O_{2(absorbed)} \rightarrow O_2^{\bullet -} \quad (18)$$

Photo-generated electrons and holes reacts with hydroxyl groups, water and oxygen to produce reactive oxygen species (ROS), such as $O_2^{\bullet -}$ and $HO^{\bullet}$, responsible for degradation of persistent organic pollutants present in water and wastewater (Han et al., 2018).

Some limitations, which bound the industrial application of the present photocatalytic system, include low-visible light absorption abilities, fast charge recombination, wide band gap energies of catalysts (E_g), low migration ability of photo-generated electrons and holes pair efficiency (Koe et al., 2019; Huang et al., 2017a, 2017b; Jo et al., 2019). Thus, the electrons and holes could recombine with each other and not participate in the photocatalytic reduction. Additionally, more energy must be absorbed for charge carrier separation to be delivered to achieve high E_g value (Micheal et al., 2019). The fast recombination rate lowers the number of photo-generated ROS available at the surface to carry out the photo-oxidation process and this significantly lowers the overall photocatalytic quantum. The limitations could be reduced however, by doping, coating, and surface organic modification (Dong et al., 2015)

1.3.5 Electrooxidation

Electrooxidation (EO), also called anodic oxidation or electrochemical oxidation is an important method for water and wastewater treatment that removes organic contaminants by anodic oxidation without the addition of chemical (Jiang et al., 2021). This technique has been used successfully:

- to degrade organic pollutants in industrial wastewater (Anglada et al., 2009), textile dye house effluent (Tsantaki et al., 2012), and paper mill effluent (El-Ashtoukhy et al., 2009; Guinea et al., 2010);
- to disinfect drinking water (Ma et al., 2011);
- to treat ballast water (Tsolaki et al., 2010);
- to facilitate remediation of polluted soils (Streche et al., 2018).

EO occurs either through direct oxidation via $HO^{\bullet}$ produced on the surface of anode during treatment process (Kapalka et al., 2010) or through indirect oxidation where oxidants like chlorine, hypochlorous acid, hypochlorite (Rajkumar & Kim, 2006), hydrogen peroxide/ozone (Guinea et al., 2010) are produced at electrodes anodically to destroy pollutants via Eqs. (19-25) (Särkkä et al., 2015).

$$2Cl^- \rightarrow Cl_2 + 2e^- \quad (19)$$

$$Cl_2 + H_2O \rightarrow HOCl + H^+ + Cl^- \quad (20)$$

$$HOCl \rightarrow H^+ + OCl^- \quad (21)$$

$$H_2O \rightarrow HO^{\bullet} + H^+ + e^- \quad (22)$$

$$2HO^{\bullet} \rightarrow H_2O_2 \quad (23)$$

$$H_2O_2 \rightarrow O_2 + 2H^+ + 2e^- \quad (24)$$

$$O_2 + O^{\bullet} \rightarrow O_3 \quad (25)$$

EO technique was used to degrade VMN in an aqueous medium; the reaction conditions were optimized (Antunes et al., 2017). This method has shown to be effective alternative as 100% of degradation occurred in 2 min of treatment under optimum conditions using 3 cm inter electrode distance, 1100 mg/L of NaCl and 400 mA current supply. It was noted that EO efficacy increased with higher currents and higher concentrations of support electrolyte applied (NaCl, however chloride ions are formed due to the indirect oxidation of molecular chlorine yielded in the medium) (Wu et al., 2016) or $HO^{\bullet}$ (Singh et al., 2016).

1.3.6 Activated hydrogen peroxide processes

Hydrogen peroxide can be activated to form $HO^{\bullet}$ by thermal reduction, transition metal ions, UV radiation, and electrophilic activation (Huber et al., 2003; Heo & Park, 2018).

Photolytic degradation of hydrogen peroxide in the presence of UV radiation at 254 nm in water produces $HO^{\bullet}$ via Eq. (26) (Andreozzi et al., 1999).

$$H_2O_2 + hu \rightarrow 2HO^{\bullet} \text{ (hu: } \lambda<300 \text{ nm)} \quad (26)$$

Hydroxyl radicals produced from H_2O_2-based AOPs play an important role especially in sludge treatment by removal of refractory organic matters, traceable organic and inorganic contaminants (Deng and Zhao, 2015). $HO^{\bullet}$ has high reaction rate and enhance recycling, which leads to lesser footprint in the treatment plant (Guan et al., 2018). The use of activated hydrogen peroxide processes has also been studied successfully for textile effluent treatment (Krishnan et al., 2017) and for purification of drinking water on industrial scale (Munter, 2001). The addition of H_2O_2 to a water/wastewater treatment plant can be done at one or multiple points in the technological scheme. This is because excess H_2O_2 reacts with other contaminants resulting in complex materials (Krishnan et al., 2017). Activated H_2O_2 however, can be used to appropriately design and scale up industrial batch reactors for wastewater treatment (Vaferi et al., 2014). The disadvantage of UV/H_2O_2 process, however, is that hydrogen peroxide has poor UV light absorption characteristics, which result in energy wastage.

The application of UV and hydrogen peroxide photolysis for treatment of water and wastewater has been established over the years especially in eliminating pharmaceutical waste in surface water among other uses (Ryan et al., 2011; Adams et al., 2002; Yuan et al., 2011). These processes are best suited for removal of organic pollutants that exhibit low reactivity towards ozone and are photoactive (Homem & Santos, 2011).

1.3.7 Activated peroxymonosulfate and peroxydisulfate processes

Recently, attention has been drawn to $SO_4^{\bullet -}$-based technology, mainly activated peroxymonosulfate and peroxydisulfate processes. (Lutze et al., 2015). Some of the advantages $SO_4^{\bullet -}$-based AOPs have over $HO^{\bullet}$-based AOPs are higher selectivity level, higher oxidation potential, greater efficiency to oxidize pollutants containing unsaturated bonds or an aromatic ring, and efficacy over a wider pH range (Wang & Wang, 2018).

Peroxymonosulfate ion (HSO_5^-) is a strong oxidant with redox potential of 1.82 V (Wang & Wang, 2018). PMS exists as a whitish powder and it is acidic in liquid form or water

solution. PMS can be activated via Eq. (27) by alkaline conditions, ultraviolet light, activated carbon, transition metal ions, ultrasound, and hydrogen peroxide to form sulfate radicals (Devi et al., 2016; Yang et al., 2011).

$$HSO_5^- + \text{activator} \rightarrow SO_4^{\bullet-} + (HO^{\bullet} \text{ or } HO^-) \quad (27)$$

Just like PMS, PDS is also a strong oxidant with redox potential of 2.01V (Wang & Wang, 2018). PDS is either colorless or white crystal salt with high stability and solubility in water. Peroxydisulfate ion ($S_2O_8^{2-}$) is most widely used due to its diverse reactivity for industrial processes like polymerization, metal surface oxidation, manufacture of organic chemical (Watts & Teel, 2006). Peroxydisulfates exist as sodium, ammonium, or potassium salts. Sodium peroxydisulfate salt is the most preferred form due to its high solubility in water (Huling & Pivetz, 2006). The base compound for the formation of PDS is persulfuric acid ($H_2S_2O_8$), which is produced by electrolysis of sulfate salts (Huling & Pivetz, 2006). PDS can be activated via Eqs. (28-29) by heat, alkali, UV radiation, transition metal ions, ultrasound, and strong oxidants (Tsitonaki et al., 2010; Furman et al., 2010).

$$S_2O_8^{2-} \xrightarrow{\Delta/UV} 2SO_4^{\bullet-} \quad (28)$$

$$S_2O_8^{2-} + M^{n+} \rightarrow SO_4^{\bullet-} + SO_4^{2-} + M^{(n+1)+} \quad (29)$$

$SO_4^{\bullet-}$-based AOPs are considered an excellent chemical oxidation solution used for the degradation of refractory organic pollutants especially in the remediation of soil and water/wastewater (Tsitonaki et al., 2010; Duan et al., 2020). When compared with $HO^{\bullet}$, $SO_4^{\bullet-}$ possess equal or even higher redox potential based on their activation methods of 2.5-3.1 V (Neta et al., 1988; Gao et al., 2016). Also, $SO_4^{\bullet-}$ in some cases, have shown higher selectivity with longer half-life than $HO^{\bullet}$ (Ghanbari & Moradi, 2017). However, the process requires a large amount of peroxydisulfate activators (for example, PDS/Fe^{2+} system), which often generate toxic organic by-products (Chen et al., 2019).

