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The Removal of Pharmaceuticals from Wastewater by Wet-Air Oxidation

Miao Sun

University of Denver

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The Removal of Pharmaceuticals From Wastewater by Wet-Air Oxidation

A Thesis
Presented to
the Faculty of Natural Sciences and Mathematics
University of Denver

In Partial Fulfillment
of the Requirements for the Degree
Master of Science

by
Miao Sun
June 2013
Advisor: Keith E. Miller
ABSTRACT

The ubiquitous occurrence of pharmaceuticals and personal care products (PPCPs) in aquatic environments has raised concerns about potential adverse effects on aquatic ecology and human health. Certain pharmaceuticals have recently become a major focus of research to better understand the routes and persistence of these compounds once they enter into aquatic system.

In this research, two model compounds were selected to represent pharmaceuticals that have been identified by recent research as being persistent; specifically, these compounds were trimethoprim (TMP, a basic antibiotic) and gemfibrozil (GEM, an acidic lipid regulator). Treatment of synthetic wastewater that contained these drugs was accomplished using wet-air oxidation (WAO). Pre- and post-treatment drug concentrations were determined by reversed-phase liquid chromatography. The influences of different operational conditions on removal efficiency of the drugs by WAO were evaluated, namely reaction time, initial drug concentration, oxygen concentration, and the amount and composition of additional organic matter used during WAO. The optimum removal efficiencies were found to be 91.9 % for TMP and 95.5 % for GEM.
ACKNOWLEDGEMENTS

I wish to thank Keith E. Miller for his continuous support through my two-year study and research at the University of Denver. I specifically want to thank Keith for giving me the guidance all the time of research and writing of this thesis, supporting me to do my non-thesis seminar, offering me the summer work opportunities in this groups, helping me fix the HPLC and VTR problems and giving me the freedom when my family need me. I would appreciate for all his patience, motivation, enthusiasm, and immense knowledge.

My sincere thanks go to the Dr. Sandra S. Eaton, Dr. Gareth R. Eaton, Dr. Andrei G. Kutateladze and Dr. Martin Margittai, for teaching me the excellent core courses during my first year study. They made several challenges in my early graduate career into an opportunity for learning, and I am richer for the experience.

I would also like to thank all the member of my thesis committee: Prof. Brian Majestic, Prof. Martin Margittai, and Prof Michael W. Kerwin, for their encouragement and insightful comments.

Last but not the least, I need to thank the constant support of my friends, especially Kellen J. Sorauf and Morgan S. Schmidt for their helps during our 2012 summer project. Special thanks goes to Darrel Hundley, Nitika Dewan, John Haynes, Zhelin Yu, as well as past and current members of the analytical section. I would also express my gratitude to my parents, for supporting me spiritually throughout my two-year US life.
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<tr>
<td>PPCP</td>
<td>Pharmaceuticals and personal care product</td>
</tr>
<tr>
<td>TMP</td>
<td>Trimethoprim</td>
</tr>
<tr>
<td>GEM</td>
<td>Gemfibrozil</td>
</tr>
<tr>
<td>COD</td>
<td>Chemical oxygen demand</td>
</tr>
<tr>
<td>BOD</td>
<td>Biochemical oxygen demand</td>
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<tr>
<td>WAO</td>
<td>Wet-air oxidation</td>
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<tr>
<td>CWAO</td>
<td>Catalytic wet-air oxidation</td>
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<tr>
<td>TSC</td>
<td>Thermal sludge conditioning</td>
</tr>
<tr>
<td>RPDM</td>
<td>Refinaria de Petroleos de Manguinhos</td>
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<tr>
<td>LPO</td>
<td>Low pressure oxidation</td>
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<tr>
<td>WWTP</td>
<td>Waste Water Treatment Plant</td>
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<tr>
<td>MBR</td>
<td>Membrane bioreactor</td>
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<tr>
<td>UV</td>
<td>Ultra-violet</td>
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<tr>
<td>NSAID</td>
<td>Non-steroidal anti-inflammatory drugs</td>
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<tr>
<td>VLDL</td>
<td>Very low-density lipoprotein</td>
</tr>
<tr>
<td>STP</td>
<td>Sewage treatment plant</td>
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<tr>
<td>RPLC</td>
<td>Reversed-phase liquid chromatographic</td>
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<td>VTR</td>
<td>Vertical tube reactor</td>
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<tr>
<td>AR</td>
<td>After reaction</td>
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<td>ACN</td>
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CHAPTER 1 INTRODUCTION

1.1 WASTEWATER

Water is indispensable for all forms of life. It is needed in almost all of human activities. The world’s population is growing by approximately 80 million people a year, implying an increase in freshwater demand of about 64 billion cubic meters a year (UNESCO 2009). The rapid increase in population and the increased demand for domestic, industrial, and agricultural establishments to meet human requirements have created problems such as overexploitation of available natural resources, leading to pollution of the land, air and water environments (Pokhrel and Viraraghavan 2004). Today, the topic of wastewater causes great concerns to both the public and researchers. This Chapter is separated into three parts, mainly to introduce the current context of water scarcity, the sources that result in water scarcity, and the related treatment technologies that are helping to reduce and solve the water scarcity issues.
1.1.1 WATER SCARCITY

Approximately 71% of the earth’s surface is covered by water. However, a small fraction (0.014%) of the world’s total water supply is readily available freshwater (Shiklomanov 1998, Tsuchida, Tamanoi and Murota 1984). Water is a renewable resource, but in many parts of the world, water resources have become so depleted or contaminated that they are unable to meet an ever-increasing demand. The challenges are more acutely felt in developing countries where 95% of the world’s new population is born each year (UNEPFI, SIWI 2005). Thus, water scarcity is currently an issue attracting attention worldwide, especially in regions where renewable water is limited (Table 1.1).

Because of the scarcity of water in many regions of the world exist, a host of problems, like socio-economic, environmental, and political conflicts/issues have resulted. In addition to these concerns, the lack of safe water is also the leading cause of disease, hunger and poverty in the developing world today. Right now, countless communities in over 50 nations are suffering because local water supplies are scarce, contaminated, or non-existent (MICATZ 2013).

A 2008 report by the World Health Organization indicated that more than 3.4 million people died each year from water, sanitation, and hygiene-related causes. Nearly all the deaths (99 %) occurred in the developing world (WHO 2008). For comparison, this is equivalent to almost the entire population in the city of Los Angeles in the United States. In addition, tens of thousands of people die
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Table 1.1 Population size and growth and renewable freshwater availability in water-scarce countries, 1995 and 2025 (Egelioğlu and Agboola 2012)
from causes directly related to contaminated water, and for those who survive, without good health, there is little chance for a normal and productive life (Project Humanity 2013). Throughout the world, water supplies in developing countries are contaminated with a wide variety of micro-organisms including viruses, bacteria and protozoans that cause typhoid, diarrheal diseases, amoebic dysentery, cholera, and other notoriously virulent diseases. Diarrhea is the most important public health concern that is directly related to water and sanitation. About 4 billion cases of diarrhea per year cause 1.8 million deaths, over 90 per cent of them (1.6 million) among children under five. Repeated episodes of diarrheal disease make children more vulnerable to other diseases and malnutrition (UNICEF 2003). Unfortunately, there has been a dramatic increase in the past 10 years of the number of deaths from the consumption of contaminated drinking water around the world.