Overall, $SO_4^{\bullet-}$ are generated *in situ* by the activation of PMS or PDS, which act as precursors through physical activation methods such as:

- heat (Ji et al., 2016),
- light radiation (Khan et al., 2017),
- ultrasound (Deng et al., 2015),

and the chemical activation approaches such as:

- transition metal ion activation (Chen et al., 2019),
- alkaline activation (Tsitonaki et al., 2010),
- strong oxidants activation (hydrogen peroxide, ozone) (M'Arimi et al., 2020),
- electrochemical activation (Tsitonaki et al., 2010).

Thermal activation

This is one of the easiest and effective method to activate PDS and PMS (Waldemer et al., 2007; Hori et al., 2008). Thus, at room temperature of about 22°C, PDS is activated (Zrinyi, 2017). However, the resultant effect of this is the high cost and demand of energy input and increased temperature can as well accelerate side reaction thereby lowering the removal efficiency of targeted pollutants (Johnson et al., 2008; Matzek & Carter, 2016). During the thermal activation of PDS process, $SO_4^{\bullet-}$ can also be transformed into $HO^{\bullet}$ (Eq. 30):

$$SO_4^{\bullet-} + H_2O \rightarrow SO_4^{2-} + HO^{\bullet} + H^+ \quad (30)$$

The rate of this reaction is quite very slow ($<2 \cdot 10^{-3}$ 1/s) at room temperature, hence the need for higher temperature (Yang et al., 2011). Wang et al. (2017) reported that degradation efficiency of aromatic hydrocarbon by PDS/heat system decreased when the temperature got over 60°C.

Alkaline activation

The impact of pH value on the decomposition of PMS and PDS is significant. Under alkaline conditions, namely, at a high concentration of alkali, PMS and PDS decompose to form $SO_4^{\bullet-}$, which is then converted to $HO^{\bullet}$ (Tsitonaki et al., 2010).

For example, removal efficiency of about 30% was reported on decabromodiphenyl ether (a bromine flame retardant added to plastic and textile), which degraded at 25°C using alkali-activated PDS system. Qi et al. (2016) reported that the application of alkali-activated PMS resulted in effective Acid Orange 7 decomposition (decolorization efficiency of 90%) at 25°C.

Radiation activation

PDS and PMS can be activated with radiation such as UV, gamma ray and ultrasonic. UV-C radiation is the most cost-effective and benign to activate PDS and PMS. The use of PDS and PMS photolysis has been reported to improve degradation of organic contaminants, such as imidacloprid, ciproflaxin, etc. (Ghanbari & Monradi, 2017; Lee et al., 2005; Xia et al., 2011; Wang et al., 2020a; Mahdi-Ahmed & Chiron, 2014). Guerra-Rodriguez et al. (2021) studied degradation of micropollutants in secondary treated

wastewater by UV-A/PMS system. The results showed 80% degradation of the target compounds within 5 min of treatment, as well as a decrease in phytotoxicity.

Depending on the contaminant concentration, the required concentration of PDS and PMS can be estimated. UV radiation has limited penetration into water, which limits the scope of application, in contrast to gamma radiation, which has a higher penetration (Shah et al., 2016).

Transition metal ions and metal oxide activation

Generally, transition metal and metal oxides can be divided into homogenous and heterogeneous activators. For homogenous transition metal ions, silver ion (Ag^{+}) is the most effective for activating PDS (Anipsitakis et al., 2004), while cobalt ion (Co^{2+}) is the best-suited activator for PMS (Hu & Long, 2016). Iron (Fe^{2+}, Fe^{0}) and its oxide are widely studied due to its non-toxicity and environmental-friendly attributes (Rastogi et al., 2009). However, it is difficult to recover metal ions from effluents and to ensure the stability of the oxides (Hu & Long, 2016).

Carbon-based activation

Carbonaceous materials possess relatively high surface area as well as high pore volume (Devi et al., 2016). The most widely used carbonaceous materials are activated carbon, biochar and graphene, which can serve both as activator and adsorbent for PDS and PMS (Karthikeyan et al., 2015; Fang et al., 2015). Due to surface deactivation after a period of use, carbonaceous materials may lose its activation capacity (Wang & Wang, 2018).

1.4 Aims of the study

The aim of this study was to evaluate the efficacy of photochemical oxidation of antibiotic vancomycin by UV-C photolysis, UV-C/H_2O_2, UV-C/PMS and UV-C/PDS systems. The research focused on comparing the application of different UV-C-activated peroxy-compounds based processes for the oxidation of the target compound in water matrix for the first time.

The specific objectives of the research study include:

- To study VMN oxidation by UV-C photolysis and selected AOPs;
- To assess the acute toxicity to luminescent bacteria of the initial and treated VMN aqueous solutions;
- To evaluate and compare the efficacy of VMN degradation and mineralization in selected AOPs under different treatment conditions;
- To assess the effectiveness of the utilization of peroxy-compounds in the studied treatment processes.

2. EXPERIMENTAL

2.1 Chemicals

Vancomycin salt ($C_{66}H_{75}Cl_2N_9O_{24}$, ≥99%), hydrogen peroxide (H_2O_2), potassium iodide (KI, ≥99%), potassium peroxymonosulfate compound ($KHSO_5 \cdot 0.5KHSO_4 \cdot 0.5K_2SO_4$, OXONE®, >4.0% active oxygen basis), sodium peroxydisulfate ($Na_2S_2O_8$, ≥99%), sodium bicarbonate ($NaHCO_3$, ≥99%) and sodium sulfite (Na_2SO_3 ≥98%) were obtained from Sigma-Aldrich. Methanol (CH_3OH, ≥99%) was supplied by Merck KGaA. All the chemicals used were of high analytical grade so no extra purification was required.

Double-distilled water (>18.2 MΩ cm) or ultrapure water (UW) (Millipore Simplicity® UV System, Merck) was used for the preparation of stock solution all through the experimental study.

2.2 Experimental Procedure

The bench scale experiments on photochemical oxidation of VMN were carried out in a batch and at ambient room temperature (22±1°C). VMN stock solutions (13.4 µM, 0.8 L) were treated in a 1 L cylindrical glass reactor for 180 min with UV-C photolysis, UV-C/H_2O_2, UV-C/PMS, and UV-C/PDS systems. With the aid of magnetic stirrer at a permanent agitation speed (~300-400 rpm), uniformity was maintained in the solution. The oxidation experiment was carried out at the initial pH (5.5±0.3) of the VMN solution or at pH adjusted to 3 or 11 by adding aqueous solutions of sodium hydroxide and/or sulphuric acid. In the case of UV-C/oxidant systems, the oxidation was initiated by the addition of oxidant (H_2O_2, PMS, or PDS) followed by exposure to UV-C radiation. A low-pressure mercury germicidal lamp (11 W, Philips TUV PL-S) sited in a quartz tube inside the cylindrical glass reactor was used as an UV-C source. To ensure constant output of the UV-C lamp, it was firstly switched on and left to warm up for 5-10 min before placing it in the reactor. The average irradiance entering the solution in the reactor was measured using spectrometer (Ocean Optics USB2000+) equipped with SpectraSuite software was 2.6 mW/cm^2. A constant temperature was maintained in the reactor throughout the experiment using a water-cooling jacket.

The VMN/H_2O_2, VMN/PMS, and VMN/PDS molar ratios of 1/1, 1/5, 1/10, corresponding to a molar concentration of peroxy-compounds ranging between 13.4-134 µM, were studied. The experiments on VMN oxidation with non-activated H_2O_2, PMS and PDS were conducted in identical reactor and treatment condition for the respective UV-C-induced

oxidation experiments. Samples for analysis were taken at pre-determined intervals. The oxidation quenching was done by the addition of methanol (sample/methanol volume ratio of 10/1) to measure VMN concentration measurement by high-performance liquid chromatography and the addition of sodium sulfite (oxidant/SO_3^{2-} molar ratio of 1/10) for total organic carbon analysis.