1.1.2 WASTEWATER SOURCE

An understanding of the nature of wastewater is important for the appropriate design of wastewater treatment plants and the effective selection of treatment technologies. Wastewater originates predominantly from water usage by residences, commercial and industrial establishments, together with groundwater, surface water and storm water.

The growing public awareness of the fate of the pollutants and stringent regulations established by the various governmental authorities such as provincial
and federal agencies are forcing the industry to treat effluents to the required compliance levels before discharging the treated water to the environment (Padmapriya, Murugesan and Dhamotharan 2012). However, improperly disposed effluents from some industries still cause slime growth, thermal impacts, color problems, scum formation, and loss of aesthetic beauty in the environment (Schmidt and Kannenberg 1998). They also increase the amount of toxic substances in the water, causing death to the zooplankton and fish, as well as profoundly affecting the terrestrial ecosystem.

The Organization for Economic Cooperation and Development reported in 2001 that within the industrialized countries, the chemical industry was the single largest consumer of water (43%) followed by metals processing (26%), pulp and paper (11%), with other uses (20%) (Environmental Outlook for the Chemicals Industry 2009). Critical sources of water pollution include chlorine for water treatment in pulp and paper processing, semi-conductor manufacturing, photographic processing, pharmaceutical manufacturing, textile dyeing and cleaning, and processes as varied as metals. Several types of industries that are supposed to help improve the quality of life for humans are at the same time, discharging wastes from their processes that have now been identified as problematic groups of pollutants.

A. Pulp And Paper Processing

Wood consists of two primary components: cellulose and lignin. Pulping is
the process depending on the systematic separation of lignin from cellulose. The Kraft and sulphite process are the two significant chemical processes for pulp and paper industry to separating these two components (EPA 1997). During the biodegradation process, the use of a limited suite of enzymes: ligninase, glyoxal oxidase, and Mn peroxidase are needed. To achieve the same oxidation of these compounds, for which nature uses only oxygen, industry has substituted chlorine compounds, resulting in the release of phenolic compounds and environmentally persistent organo-chorine compounds (Hjeresen 2001).

In Canada, the pulp and paper industry accounts for a major portion of the country's economy in terms of value of production, but on the other hand, it is responsible for 50% of all wastes dumped into Canada's waters (Environment Canada 2012).

B. Textile And Dyeing Industry

Dye wastes are often rich in color and can be easily identified by the human eye. They contain residues of reactive dyes and chemicals, such as complex components, many aerosols, much more hard-degradation materials that result in a high chemical oxygen demand (COD) and biochemical oxygen demand (BOD) (Wang, et al. 2011). At present, most dyes are mainly heterocyclic, aromatic compounds, and color-display groups, which structure are more complicated and stable, thus, resulting in greater difficulty to treat effluent from printing and dyeing operation (Ding, Li and Wang 2010).
With the increasing demands of human consumption, the textile and dyeing industries consume large volumes of water, and thus produce large quantities of wastewater from different steps in the dyeing processes. According to the report, the textile and dyeing industries in China produced about 70 billion tons of wastewater each year, which required proper treatment before being released into the environment (State Environmental Protection Administration 2010).

C. Pharmaceuticals Manufacturing

Pharmaceutical companies are devoted to discovering and developing new medicines that will enable patients to live longer, healthier and more productive lives. But at the same time, they generate both hazardous and non-hazardous wastes, and the insufficient treatment of these wastes leads to surface and groundwater contamination that poses risks to the health of the aquatic ecosystems and the surrounding environment (Zorita, Martensson and Matthiasson 2009).

The pharmaceutical compounds reach the aquatic environment as effluents of the hospital structures, pharmaceutical industries, municipal sewage treatment plants, as well as residues of their use in agriculture and breeding (Nikolaou, Meric and Fatta 2007). Several investigations have shown evidence that some substances of pharmaceutical are detectable in the environment with concentration levels up to the µg /L due to incompletely removal during conventional wastewater treatments (Gòmez, et al. 2007, Comoretto and Chiron 2005).
Presently, the effects of pharmaceutical wastes on aquatic organisms are the apparent major concern, including inhibition of growth, production of stress hormone (abscisic acid), feminization and behavioral changes (Ngwuluka 2011). Furthermore, ibuprofen, fluoxetine and ciprofloxacin have been shown to cause mortality of fish in the μg/L range (Richards 2004).

1.1.3 WASTEWATER TREATMENT TECHNOLOGIES

Because water shortage is an ever increasing concern, a solution to increase the water availability and quality for several uses can be the reuse of sewage treatment plants effluents. Before the 1880s, people began to realize that the understanding and developing effective wastewater treatment technology was significant for human being’s healthy lives and was environmentally important. In 1899, the first wastewater treatment plant was set up and located near Yahara River at East Washington Avenue Madison, WI (Madison Metropolitan Sewerage District 2004). Over the past ten decades, the concern over increasing needs for drinking water and awareness for development of systems to improve water quality have provided incentives to develop new innovations and technologies and improve performance of existing technologies.

The general components in wastewater treatment processes could be categorized as physical, chemical and biological unit operations. Table 1.2 lists the unit operations included within each category. In order to achieve different levels of contaminant removal, individual wastewater treatment procedures are combined
into a variety of systems, classified as primary, secondary, and tertiary wastewater treatment. Normally, physical processes are used initially followed by chemical processes, like precipitation if needed. In sewage treatment plants, biological methods are generally the primary method for the treatment.

<table>
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<th>Physical unit operation</th>
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<th>Biological unit operation</th>
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<td>Anaerobic digestion</td>
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<td>Biological nutrient removal</td>
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Table 1.2 Wastewater treatment unit operations and processes (United Nations 2003)
This section mainly summarizes various conventional and advanced physical and chemical technologies in current use and explains how they are applied for the effective treatment of municipal wastewater.

A. Physical Operations

The main aim of physical treatment process in a water treatment system is to protect the main treatment systems from possible damage or clogging. Various processes are used to remove large floating and suspended material. The three widely used types of physical unit operations are described (Ramalho 1977).

i. Screening

Screening, one of the oldest treatment methods, is employed for removing gross pollutants from the waste stream to protect downstream equipment from damage and avoid interference with plant operations.

ii. Sedimentation

Sedimentation, a fundamental and widely used unit operation in wastewater treatment, is utilized to separated suspend solids from wastewaters. Removal by sedimentation is based on the difference between densities of solids and wastewater due to gravity.

iii. Flotation

Flotation is a process used to separate lower density solids or liquid particles from a liquid phase by introducing gas bubbles into the liquid phase. The
significant advantage of flotation over others is that very small or light particles can be removed more completely and in a shorter time.