Most of the experiments were conducted in replicates. The results of the analysis are presented as the mean with a standard deviation using at least three parallel replicates less than 5%.

2.3 Analytical methods

VMN concentration was monitored using a high performance liquid chromatography combined with diode array detector (HPLC-PDA, Shimadzu, Japan) equipped with a Phenomenex Gemini (150 mm) NX-C18 (5 µm) column. The analysis was conducted using an isocratic method with a mobile phase mixture of 9% acetonitrile (with 0.3% formic acid) and 91% formic acid (0.3%) aqueous solution. The flow rate was kept at 0.25 mL/min. Samples (75 µL) were analyzed at a wavelength of 220 nm.

The pH was measured using a digital pH/Ion meter (Mettler Toledo S220). The TOC was measured by a TOC analyzer multi-N/C® 3100 (Analytik Jena).

The residual hydrogen peroxide concentration in the treated samples was measured spectrophotometrically at a wavelength of 410 nm with titanium sulfate by a H_2O_2-Ti^{4+} complex formation (Eisenberg, 1943). Accordingly, 0.5 mL of complex solution was added to the treated sample (4.5 mL), hand-shaken, and then analyzed with a GENESYS 10S spectrophotometer (Thermo Scientific).

The measurement of residual PMS and PDS concentration in the treated samples (0.4 mL) was done spectrophotometrically at a wavelength of 352 nm by an excess potassium iodide reaction with PMS or PDS towards the formation of I_2 (Liang et al., 2008). Blank samples were withdrawn from the reactor at the pre-determined time intervals of 60, 120, 180 min and were used to zero and standardize the spectrophotometer. Both zero-sample and resulting treated sample solutions were hand-shaken and allowed to wait 15 min before being analyzed with a GENESYS 10S spectrophotometer (Thermo Scientific). Residual concentration of PMS and PDS was determined by using the standard multipoint calibration.

The acute toxicity of VMN was studied using the Microtox® method (Model 500 Analyzer SDI) (ISO 11348-3:2007). The solution for reconstitution was prepared and used to activate freeze-dried *Vibrio fischeri*. In order to maintain the suspension osmotic

pressure of the test bacteria, concentrated salt solution (2% NaCl) was introduced to achieve 2% salinity. The salt solution served as control. Analysis samples were prepared by using the initial VMN solution (13.4 μM) and treated VMN solutions that had undergone 3 h of oxidation. Each toxicity test was performed in 10 dilutions, and the luminescence was measured after 15 min of exposure. The bacterial luminescence inhibition (INH%) was calculated via Eqns. (31-32).

$$INH\% = 100\text{-}IT_{15}\cdot 100/(KF\cdot IT_0) \quad (31)$$

$$KF = IC_{15}/IC_0 \quad (32)$$

Where: KF - correction factor, IC_{15} – control luminescence intensity after 15 min of contact time, IC_0 - initial luminescence intensity of control sample, IT_{15} - luminescence intensity of test sample after 15 min of contact time, and IT_0 - initial luminescence intensity of the test sample.

3 RESULTS AND DISCUSSION

The efficiency of direct UV-C photolysis for VMN decomposition was firstly evaluated. The values obtained were compared with the efficiency of UV-C/H_2O_2, UV-C/PMS, and UV-C/PDS processes at a VMN/oxidant molar ratio of 1/5 in VMN degradation in aqueous solution (Figure 4). The direct UV-C photolysis and UV-C-induced peroxy-compound-based processes studied were effective in the target compound oxidation, since they led to the complete degradation of VMN in less than 15 min.

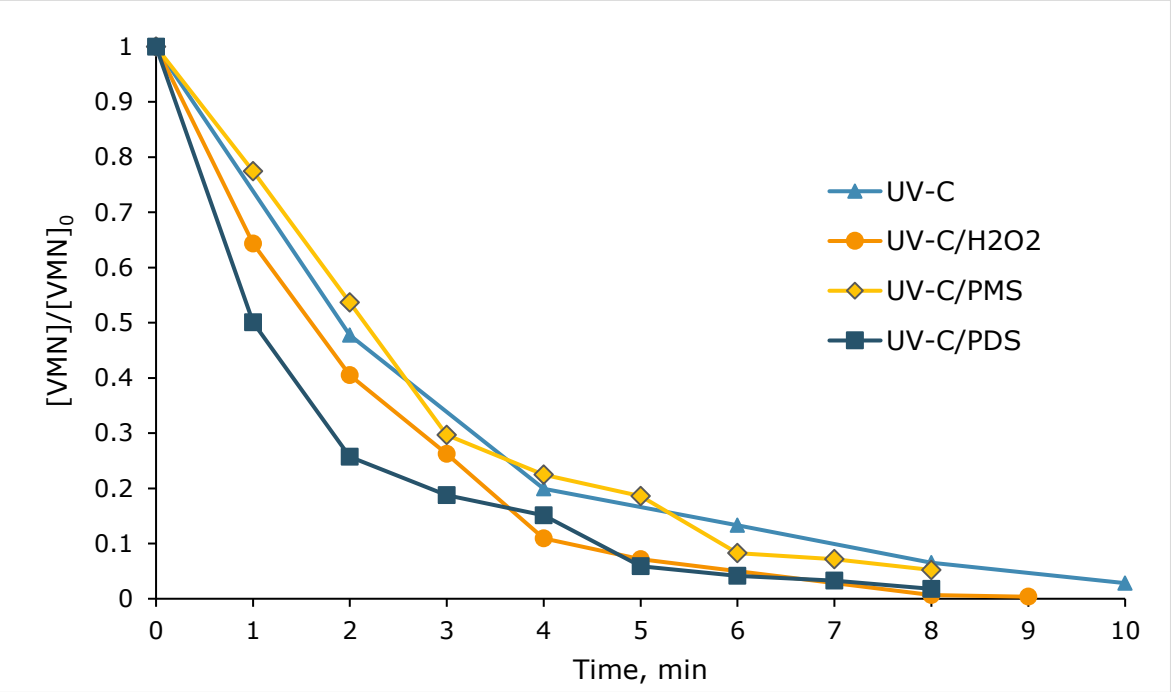

Figure 4. VMN decomposition by the UV-C photolysis, UV-C/H_2O_2, UV-C/PMS and UV-C/PDS processes ($[VMN]_0$=13.4 μM, $[H_2O_2]_0$=$[PMS]_0$=$[PDS]_0$=67 μM, pH initial)

The result of the conducted experiments clearly showed that VMN degradation in the UV-C photolysis and UV-C-activated systems followed a pseudo-first order kinetics law ($r^2 \geq 0.98$) and can be described in relation to the VMN concentration using eqn (33):

$$\frac{dC_{VMN}}{dt} = -k \times C_{VMN} \quad (33)$$

where k is the apparent pseudo-first-order rate constant and C_{VMN} is the VMN concentration. The rate constant (k) was determined from the slope of straight line by plotting ln (C_t/C_0) as a function of time (t) through linear regression (Figure 5).