**B. Chemical Operations**

Chemical processes used in wastewater treatment are designed to alter the compounds in the wastes by chemical reactions. This section mainly discusses the chemical unit processes, including chemical precipitation, adsorption, disinfection and other applications.

**i. Chemical Precipitation**

In this method, chemicals are added to the wastewater, converting undesired soluble substances into an insoluble precipitate that can be removed. Chemical coagulation of raw wastewater before sedimentation increase the removal efficiency, and it has a greater feasibility of using higher overflow rates. When removing the BOD from plain sedimentation, the reported removal percentages was only 25-40%, while for the prepared chemical precipitation, it increased up to 90% (WEF 1992).

**ii. Adsorption**

In wastewater treatment, adsorption with activated carbon aims to remove a portion of the remaining dissolved organic matters. Activated carbon has a unique property that is highly porous over a broad range of pore sizes from visible cracks to crevices of molecular dimensions. Intermolecular attractions in these smallest pores result in adsorption forces, which causes the adsorption of solutes from
solution into these molecular scale pores. The two most common types of activated carbon were granular activated carbon, which had a diameter greater than 0.1 mm, and powdered activated carbon, which had a diameter of less than 0.074 mm (Metcalf and Eddy 1991).

**iii. Disinfection**

Disinfection refers to the selective destruction of any pathogens, including viruses, bacteria such as Escherichia coli, Campylobacter and Shigella, and other Cryptosporidium, which pass through some water filters (Tansel 2008). This process is important in drinking water treatment. Traditional disinfection processes, such as chlorination and ozonation, are widely used in wastewater treatment plants (Pablos, et al. 2013). However, the most notable disadvantage of this technique is that disinfection produces chlorinated and brominated disinfection by-products with potential carcinogenic effects on mammals (Ikehata, Naghashkar and Gamal El-Din 2006).

**iv. Other Chemical Applications**

In addition to the chemical processes described above, various other applications are necessarily encountered in wastewater treatment. Dechlorination is the removal of free and total combined chlorine residues from chlorinated wastewater effluent. Wet-air oxidation treats wastewater in the presence of oxygen at a high temperature under high pressure to oxidize and decompose oxidizable substances. Ion exchange systems can exchange ions according to an equilibrium
reaction, which helps the softening or demineralization of water for industrial use (Tansel 2008).

1.1.4 SUMMARY

Water is life, it is an essential substance for living systems. However, the growing global crisis in water resources provides an important illustration of the influence of upstream pollution prevention. For the past decade, a large amount of patents applications for water and wastewater treatment were developed and have addressed improvements for reliability and maintainability and improved water quality, including the physical, chemical and biological technologies.

With the rapid increase in population and the increased demand to meet human requirements, new technological advancements are still needed to improve water quality. In the near future, with the advancements in materials science, nano technology, and information technology, it is likely that there will be new developments in the area of disinfection, oxidation methods, ion exchange resins, sorption technologies, and advanced biological methods such as membranes filtration and anaerobic digestion.
1.2 WET-AIR OXIDATION

Given the vast quantities of hazardous wastewater production from industrial and domestic activities, it is not surprising that environmental concerns have focused research on the development of efficient wastewater treatment technologies. Wet-air oxidation (WAO) is considered an emergent technology that can effectively treat organic wastewaters in order to meet the progressively more stringent environmental regulations.

As an established technology, WAO is useful for the treatment of hazardous, toxic, and non-biodegradable waste streams, without emissions of NO\textsubscript{x}, SO\textsubscript{2}, HCl, dioxins, furans and fly ash (Luck, Wet air oxidation: past, present and future 1999). Therefore, this technique has potential to help reduce the world’s water scarcity issue.

WAO has more than 80 years of commercial history. It originally developed in the 1930s as a process to produce artificial vanilla by wet-air oxidation of lingo sulphonic acids. It was patented as a waste treatment process in 1950 (Chemical Materiel Agency 2000). WAO was employed as an alternative method to treat special black liquors from paper mills. Because of their very high silica content, the usual evaporation and combustion method (Kraft process) was unsuitable (Zimmermann 1954). Since then, applications for the wet-air oxidation process had become as various as its history was long. For example, it has received significant interest as a means of removing organics from refineries and acidic
material from industrial plants as well as for pretreating sewage sludge (SIEMENS 2011, Chauzy, et al. 2010, Luck, Djafer, et al. 1999).

1.2.1 SYSTEM OVERVIEW

Wet-air oxidation is an aqueous phase oxidation process that uses molecular oxygen contained in air (or any other oxygen containing gas) as an oxidant. The process operates at elevated temperatures (120-320 °C) and pressures (110-3,000 psi) (Claude, Robert and Brandenburg 1994).

The typical wet-air oxidation system uses equipment to raise the feed stream and air (or oxygen) to the required operating pressure. This process is applicable for aqueous waste streams, which are too dilute to incinerate and sometimes too concentrated for biological treatment. Residence times may range from 15 to 120 min, and the COD removal may generally be about 75–90% (Luck, 1999).

The basic flow schematic of a wet-air oxidation system is provided in Figure 1.1. It consists of a high-pressure pump, an air or oxygen compressor, a heat exchanger as well as a reactor with a relief valve and a downstream separator.

The wastewater or feed liquor is first pressurized by high pressure feed pumps. In most case, a gas stream, containing sufficient oxygen to meet the oxygen demand requirements, is injected into the pressurized waste stream. Heat exchangers are routinely employed to preheat the feed/air mixture. When the mixture reaches the required reaction temperature, the mixture remains in the
reactor for a sufficient period of time to allow the oxidation reaction to approach the design reduction in chemical oxygen demand. Since the oxidation reaction is exothermic, producing a temperature rise in the reactor, this allows the wet-air oxidation system to operate without any additional heat input. After heating the reactor feed, the reactor effluent usually requires further cooling before discharge. The final step is to reduce the pressure of the reactor effluent stream and separate the vapor and liquid. The liquid is finally discharged for other treatments, if needed (Claude, Robert and Brandenburg 1994).

The primary variables in the design of a wet-air oxidation system are significant for the effective application of an integrated process. These variables includes:

- Reactor Temperature
- Reactor Pressure
- Reaction Retention Time
- Initial Oxygen Pressure (which is obtained from initial air pressure)

Of these variables, temperature is most sensitive factor for the degree of oxidation (Mishra, Mahajani and Joshi 1995). This is because WAO is known to follow a free-radical mechanism. The chemical bond’s breaking is under the direct influence of the reaction temperature (Bachir, et al. 1998). Higher temperatures will provide enough energy to break chemical bonds. To a certain extent, the more the reaction temperature is raised, the more efficient the breakage of the bonds is.
Figure 1.1 Flow diagram of a wet-air oxidation process (Luck, Wet air oxidation: past, present and future 1999).
The system is pressurized to control vaporization of the liquid water, thus maintaining the water in a sub-critical state. The reactor pressure is also a function of reactor temperature. As temperature and initial air pressure are increased, the required system operating pressure will also increase. The phase boundary between liquid and gas does not continue indefinitely. Instead, it terminates at a point called the critical point. This reflects the fact that, at extremely high temperatures and pressures, the liquid and gaseous phases become indistinguishable (Papon, Leblond and Meijer 1999). For the WAO conditions, they mainly stay in the liquid phase.

For the reaction retention time, 45-90 minutes are typical of wet-air oxidation system designs with operating temperatures above 150°C (302°F). At lower operating temperatures, longer retention times are typically required.

1.2.2 WET-AIR OXIDATION MECHANISM

The WAO process converts organic compounds into carbon dioxide, water and biodegradable, short-chain organic acids. Inorganic constituents such as sulfides and cyanides can also be oxidized. The wet-air oxidation process can involve any or all of the following reactions (Eftaxias, et al. 2001):

\[
\text{Organics} + O_2 \rightarrow CO_2 + H_2O + RCOOH^* \]

\[
\text{Sulfur Species} + O_2 \rightarrow SO_4^{2-} \]

\[
\text{Organic Cl} + O_2 \rightarrow Cl^- + CO_2 + RCOOH^* \]
Organic $N + O_2 \rightarrow NH_3 + CO_2 + RCOOH^*$

Phosphorus $+ O_2 \rightarrow PO_4^{3-}$

*Short chain organic acids such as acetic acid and formic acid make up the major fraction of residual organic compounds*

Catalytic wet-air oxidation (CWAO) has been shown to be an effective technique for eliminating organic compounds, such as phenol (Levec 1997). Nowadays, phenol and its derivatives have received great attentions, because phenol commonly appears in aqueous effluents from sources such as petrochemical, chemical and pharmaceutical industries (Fortuny, et al. 1999). Phenolic wastewaters are considered refractory in conventional bio-treatments because of their bactericidal properties (Autenrieth 1991). Hence, phenolic compounds must be specifically targeted for removal by subsequent treatment in conventional sewage plants.

The complete oxidation of phenol into carbon dioxide and water follows an extremely complex pathway composed by parallel and consecutive reactions. In 1999, (Fortuny, et al. 1999) did an exhaustive analysis of the stream containing intermediates by a validated reversed-phase liquid chromatographic (RPLC) protocol. The analyses showed the main partial oxidation products to be light carboxylic acids such as oxalic, acetic and formic. Malonic, maleic and its isomer, fumaric acid, were also detected in trace amounts. Over 50 different reaction models have been proposed, Eftaxias summarized many of the related reactions, and a simplified reaction network is shown in Figure 1.2.
Figure 1.2 Simplified reaction pathway for catalytic wet-air oxidation of phenol (Eftaxias, et al. 2001)
1.2.3 WET-AIR OXIDATION INDUSTRIAL APPLICATIONS

As a well-established technique for wastewater treatment, WAO has been used operationally for treatment of toxic, highly organic wastewater and sludge worldwide since 1950s. The wet-oxidation reaction generally takes place between 100°C and 372°C at elevated pressures to maintain water in the liquid phase. Depending on its different industrial applications, the temperature ranges can be subdivided into low (100-200°C), medium (200-260°C), and high temperature (260-320°C) operation. The typical non-catalytic WAO waste treatment applications are listed below according to required reaction temperature (Maugans and Ellis 2002):

- Low temperature oxidation (100-200°C) includes the low pressure thermal conditioning of sludge and low strength sulfides typically found in spent caustic waste streams. Other industrial wastes including cyanide and phosphorus as well as non-chlorinated pesticides could also been treated by low temperature oxidation.

- Medium temperature (200-260°C) oxidation is used for typical ethylene spent caustics, as well as for autothermal thermal sludge conditioning (TSC), and some industrial wastes.

- High temperature (260-320°C) oxidation is used for refinery spent caustic, sludge destruction, and most WAO treated industrial wastewaters.

The spent caustic treatment and sludge treatment and destruction are two types of the key historic and commercial WAO applications currently.
A. Spent Caustic Treatment

One of the most common industrial applications for the wet-air oxidation process is treatment of spent caustic wastewater streams generated by ethylene plants and refineries. Due to the high levels of sulfides, the waste stream can create odor and safety problems when liberated as a gas, and other problems associated with discharge to a plant's wastewater treatment plant (Claude, Robert and Brandenburg 1994). The WAO process is used for complete oxidation to eliminate or reduce sulfur species such as sulfides and mercaptans, and other complex organic contaminants such as phenols prior to discharge to a conventional biological treatment process.

In 1995, a WAO system was put into operation for treatment of refinery spent caustic at the Refinaria de Petroleos de Manguinhos, S.A. (RPDM) in Rio de Janeiro (Carlos and Maugans 2000). As Table 1.3 shows, in this system, approximately 80% destruction of COD is achieved, with near complete phenols destruction and sulfide levels reduced to below detection limits.

B. Sludge Treatment and Destruction

Nowadays, major cities are facing a common challenge dealing with sludge disposal. Therefore, the wet-air oxidation process has another widespread application that is for treatment of municipal sludge. The majority of these systems are low temperature and pressure designs, commonly referred to as low pressure oxidation (LPO). An LPO system operates at 175-200°C (350-395°F) and
<table>
<thead>
<tr>
<th></th>
<th>Reactor Inset</th>
<th>Reactor Effluent</th>
</tr>
</thead>
<tbody>
<tr>
<td>COD (mg/L)</td>
<td>72,000</td>
<td>15,000</td>
</tr>
<tr>
<td>COD reduction</td>
<td>--</td>
<td>79.2%</td>
</tr>
<tr>
<td>BOD/COD</td>
<td>--</td>
<td>0.515</td>
</tr>
<tr>
<td>Phenols (mg/L)</td>
<td>1,700</td>
<td>3</td>
</tr>
<tr>
<td>Sulfide (mg/L)</td>
<td>2,700</td>
<td>&lt;1*</td>
</tr>
<tr>
<td>Mercaptans (mg/L)</td>
<td>2,800</td>
<td>2</td>
</tr>
<tr>
<td>Thiosulfate (mg/L)</td>
<td>640</td>
<td>&lt;26*</td>
</tr>
<tr>
<td>pH</td>
<td>13.43</td>
<td>8.24</td>
</tr>
</tbody>
</table>

Table 1.3 RPDM spent caustic WAO performance (T=246°C) (Carlos and Maugans 2000)

200-500 psi. Under these conditions, sludge/water mixtures are allowed to drain more effectively, thus to be broken down to become the mixtures that have better dewaterability (SIEMENS 2011). The final products are then dewatered and dried to over 90% solids content, prior to being disposed as a cover product for landfills. When higher temperature and pressure is applied, destruction of volatile solids occurs and wet-air oxidation can be used for sludge destruction, a possible alternative to incineration.