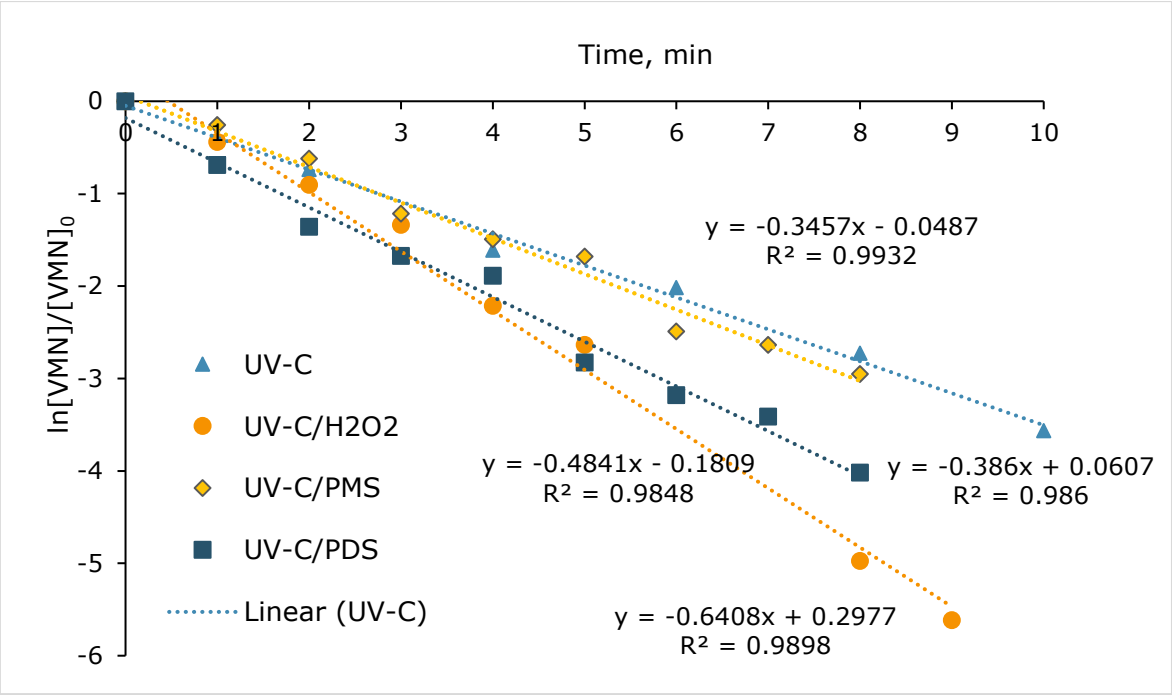

Figure 5. VMN decomposition by the UV-C photolysis, UV-C/H_2O_2, UV-C/PMS and UV-C/PDS processes: k values calculation through linear regression ($[VMN]_0$=13.4 μM, $[H_2O_2]_0$=$[PMS]_0$=$[PDS]_0$=67 μM, pH initial)

3.1 UV-C photolysis

Experiments on direct photolysis of UV-C were conducted at various pH values in an unbuffered solution to assess the effect of the pH of the medium on the efficiency of VMN decomposition (Figure 6). Thus, the trials were conducted at the initial pH (5.5±0.3) of VMN aqueous solution as well as at adjusted pH to 3 and 11. Measurements of the final pH values after 3 hours of treatment showed that noticeable changes in pH were observed only in the experiment at the initial pH value (Table 2). While in adjusted acidic (pH 3) and alkaline (pH 11) solutions, there was practically no change in pH.

The calculated values of the kinetic rate constants for the degradation of targeted compound at given treatment conditions are presented in Table 2. Comparison of the calculated kinetic rate constants showed that VMN degradation at initial pH and adjusted to pH 3 resulted in similar values (0.340 and 0.346 1/min, respectively), while treatment at pH 11 had higher performance and resulted in k of 2.191 1/min.

Similarly, VMN mineralization, measured as TOC removal, was the highest (TOC removal of 29.5%) after a 3-h UV-C photolysis at pH 11 (Table 2). Regardless of the treatment

conditions, the mineralization of VMN was less efficient than its decomposition, which indicates the formation of recalcitrant by-products.

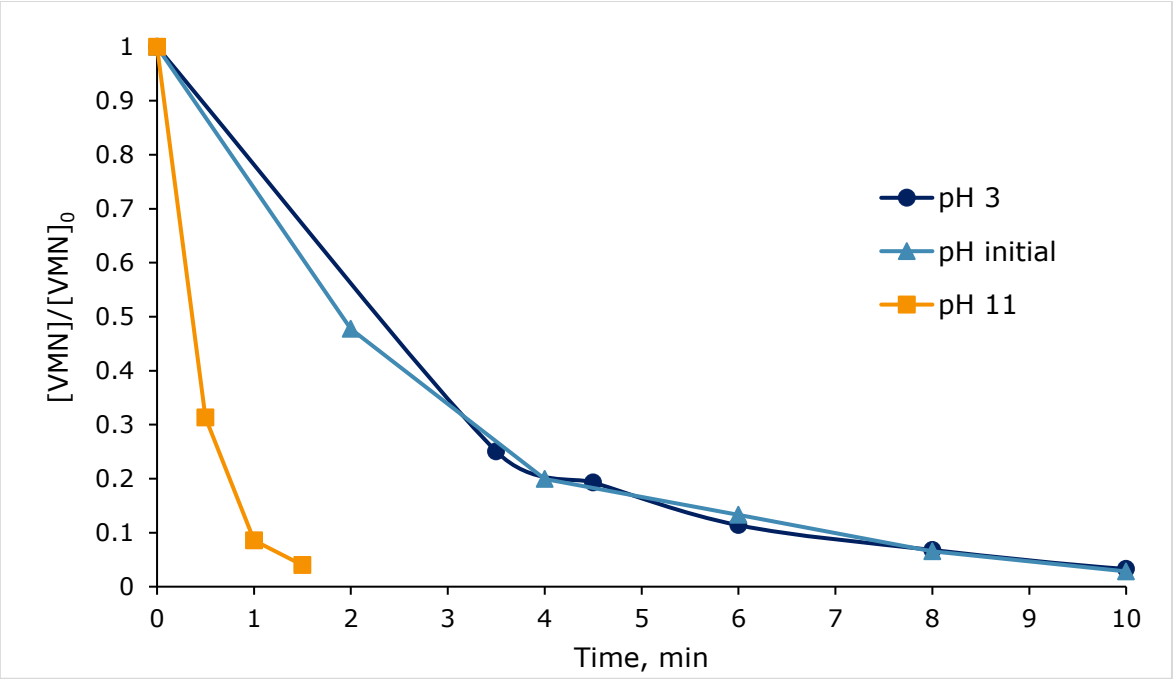

Figure 6. VMN decomposition by the UV-C photolysis at different pH values ($[VMN]_0$=13.4 μM)

Table 2. Residual pH, pseudo-first order rate constants and TOC removal for VMN decomposition by the UV-C photolysis ($[VMN]_0$=13.4μM, t=180 min)

pH_0	pH_{180}	k, 1/min	TOC removal, %
3.00	2.96	0.340 ± 0.009	6.2
5.67	4.48	0.346 ± 0.014	4.1
11.02	10.81	2.191 ± 0.159	29.5

To improve the efficiency of VMN removal from water using UV-C photolysis, the addition of peroxy-compounds, such as hydrogen peroxide, peroxymonosulfate and peroxydisulfate, to the treatment system was studied.

3.2 UV-C/H_2O_2 process

The effect of adding hydrogen peroxide to the UV-C system on VMN decomposition performance was examined at different VMN/H_2O_2 molar ratios as shown in Figure 7. Accordingly, an increase in the dosage of oxidant resulted in a faster degradation of the target compound in the UV-C/H_2O_2 system. Most likely, increase in the oxidant dosage led to an improved removal efficiency of the system by generating more hydroxyl

radicals. This observation can be confirmed by Eq. (26), where hydrogen peroxide is activated by UV radiation to form $HO^{\bullet}$.