The Athos™ Process (Luck, Djafer, et al. 1999) is a wet-oxidation system dedicated for oxidation of residual sludge from municipal wastewater treatment facilities. It was installed at the North Brussels Waste Water Treatment Plant (WWTP) and started-up in 2007. With homogeneous copper (II) ion as the catalyst and pure oxygen as the oxidative agent, 75 to 90% COD mineralization is
achieved and a solids volume reduction of 90 to 95% can be achieved (Chauzy, et al. 2010).

1.2.4 SUMMARY

Wet-air oxidation is very attractive among the various types of wastewater treatment processes that are used for treating aqueous wastes polluted with organic matter. The basic idea of the process is to enhance contact between molecular oxygen and the organic matter to be oxidized at the condition 120-320°C for temperature, 110-3,000 psi for pressure. The WAO treatment process has been developed over many years and has been applied to a wide variety of waste treatment industrial projects, including spent caustic treatment, sludge treatment and destruction, production of vanillin and treatment of industrial wastewaters.

Because of the utilization of direct chemical oxidation process and its high thermal efficiency, WAO offers us an environmental wastewater treatment. And additional applications will surely be realized as more stringent discharge criteria are applied by regulatory agencies.

1.3 PHARMACEUTICAL CONCERNS

Pharmaceutical drugs are chemicals used for diagnosis, treatment, or prevention of illness of the human body and parts of pharmaceuticals could control symptoms instead of cure conditions. During the most recent decades, tons of
pharmacologically active substances were used annually in both human medicine for preventing illness and animal and fish farming as growth promoters or parasiticides (Diaz-Cruz, Alda and Barcelo 2003).

With the addition of new pharmaceuticals to the already large array of chemical classes, most of these substances are excreted un-metabolized or as active metabolites entering the environment (Halling-Sorensen, et al. 1998). Indeed, pharmaceutical compounds have been detected in sewage treatment plant effluents, surface and ground water and even in drinking water all over the world (Mompelat, Le and Thomas 2009) (Mompelat, Le and Thomas 2009) (Xu, et al. 2007) (Brown, et al. 2006) (D.W.Kolpin, et al. 2002) (Golet, Alder and Giger 2002). Figure 1.3 shows the main sources and routes of drugs in the environment. The principal way is through the discharge of raw and treated sewage from residential users or medical facilities. Even though advanced treatment processes are able to achieve higher removal rates, they still do not obtain complete removal of pharmaceuticals (Mompelat, Le and Thomas 2009) (Stackelberg, et al. 2007). After all these various discharge routes and subsequent treatment of wastewater, very low ng/L concentrations of pharmaceuticals have been detected in drinking water supplies (Jelic, Petrovic and Barcelo 2012).

Even through the amount of pharmaceuticals and their bioactive metabolites being disposed or discharged into the environment are probably low, their continual input into the environment may lead to a long-term, unnoticed .

25
Figure 1.3 Principal routes of environmental exposure to drugs consumed in human and veterinary medicine (Khetan and Collins 2007)
adverse effect on both aquatic and terrestrial organisms (Diaz-Cruz, Alda and Barcelo 2003)

1.3.1 ANTIBIOTIC RESIDUES IN ENVIRONMENT

Thousands of different drugs are approved for use throughout the world in human and veterinary medicine. Antibiotics, a group of pharmaceuticals, are administered to human, livestock and poultry, and fish to treat diseases and infections every year (Schneider 1994, Eckman 1994, Migliore, et al. 1997). The increasing use of these drugs during the last six decades has caused matters of great concern. Table 1.4 provides some data on the consumption of antibiotics in different cities of European Union countries.

<table>
<thead>
<tr>
<th>Human*</th>
<th>-France: 34 tons (1999); 33 tons (2001)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-Italy: 25 tons (1999); 27 tons (2001)</td>
</tr>
<tr>
<td></td>
<td>-Spain: 22 tons (1999); 19 tons (2001)</td>
</tr>
<tr>
<td></td>
<td>-Germany: 14 tons (1999); 13 tons (2001)</td>
</tr>
<tr>
<td>Veterinary</td>
<td>-EU 1,600 tons (1999)</td>
</tr>
</tbody>
</table>

* Values expresses in Defined Daily Dose per 1,000 inhabitants per day (D/D).

Table 1.4 Consumption of antibiotics in human and veterinary medicine (Diaz-Cruz, Alda and Barcelo 2003)
Indeed, the widespread use of antibiotics, coupled with their subsequent release into the environment, merit a great concern. Recent research showed that the amount of different antibiotics residues discharged to environment is increasing year by year (Xu, et al. 2007) (Brown, et al. 2006) (D.W.Kolpin, et al. 2002) (Golet, Alder and Giger 2002). These antibiotic contaminants might lead to altered microbial community structures in nature, accelerate the proliferation of antibiotic-resistant pathogens. What is worse, this can also pose threats to human health and result in some related diseases, such as thrombocytopenia, hyperkalemia and shiga toxin (Daughton and Ternes 1999). Thus, a better understanding of the occurrence and fate of antibiotics and engineered water systems is essential to assess, reduce and eliminate the risks of these compounds.

1.3.2 TRIMETHOPRIM

Trimethoprim (TMP) is among the most important antibacterial agents used in human and veterinary medicine worldwide for long years. It is mainly used in the prophylaxis and the treatment of urinary tract infection by selectively inhibiting the bacterial species of the dihydrofolate reductase enzyme (Hitching, Kuyper and Baccananari 1988). It is also used in combination with other drugs to treat certain types of pneumonia and traveler's diarrhea. Figure 1.4 is the structure of TMP and its properties are listed in Table 1.5.

TMP has been reported as one of the antibiotics most frequently detected in municipal wastewaters (vary by several hundred ng L⁻¹) and surface waters (ten to
several hundred ng L\(^{-1}\)) (Ho, et al. 2011). Another study has summarized the worldwide presence of TMP residues in water sources: at 0.6–7.6 µg/L level in hospital sewage water in Sweden, at 0.12 and 0.16 µg/L levels in wastewater effluents from East Aurora and Holland, respectively, 12.4 mg/kg level in manure and soil in a German farming area, at 40–705 ng/L in two municipal wastewater treatment plants in USA, and 0.013–0.15 µg/L in US streams (Bekçi, Seki and Yurdakoc 2006).

When trimethoprim reaches into the environmental systems, there are multiple routes for their possible removal, including physical-degradation, photo-degradation, bio-degradation and several types of chemical oxidation degradations. A summary of the removal treatments of trimethoprim that have been evaluated in recent five years follows.

A. Adsorbents

Adsorption is an effective method in removing suspended solids, odors, organic matter, and oil from aqueous solutions due to its low cost, simplicity of design, ease of operation, and insensitivity to toxic substances (Low, et al. 2011). A great variety of versatile adsorbents are used at present for the removal of pollutants from wastewater, including silica gel, alumina, activated carbons, and synthetic exchange resins.
Table 1.5 Properties of trimethoprim

(Ho, et al. 2011, Cao 1995, Roth and Strelitz 1969)
Bekçi et al. investigated montmorillonite KSF and K10 as adsorbent in the removal of trimethoprim, respectively in 2006 (Bekçi, Seki and Yurdakoc 2006) and 2007 (Bekçi, Seki and Yurdakoc 2007). Both of these adsorbents provided high surface area, high adsorption capacity and mechanical stability. Through observing the interaction between these two montmorillonites and TMP, the researchers found that the adsorptive removal of TMP from aqueous solution was pH dependent. In the range of pH 2.5 and 6.3, adsorption was increased via the attraction between the negatively charged surface of clay and protonated form of the drug. Beyond the value of 6.3, there was a decrease in the adsorption because the surface site of the clay did not favor the adsorption of neutral TMP. By performing kinetic experiments, the pseudo-second-order kinetic model provides the best fit for TMP adsorption onto KSF and K10 montmorillonites. In the optimum treatment conditions, the amount of drug adsorbed was 60 mg/g for 1 hour of contact time when its initial compound concentration was 290.3 mg/L; this resulted in a removal for TMP of 20.7%.

A low-cost carbon black has been studied as an adsorbent for the removal of TMP from aqueous solution (Dominguez-Vargas and Carrillo-Perez 2012). After analysis of the variances between temperature, pH and ionic strength, these researchers reported that an optimum removal was found at pH = 9.2, T = 47 °C, and I = 0.48 M. Under these conditions, a maximum value of removal efficiency equal to 156.2 mg of TMP per gram of adsorbent was achieved.
Membrane Reactor

Membrane bioreactor (MBR) technology combines the biological degradation process using activated sludge with a direct solid–liquid separation by membrane filtration. The key components of the MBR include a fine screen, a bioreactor tank (to achieve nitrification and de-nitrification), two parallel-submerged membrane modules (made of hollow fiber membranes) and a medium pressure ultra-violet (UV) disinfection unit.

In 2012, Schröder (Schröder, et al. 2012) evaluated a treatment of wastewater in two MBRs. The wastewater contained three non-steroidal, anti-inflammatory drugs (NSAIDs) and three antibiotics, including trimethoprim. The results showed that NSAIDs (range from 86-100%) were removed with higher efficiencies than the antibiotics (range from 55-86%) on both MBRs. At the same year, another group of research (Trinh, et al. 2012) characterized the removal of 48 trace organic chemical contaminants through a MBR in Australia. Their results indicted that the removals of most of the drugs were high (above 90%); however, others removal efficiencies were only 24-68%. For example, the initial concentration of trimethoprim was 100 ng/L in raw sewage, after 10 days sludge retention time (SRT) of the bioreactor, its final removal efficiency was only 38%. Thus, TMP has been identified as persistent compounds that are difficult to be removed through MBRs.
C. Photolysis

Photolysis is a potential means to limit the release of pharmaceuticals drug carried by wastewater effluents into the environment. Photo-degradation occurs either by an engineered ultraviolet light photolysis system or in natural sunlight.

In 2011, Ryan et al. (Ryan, Tan and Arnold 2011) studied the direct and indirect photolysis of TMP in wastewater treatment plant effluent exposed to sunlight. In the wastewater effluent tests, photolysis could be divided into 18% direct photolysis and 82% indirect photolysis, that latter including 62% reaction with hydroxyl radicals and 20% reaction with triplet excited effluent organic matter. These results indicated that allowing photolysis in wastewater stabilization ponds or wastewater treatment wetlands may lead to enhanced pharmaceutical removal prior to discharge into environment. However, some toxicity of oxidation products were observed (Sirtori, et al. 2010).

D. Oxidation Reaction

Chemical oxidation processes have been widely applied to water treatment and may serve as a tool to minimize the release of TMP into the aquatic environment. The potential of several oxidants for the transformation of TMP was listed, assessed and compared. The oxidants include ozone (O3), ferrate (VI), potassium permanganate (KMnO4; Mn(VII)), chlorine (HOCl), chlorine dioxide (ClO2), hydroxyl radicals (HO'), and UV-TiO2 photo-catalysis.
Ozonation of TMP in municipal wastewater generally yields sufficient structural modification of antibacterial molecules to eliminate their antibacterial activities (Dodd, Kohler and Gunten 2009). The study has shown a 90% removal with ozone. However, the removal may not necessarily obviate the antibacterial properties completely since the 2,4-diaminopyrimidine substructure was present in some of the degradants (Radjenovic, et al. 2009), therefore raising the concern of production of carcinogenic bromate ion in the treated water.

Anquandah et al (Anquandah, et al. 2011) presented a work that described for the first time that the oxidant, ferrate(VI) (Fe(VI)), degraded TMP completely with cleavage of the original molecule, oxidation of amino groups of the pyrimidine moiety, and finally the elimination the antibacterial activity of TMP.

Mn(VII) oxidizes a wide range of organic pollutants. Hu et al (Hu, Martin and Strathmann 2010) examined the oxidation of TMP by potassium permanganate (KMnO₄; Mn(VII)). The reaction kinetics of trimethoprim were described by second-order rate laws with apparent second-order rate constants k₂=1.6 ± 0.1 M⁻¹s⁻¹ at pH 7 and 25 °C condition. And the rates of trimethoprim oxidation exhibited marked pH dependences. The Mn(VII) reactivity with the antibiotics resulted in a removal rate range of 74-80%, which was lower than that reported for ozone.

Ho et al (Ho, et al. 2011) used a photo-catalyst accompanied with the oxidation process to remove residual TMP from water. The results indicated that TiO₂/UV photo-oxidation was effective in removing TMP, and the mineralization
is about 80% within 180 min of irradiation. Furthermore, a lower flow rate and higher detention time achieved higher percentage of TMP mineralization.

1.3.3 GEMFIBROZIL

Other non-antibiotic, active pharmaceutical for human usage also has an emerging environmental issue because of possible impacts for environment. Gemfibrozil (GEM) is a FDA-approved fibrate drug, commonly known as “lopid” in the pharmacy. Gemfibrozil is used as a hypolipidemic drug to decrease very low-density lipoprotein (VLDL) levels in the blood stream. Like a triglyceride-lowering agent, GEM promotes the lipolysis of VLDL-triglycerides through activation of lipoprotein lipase. GEM is an amphipathic carboxylic acid molecule, its chemical formula and properties are presented in Figure 1.5 and Table 1.6, respectively.

Gemfibrozil was designed first at the Parke Davis Research Laboratories at Detroit in 1968 aimed to lower serum lipid. After years of research in clinical trial, in 1976, GEM was successfully introduced in the market as a hypolipidemic drug with its profound ability to reduce plasma triglyceride level (Betteridge, Higgins and Galton 1976). It was then first marketed in the United States of America in the year of 1982 (Wysowski, Kennedy and Gross 1990).