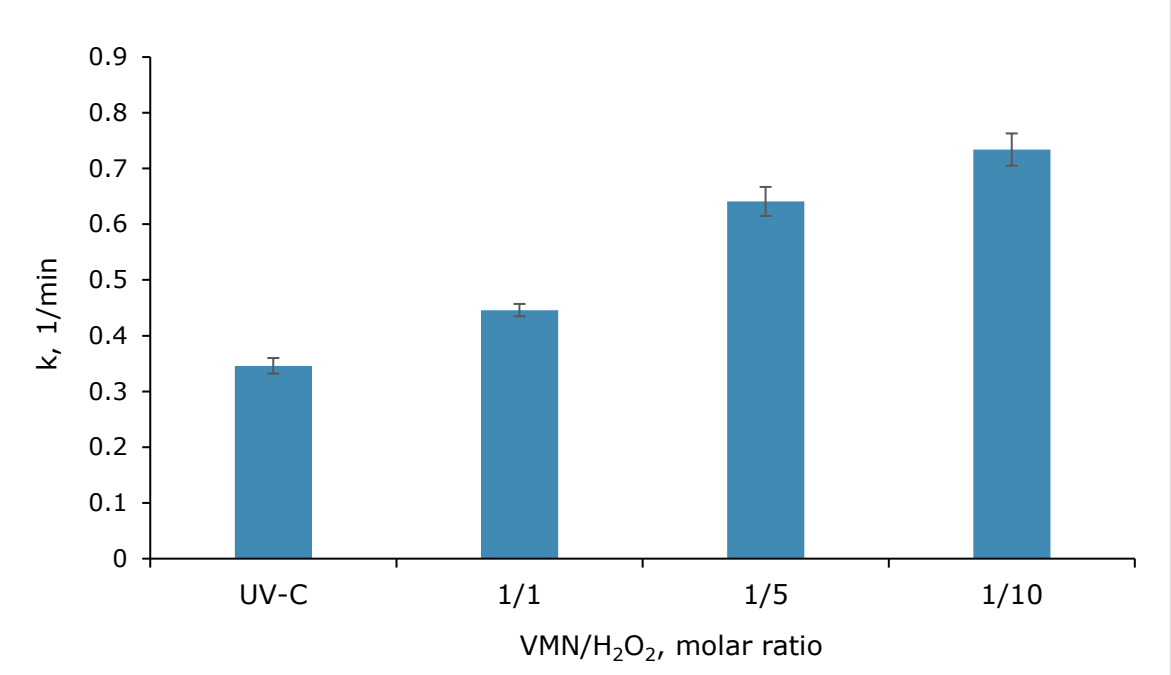

Figure 7. VMN decomposition rate constants by the UV-C photolysis and UV-C/H_2O_2 process at different VMN/H_2O_2 molar ratios ([VMN]$_0$=13.4 μM, pH initial)

The most notable effect of adding hydrogen peroxide to the UV-C system on VMN decomposition was observed when the oxidant dosage was increased to a VMN/H_2O_2 molar ratio of 1/10. Likewise, the most complete utilization of H_2O_2 after 3 hours of treatment was observed at the highest concentration of hydrogen peroxide studied, indicating the overall effectiveness of the treatment conditions (Table 3).

Table 3. Residual pH and residual hydrogen peroxide concentrations for VMN decomposition by the UV-C/H_2O_2 process ([VMN]$_0$= 13.4 μM, t=180 min)

VMN/H_2O_2, molar ratio	**pH_0**	**pH_{180}**	**Residual H_2O_2, %**
1/1	5.41	4.33	67.2
1/5	5.54	4.1	70.1
1/10	5.23	3.84	57.5
1/5	10.81	10.18	6.0

Although a higher efficiency of VMN removal by UV-C photolysis was obtained at pH 11, the UV-C/H_2O_2 oxidation experiment was carried out both at the initial pH (5.5±0.3) and at an alkaline value. The former treatment conditions were chosen to evaluate the

possibility of improving the overall VMN removal efficiency without the cost of pH adjustment.

Even the use of the lowest studied dosage of hydrogen peroxide (VMN/H_2O_2 molar ratio of 1/1) led to faster decomposition of VMN (k=0.446 1/min) compared to direct UV-C photolysis (k=0.346 1/min) (Figure 7). Furthermore, a 5-fold concentration rise of the oxidant showed an almost twice faster decomposition of the target compound with k=0.641 1/min. In turn, UV-C/H_2O_2 oxidation at a VMN/H_2O_2 molar ratio of 1/10 showed k value of 0.734 1/min and 2.449 1/min at initial pH and pH 11, respectively. Thus, the most efficient degradation of the antibiotic was still obtained under alkaline conditions with the least residual oxidant of 6%.

The efficiency of VMN mineralization by the UV-C/H_2O_2 process was also evaluated and the TOC removal results are presented in Figure 8. In experiments on hydrogen peroxide photolysis carried out at initial pH, the highest TOC removal of 38% was observed at a VMN/H_2O_2 molar ratio of 1/10. This was followed by treatment at a molar ratio of 1/5, which removed 19.7% of the TOC. The UV-C/H_2O_2 oxidation at a molar ratio of 1/1 demonstrated similar mineralization efficiency as with direct UV-C photolysis and resulted in only 4.4% TOC removal.

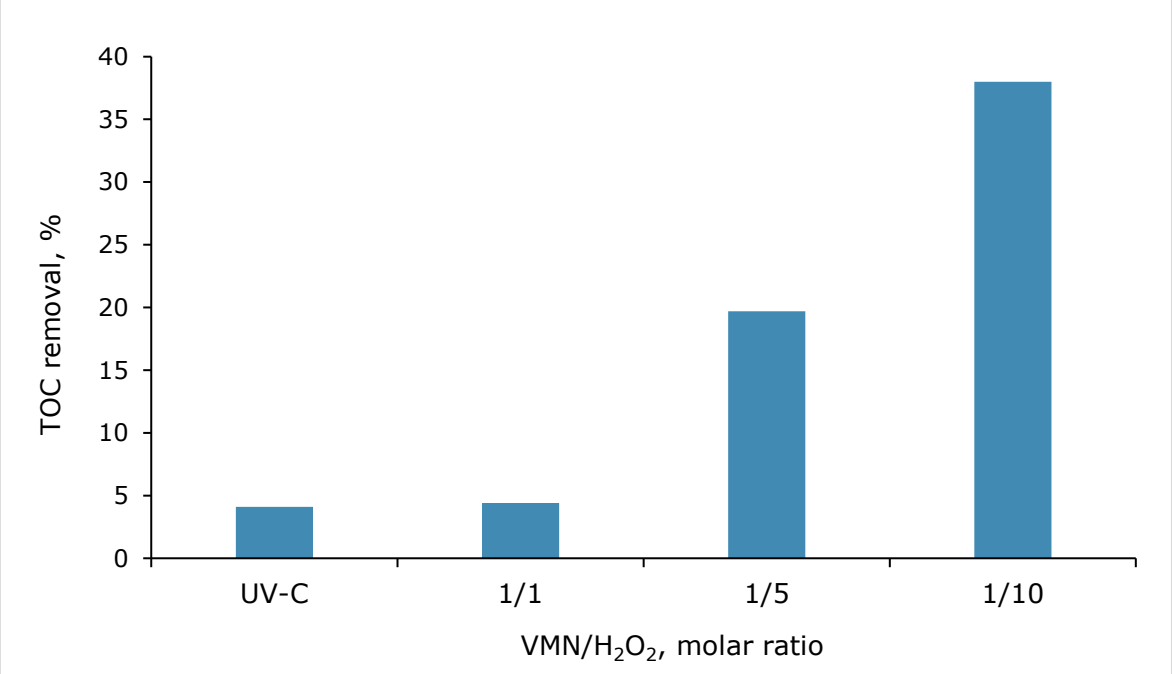

Figure 8. TOC removal by the UV-C photolysis and UV-C/H_2O_2 process at different VMN/H_2O_2 molar ratios ($[VMN]_0$=13.4 μM, pH initial, t=180 min)

It is noteworthy that the H_2O_2 oxidation was also investigated in the absence of UV-C radiation at a molar VMN/oxidant ratio of 1/10. The result showed negligible degradation of VMN with 99% residual oxidant after a 3-h oxidation, indicating the importance of the oxidant activation by UV-C radiation to obtain a real treatment effect.

3.3 UV-C/PMS process

In the UV-C/PMS systems, the effect of added oxidant dosage was also studied. Thus, the efficiency of UV-C/PMS oxidation in the degradation of VMN was examined at VMN/PMS molar ratios of 1/1, 1/5 and 1/10, as shown in Figure 9.

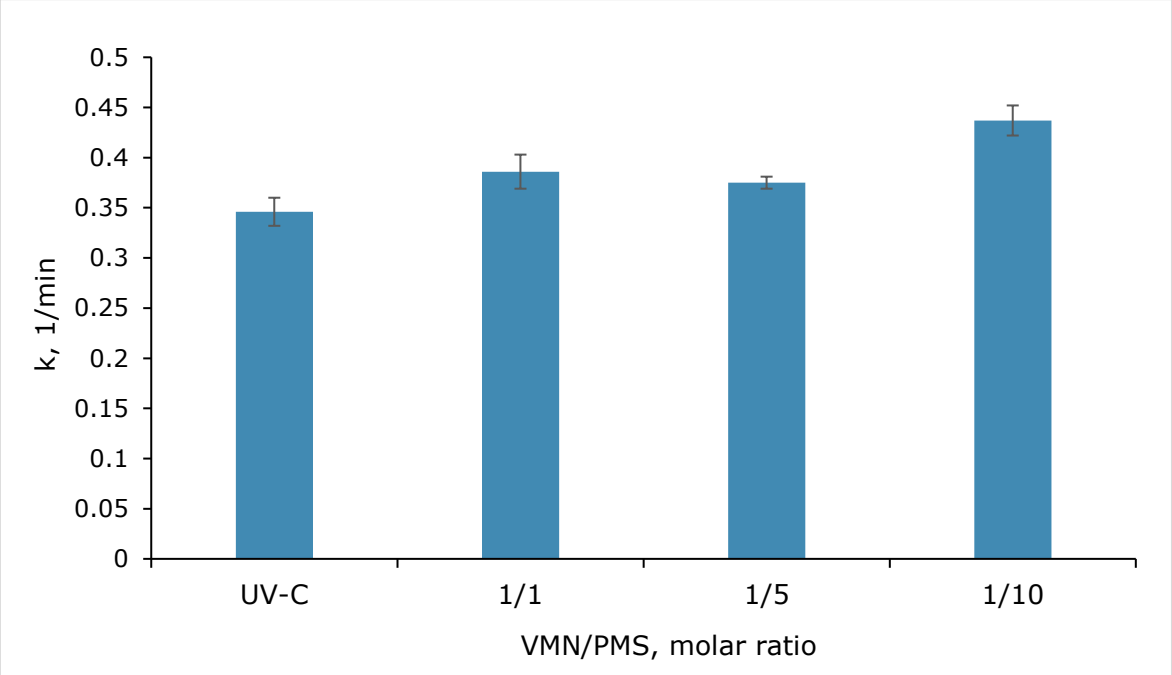

Figure 9. VMN decomposition rate constants by the UV-C photolysis and UV-C/PMS process at different VMN/PMS molar ratios ($[VMN]_0$=13.4 μM, pH initial)

The results revealed that the highest efficiency among the studied systems at the initial pH was observed when the dosage of the oxidant was adjusted to a VMN/PMS molar ratio of 1/10. Accordingly, the calculated VMN degradation rate constant was 0.437 1/min. In turn, the UV-C/PMS oxidation at a VMN/PMS molar ratio of 1/1 and 1/5 led to almost the same k values of 0.386 and 0.375 1/min, respectively. Overall, the addition of PMS to UV-C systems had a moderate impact on the degradation efficiency of VMN.

Just as the case of the UV-C/H_2O_2 system, incomplete utilization of the oxidant was observed after 3 hours of peroxymonosulfate photolysis (Table 4). In addition, bringing

the pH to an alkaline value led to more rapid VMN decomposition (k = 1.425 1/min) at a VMN/PMS molar ratio of 1/5, but did not have a positive effect on the efficiency of oxidant utilization.

The results of TOC removal using the UV-C/PMS systems at initial pH and various oxidant concentrations are presented in Figure 10. The highest extent of VMN mineralization (TOC removal 10.7%) was observed after a 3-h treatment at a VMN/PMS molar ratio of 1/1. This was followed by UV-C/PMS treatment at a molar ratio of 1/5 with a TOC removal of 7.5%. The use of the lowest PMS concentration studied did not lead to an improvement in TOC removal (4%) compared to direct UV-C photolysis (4.1%).

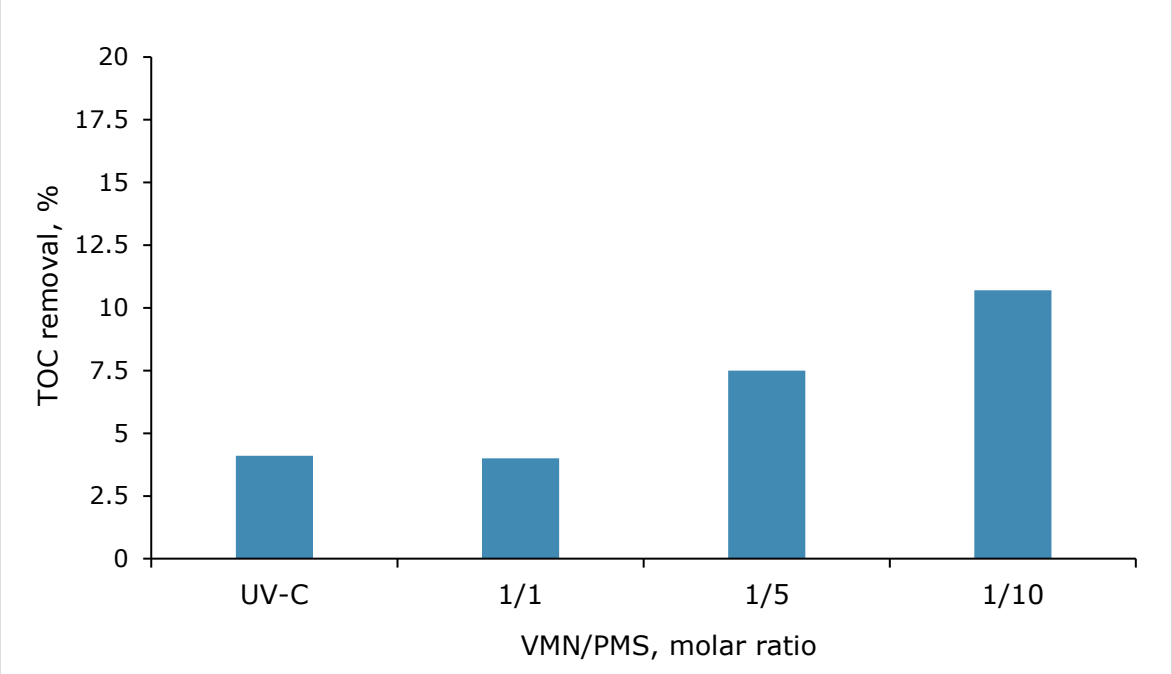

Figure 10. TOC removal by the UV-C photolysis and UV-C/PMS process at different VMN/PMS molar ratios ($[VMN]_0$=13.4 μM, pH initial, t=180 min)

Table 4. Residual pH and residual peroxymonosulfate concentrations for VMN decomposition by the UV-C/PMS process ($[VMN]_0$= 13.4 μM, t=180 min)

VMN/PMS, molar ratio	pH_0	pH_{180}	Residual PMS, %
1/1	5.45	4.1	*
1/5	5.80	4.36	46.5
1/10	5.45	4.1	60.2
1/5	10.86	10.51	63.4

*no data

Blank PMS oxidation in the absence of UV-C radiation was as well examined at a VMN/PMS molar ratio of 1/10. The results showed negligible VMN removal and less than 3% of the oxidant consumption after 3 hours of treatment.

3.4 UV-C/PDS process

The efficacy of the UV-C/PDS process in VMN degradation was studied at VMN/PDS molar ratios of 1/1, 1/5 and 1/10 at initial pH as showed in Figure 11. As in the case of hydrogen peroxide photolysis, an increase in the oxidant dosage led to an increase in the efficiency of VMN decomposition during the UV-C/PDS oxidation. Accordingly, the calculated VMN degradation rate constants were 0.388, 0.484 and 0.629 1/min for treatment carried out at a VMN/PDS molar ratio of 1/1, 1/5, and 1/10, respectively.