Gemfibrozil has some general advantages over other lipid lowering drugs. First of all, it can be administered orally which is less painful. Secondly, it generates relatively less amount of side effects compared to other lipid-lowering
Figure 1.5 The structure of gemfibrozil

<table>
<thead>
<tr>
<th>Properties</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>IUPAC Systematic Name</td>
<td>5-(2,5-dimethylphenoxy)-2,2-dimethyl-pentanoic acid</td>
</tr>
<tr>
<td>Molecular formula</td>
<td>C\textsubscript{15}H\textsubscript{22}O\textsubscript{3}</td>
</tr>
<tr>
<td>CAS</td>
<td>25812-30-0</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>250.33</td>
</tr>
<tr>
<td>Water Solubility</td>
<td>Insoluble (19 µg/mL)</td>
</tr>
<tr>
<td>Ethanol Solubility</td>
<td>Soluble (100 mg/mL)</td>
</tr>
<tr>
<td>Melting point</td>
<td>61 - 63 °C</td>
</tr>
<tr>
<td>Storage temperature</td>
<td>RT at 25 °C</td>
</tr>
<tr>
<td>pKa values</td>
<td>4.7</td>
</tr>
</tbody>
</table>

Table 1.6 Properties of gemfibrozil
(Gennaro 1995, Budavari 1995, American Hospital Formulary Service 1995)
agents. Therefore, it drug has been widely used since the early 1980s to lower serum triglycerides and raise high-density lipoprotein-cholesterol in patients.

However, its widespread use also suggests that GEM have the potential to occur commonly in wastewater and ultimately the environment via excretion with urine and feces as parent compounds, conjugated compounds, or metabolites (Xia, et al. 2005). Several studies have suggested that GEM can’t be completely removed by wastewater treatment process (Fang, et al. 2012) and has been detected in wastewater treatment plant influents, effluents, and drinking water as shown in Table 1.7. The GEM concentrations in wastewater may also vary between worldwide countries due to different national pharmaceutical consumption and wastewater production. For example, in North America, the concentration of GEM in wastes effluent was approximately 0.75 µg/L while in Europe, the concentration was about 1.5 µg/L (Sanderson, et al. 2003). In addition, GEM has a longer degradation half-lives compared with other pharmaceuticals, 17.8-20.6 days for different textures of soil (Fang, et al. 2012).

<table>
<thead>
<tr>
<th>Source</th>
<th>Concentrations of gemfibrozil (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treated wastewater</td>
<td>0.08 - 19.4</td>
</tr>
<tr>
<td>Surface water</td>
<td>0.009 - 0.51</td>
</tr>
<tr>
<td>Drinking water</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Table 1.7 The concentrations of GEM in various source of water (Skolness, et al. 2012)
Even though the environmental risks associated with the presence of GEM in water are unknown and little information exists about the effect of GEM in aquatic organisms, gemfibrozil residue in wastewater has attracted much interests due to its consumption, physical and chemical properties, toxicity, and water persistence. GEM has been included in the current contaminant candidate list published by US EPA (US EPA 2009). Considerable work has been carried out on the degradation of gemfibrozil by a variety of wastewater techniques.

P. Falås et al (Falås, et al. 2012) studied the influent and effluent pharmaceuticals concentrations compiled from the Swedish wastewater treatment plants. Swedish WWTPs comprised a large spectrum of biological wastewater treatment technologies, where organic micro-pollutants could be stripped to air, absorbed to the biomass, and degraded by microorganisms. The final reduction degrees were observed for GEM in activated sludge plants with extended nitrogen is 32%.

Ying (Ying, Kookanab and Kolpin 2009) investigated eight selected pharmaceutically compounds (including GEM) in effluents from fifteen sewage treatment plants (STPs) across South Australia. The removals of these compounds in four STPs were carried out by different technologies (Plant A: conventional activated sludge; plant B: two oxidation ditches; plant C: three bioreactors; and plant D: ten lagoons in series). Plant A was a large conventional, municipal, activated STPs and the other three plants were small, rural STPs. The table 1.8 shows more details of these technologies and includes the removal efficiencies of
GEM. Gemfibrozil exhibited variable removal efficiencies within the four STPs. Biodegradation (Plant B) had a significant concentration decreases between influent and effluent and was found to be the main mechanism for removing concentrations from the liquid waste stream for GEM within the four STPs, while Plant D had the least efficient.

<table>
<thead>
<tr>
<th>Plant</th>
<th>Treatment process</th>
<th>Discharged</th>
<th>Removal efficiencies</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>conventional activated sludge</td>
<td>primary sedimentation secondary activated sludge process tertiary stage of six lagoons.</td>
<td>1) sea 2) irrigation reused</td>
</tr>
<tr>
<td>B</td>
<td>two oxidation ditches</td>
<td>biological process with two oxidation ditches followed by chlorination</td>
<td>small creeks</td>
</tr>
<tr>
<td>C</td>
<td>three bioreactors</td>
<td>an activated sludge process with three bioreactors followed by UV disinfection and chlorination</td>
<td>small creeks</td>
</tr>
<tr>
<td>D</td>
<td>ten lagoons in series</td>
<td>10 lagoons operated in series: 2 parallel anaerobic lagoons followe by 8 aerobic lagoons with only lagoon 3 aerated</td>
<td>small creeks</td>
</tr>
</tbody>
</table>

Table 1.8 The GEM removal efficiencies (%) in the four sewage treatment plants

Oxidation techniques have also been proven as an effective method to remove potential pollutants in wastewater that cannot be degraded biologically with the benefits of disinfection effect. As the same as the oxidants that used for trimethoprim, various oxidants can be employed in the wastewater treatment, such as Ozone (O₃), chlorine, chlorine dioxide (ClO₂) and peracetic acid (PAA).
To explore the efficiency of those oxidants that have not been extensively studied, Hey et al (Hey, et al. 2012) studied the effectiveness of ClO$_2$ and PAA on the removal of GEM in biologically treated wastewater. Their result showed that GEM was removed only when treated with higher dose of ClO$_2$ (20 mg/L) in the low COD wastewater, whereas higher removal was observed in medium and high COD wastewater at much lower ClO$_2$ dose (1.25 mg/L). In the case of PAA, GEM was less reactive at lower PAA dose in all COD effluents, but it was gradually removed for 25% with increasing PAA dose to 15 mg/L. The higher removal efficiency (75%) occurred at 15 mg/L PAA dose. However for the medium and high COD wastewater, the best removal efficiency was only 20% achieved by the highest oxidant dose. Hence, ClO$_2$ is more effective than PAA at removing GEM in wastewater.

1.3.4 SUMMARY

Pharmaceutical residues are widespread in the environment at trace quantities. Most of them come from excreta of human and animals, waste effluents of manufacturing processes, and disposals of unused or expired drug products. Researchers have detected them in drinking. These residues indicate that the applied water treatment technologies are not efficient enough to eliminate pharmaceutical from natural waters. Therefore, it’s difficult to predict human health risks from exposure at the drinking water that includes innumerable pharmaceutical drugs and their transformation products.
This section mainly showed the occurrences, fates and removal technologies of two substances including an antibiotic (trimethoprim) and a fibrate drug (gemfibrozil). Both of these drugs have been found in several countries’ wastewater effluent. Even though large amounts of technologies have been researched and developed to help remove these pharmaceuticals, these drugs still persist in treated wastewaters.