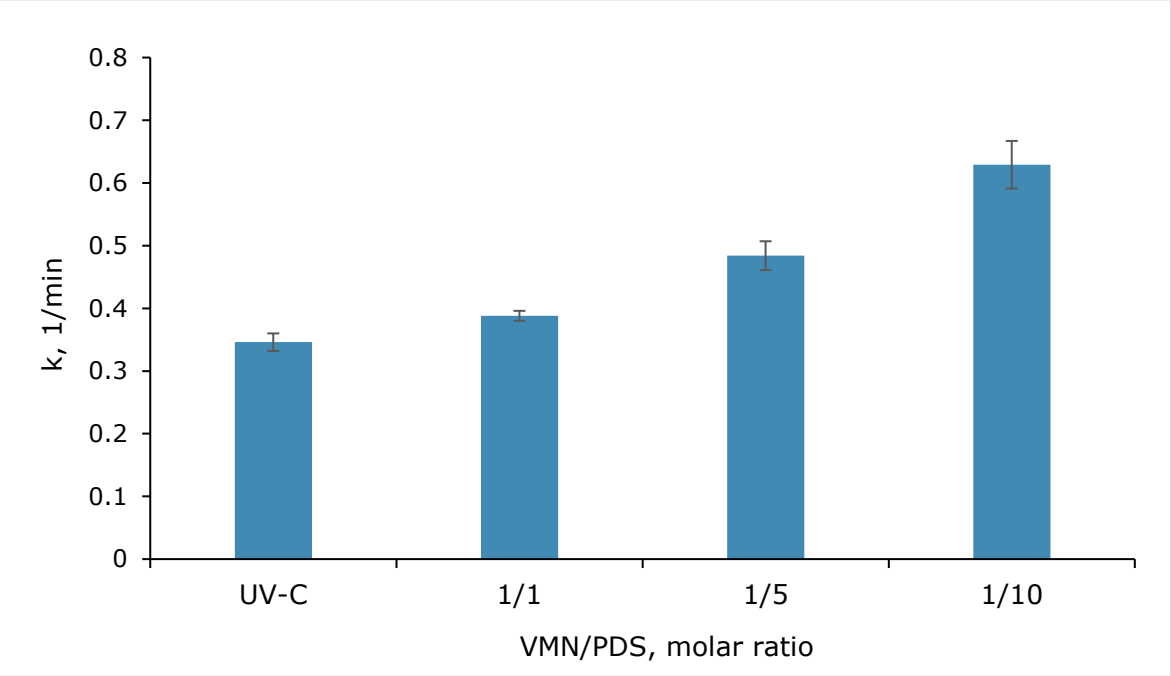

Figure 11. VMN decomposition rate constants by the UV-C photolysis and UV-C/PDS process at different VMN/PDS molar ratios ($[VMN]_0$=13.4 μM, pH initial)

The extent of VMN mineralization, measured as TOC removal, by the UV-C/PDS process was also assessed and the results are illustrated in Figure 12. The highest TOC removal (21.5%) was achieved after 3 hours of treatment at a VMN/PDS molar ratio of 1/10. In turn, the UV-C/PDS treatment at a molar ratio of 1/5 showed moderate efficiency with 11.1% of TOC removed, while oxidation at a molar ratio of 1/1 resulted in 7.2% TOC removal.

The residual PDS concentration in the UV-C/PDS system after 3 hours of treatment was also evaluated (Table 5). The results obtained showed that regardless of the pH values at which the treatment was carried out, the utilization of PDS was incomplete. Thus, 40.2 and 48.4% residual PDS was observed in the treated solution after UV-C/PDS oxidation (VMN/PDS molar ratio of 1/5) at initial pH and pH 11, respectively. On the other hand, a 3-h oxidation period at a VMN/PDS molar ratio of 1/1 and 1/10 resulted in the residual PDS concentration of 29 and 31.2%, respectively.

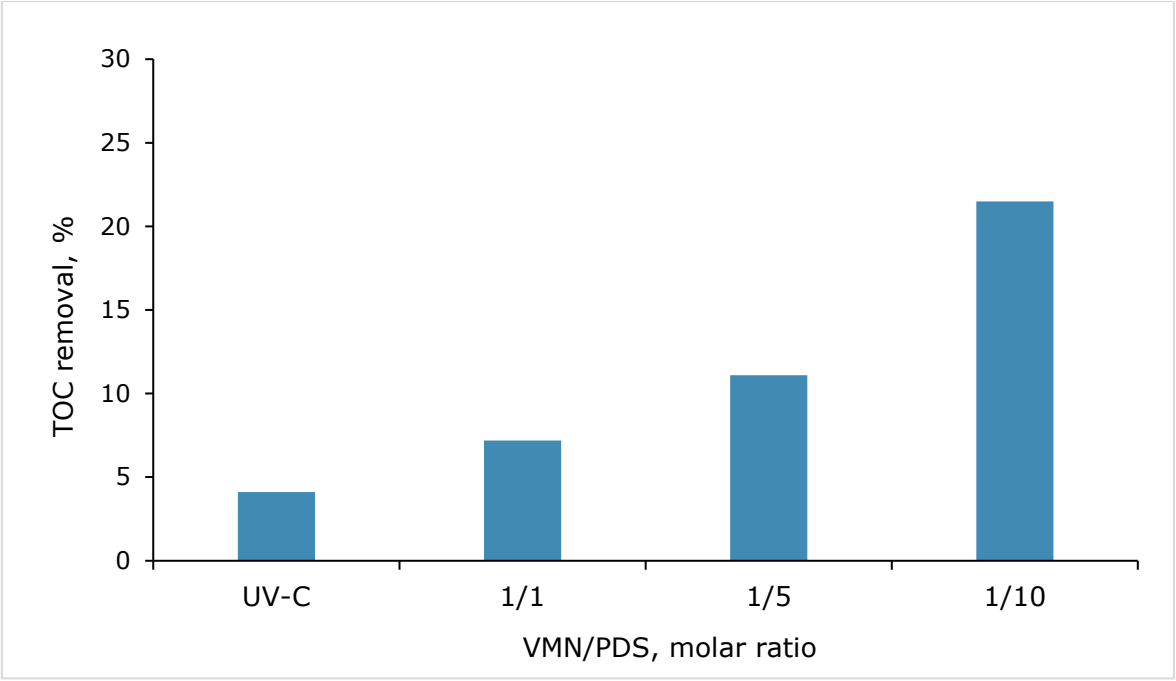

Figure 12. TOC removal by the UV-C photolysis and UV-C/PDS process at different VMN/PDS molar ratios ($[VMN]_0$=13.4 μM, pH initial, t=180 min)

The drop in pH noted in all studied UV-C-induced PDS systems was due to the formation of acidic intermediates as well as the acidity of the PDS (Table 5).

Table 5. Residual pH and residual peroxydisulfate concentrations for VMN decomposition by the UV-C/PDS process ($[VMN]_0$= 13.4μM, t=180 min)

VMN/PDS, molar ratio	**pH_0**	**pH_{180}**	**Residual PDS, %**
1/1	5.36	4.04	29.0
1/5	5.66	3.66	40.2
1/10	5.75	3.47	31.2
1/5	11.05	10.45	48.4

It should be noted that the target compound degradation efficacy of PDS oxidation in the absence of UV-C radiation has also been evaluated. Similar to the blank H_2O_2 and PMS oxidation, a 3-h treatment at a VMN/PDS molar ratio of 1/10 resulted in negligible VMN removal and PDS consumption.

3.5 Comparison of the efficiencies of UV-C photolysis, UV-C/H_2O_2, UV-C/PMS and UV-C/PDS processes

To compare the efficiency of the studied treatment processes in the degradation and mineralization of VMN, a fixed oxidant concentration of 67 μM was chosen for UV-C-induced peroxy-compound-based systems (Figures 13 and 14). In addition, the effect of two pH values, namely initial and pH 11, was evaluated. Finally, the results obtained were compared with direct UV-C photolysis under similar treatment conditions.

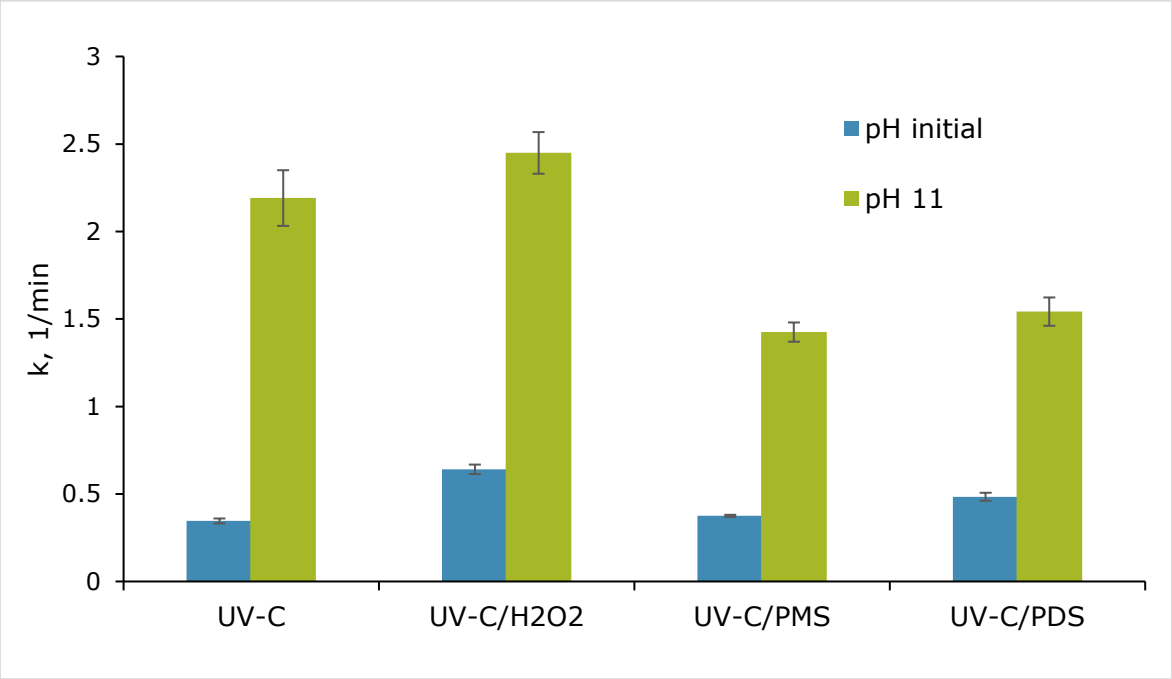

Figure 13. VMN decomposition rate constants by the UV-C photolysis, UV-C/H_2O_2, UV-C/PMS and UV-C/PDS processes ($[VMN]_0$=13.4 μM, $[H_2O_2]_0$=$[PMS]_0$=$[PDS]_0$=67 μM)

The application of direct UV-C photolysis and UV-C/H_2O_2 process at alkaline pH turned out to be most effective for the decomposition of VMN with high rate constants of 2.191 and 2.449 1/min, respectively. In turn, the use of UV-C/PMS and UV-C/PDS processes at pH 11 resulted in k values of 1.43 and 1.542 1/min, respectively, which was better than the achievements at initial pH, but lower than with direct UV-C and H_2O_2 photolysis at alkaline pH.

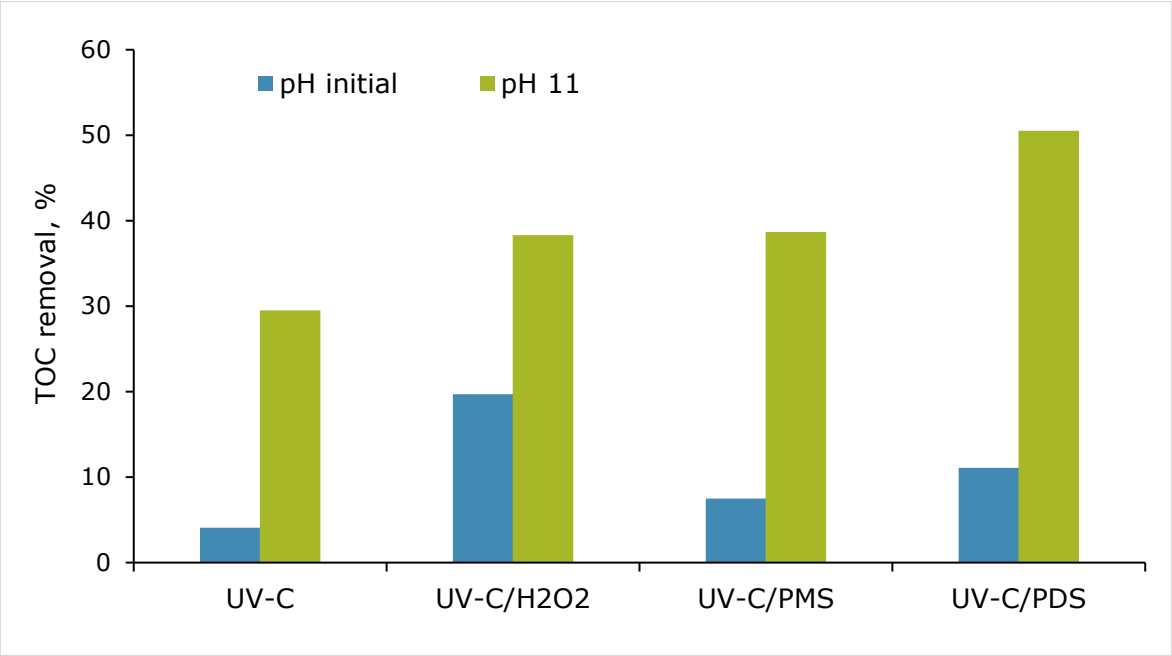

Figure 14. TOC removal by the UV-C photolysis, UV-C/H_2O_2, UV-C/PMS and UV-C/PDS processes ($[VMN]_0$=13.4 μM, $[H_2O_2]_0$=$[PMS]_0$=$[PDS]_0$=67 μM, t=180 min)

In initial pH experiments, the direct UV-C photolysis proved less effective among studied treatment processes with k value of 0.346 1/min. The fastest VMN degradation was observed in the UV-C/H2O2 systems with k values of 0.641 1/min surpassing other systems. Similar to the target compound degradation results at initial pH, the most efficient TOC removal was achieved with the UV-C/H_2O_2 system (19.7%), followed by the UV-C/PDS process (11.1%).

Regardless of the treatment process studied, VMN mineralization was higher at pH 11. Thus, the use of the UV-C/PDS system resulted in a maximum TOC removal of 50.5% after 3 hours of treatment. Other systems showed the following TOC removal: UV-C photolysis (29.5%), UV-C/PMS process (38.7%) and UV-C/H_2O_2 process (38.3%).

Overall, it can be assumed that pH 11 is more favorable for the removal of VMN from water by UV-C-induced processes and direct UV-C photolysis. In addition, the combination of UV-C radiation with peroxy compounds, especially H_2O_2 and PDS, can be a very promising solution for effectively treating vancomycin-contaminated water.

It is noteworthy that the toxicity of the original and photochemically treated VMN solutions were tested using the bioluminescent bacteria *Vibrio fischeri* in a luminometer. The results revealed that both the initial VMN solution and the samples subjected to photochemical treatment turned out to be non-toxic to bacteria.

SUMMARY

The main goal of this study was to investigate the potential of UV-C-induced peroxy-compound-based processes for the degradation and mineralization of the antibiotic vancomycin in aqueous solution. The peroxy-compounds considered were hydrogen peroxide, peroxymonosulfate, and peroxydisulfate. The results obtained were compared with the efficiency of direct UV-C photolysis for the decomposition of the target compound. The effects of different concentrations of peroxy-compounds as well as pH values on the effectiveness of treatment with UV-C/H_2O_2, UV-C/PMS and UV-C/PDS systems were investigated. Regardless of the studied process and treatment conditions, the degradation of VMN was considerably more efficient than its mineralization. However, the use of combined UV-C/oxidant systems resulted in an improved extent of VMN mineralization compared to direct UV-C photolysis. In the case of initial pH experiments, the fastest target compound degradation was observed in the UV-C/H_2O_2 systems with k values surpassing other systems. Similarly, the most efficient TOC removal was achieved with the UV-C/H_2O_2 process (38%) followed by the UV-C/PDS process (21.5%), in both cases at a VMN/oxidant molar ratio of 1/10. The use of direct UV-C photolysis and UV-C/H_2O_2 process at alkaline pH resulted in the fastest decomposition of VMN. However, the use of the UV-C/PDS system showed the highest TOC removal (50.5%) after 3 hours of treatment at pH 11, followed by the UV-C/PMS system (38.7%) and the UV-C/H_2O_2 system (38.3%).

Therefore, it can be suggested that pH 11 is more favorable for the removal of VMN from water by direct UV-C photolysis and UV-C-induced H_2O_2, PMS, and PDS processes. Additionally, the combination of UV-C radiation with peroxy-compounds, especially hydrogen peroxide and peroxydisulfate, can be a very promising solution for effective treatment of VMN-contaminated water.

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