1.4 RESEARCH OBJECTIVES

The research objectives of this study were to 1) evaluate wet-air oxidation as a treatment technique for two persistent pharmaceutical compounds in wastewater and 2) evaluate the importance of organic matter content on the removal capability of wet-air oxidation.

With the rapid increase in population and the increased demand to meet human requirements, new technological advancements are needed to improve water quality, even through various conventional and advanced technologies are used currently. From an economic point of view, it is also interesting to develop some knowledge and methods on the energy balance of the process, along with energy recovery and savings. This concern is very important when high quantities of wastewater are to be treated.

Wet-air oxidation is considered an effective treatment of hazardous and toxic wastes, without emissions of any toxic effluent and gas. To determine the
optimal removal efficiency of certain pharmaceuticals, this study tried to explore the relationships between different operation parameters of the oxidation process. The operation parameters discussed in the thesis including the reaction time, target concentration, sample volume, oxygen supply (as a function of applied air pressure) and external organic matters. Trimethoprim and gemfibrozil were chosen as the two pharmaceutical contaminants to evaluate in this work because of their frequent appearance in surface and drinking water, implying these drugs resist removal and/or treatment in typical wastewater treatment operations and thus are detected in aquatic systems.

Trimethoprim as an important antibacterial agent has been used in human and veterinary medicine worldwide for long years. However, the widespread use of the antibiotics, coupled with their subsequent release into the environment merit a great concern. Gemfibrozil, as a hypolipidemic drug, has recently been detected in multiple water sources. Even though little information exists about the effect of GEM in aquatic organisms, gemfibrozil residues in wastewater are of concern due to its persistence in water after treatment.

Analytical methods needed to be developed to detect and quantify these pharmaceutical compounds during the experiments needed to meet the research objections. These methods required quantification of the drugs using calibration curves, and using these values to determine the removal efficiency of the drugs by comparing drug concentrations before and after sample treatment by WAO. Reversed-phase liquid chromatographic techniques were a first step in the
development of analytical techniques since the major focus of this research is in aqueous systems. The appropriate selections of RPLC columns, mobile phase solutions, flow rate, injection volume and detection wavelength where significant and important steps needed to develop a sensitive RPLC detection method.
CHAPTER 2 TRIMETHOPRIM

2.1 INTRODUCTION

Trimethoprim is among the most commonly human-used antibacterial compounds that are prescribed worldwide to treat various bacterial infections for a number of years (Ryan, Tan and Arnold 2011). As described in Chapter 1, detectable concentrations of the drug are detected in the treated wastes from wastewater treatment plants. The discharge of effluent to surface waters leads to the potential contamination of environmental systems with the residual pharmaceutical. Concerns about TMP include the potential for the development of bacterial resistance to due to increased use, the alteration of microbial communities and risks to the health of humans (Kublin, et al. 2010) (Lindsey, Meyer and Thurman 2001)(Golet, Alder and Giger 2002).

This chapter discusses the application of wet-air oxidation in the removal of TMP from water solutions. The wastes resulting from WWTPs are very complex. To avoid the effects of environmental factors and minimize the hazards associated with handling sewage, a synthetic wastewater is used in the studies.
reported here that contains only TMP and a surrogate organic material to simulate sewage instead of using the real wastes from natural microbial community that contains TMP. The aim of this chapter is to explore the relationships between three experimental parameters of the wet-air oxidation process and optimize reaction conditions to obtain the best removal efficiency.

### 2.2 MATERIAL / EXPERIMENT DESIGN

#### 2.2.1 CHEMICALS

Trimethoprim (purity = 99.5%) were purchased from Sigma (St. Louis, MO). Acetonitrile (ACN) of reversed-phase liquid chromatography (RPLC) grade was supplied by Sigma, and analytical grade ammonium acetate by Panreac (Barcelona, Spain). RPLC grade water was obtained from a Thermo Scientific water purification system. A 1,000 mg/L stock solution of TMP was prepared by dissolving 0.05 g of TMP in ACN and diluting to 50 mL with ACN in a volumetric flask. The stock solution was stored in stoppered flasks until needed at 4 °C in the dark.

#### 2.2.2 WET-AIR OXIDATION

**A. Vertical Tube Reactor Introduction**

A detailed schematic diagram of the laboratory vertical tube reactor (VTR) is provided in Figure 2.1. Briefly, the laboratory VTR contains a sample charge
Figure 2.1 Schematic of the detailed rotating vertical tube reactor
Inset: Liquid sample introduction apparatus
(Connors 2009)
Figure 2.2 The control board of VTR with monitors and switches
vessel that is constructed of stainless steel and is connected to a low-pressure air source. Samples are “charged” to the reactor chamber, that is approximately 1L, using the low-pressure air source. The typical liquid sample volumes were 500mL in order to provide adequate mixing space with the vapor phase (Connors 2009).

The reactor tube was rotated via an air actuator (Pneuturn®, Bimba, Monee, Il), which is controlled with a regulated nitrogen cylinder. The outside of the reactor vessel is wrapped with heat tape and conductive heating wire that are used to control the temperature of the reactor. Control of the heat tape is accomplished using a rheostat. Three K-type thermocouples are used to monitor the reaction temperature at each end and the middle of the tube, and the reactor temperature is reported on the front of the VTR console as shown in the Figure 2.2. The pressure is monitored via a pressure sensor during all phases of an experiment (See Figure 2.2). In order to facilitate rapid cooling of the reaction chamber after completion of the heating cycle and to simulate the transit of wastewater through a full-scale VTR treatment system, house air is connected to a cooling tube running alongside the reaction tube that results in an increase of heat removal from the reaction vessel. An evacuation valve is placed at the end of the reactor tube for the release of treated sample. As shown in the Figure 2.2, in addition to the temperature and pressure monitors, there is a power switch, a rotation switch, a voltage switch (to control the temperature increase rate) and an air pressure control control switch (to determine the initial pressure of breathing air charged to the reactor).
B. Sample preparation

To achieve the necessary concentrations (1, 5, 10, 20 ppm, respectively) for calibration standards and samples, the TMP stock solution was diluted with pure water to the final sample volume (500 ml). An additional 2.25g sucrose (4,500 ppm) was added to and dissolved in the sample to provide the necessary organic matter to simulate organic matter that would be present in wastewater.

C. WAO operation procedures

The basic WAO operation procedures for adding a sample to the reactor and completing one test run are described below:

1. Clean the wet-air oxidation reactor using water. [Note, if needed, treat with a 1% (v/v) solution of nitric acid to remove scale buildup. After acid treatment, flush the reactor with clean water until pH is neutral.]
2. Charge the sample liquid (500 ml) into the reactor by pressuring the flask with house air pressure (23 psi).
3. Open the valve from the breathing air tank to add breathing air to inside the reactor chamber.
4. Set the pressure at 300 psi (or other pressure desired for experiment) and close the breathing air pressure control to isolate the system.
5. Switch the rotation control to start rotating the vertical tube reactor.
6. Start heating (this point was defined as “zero time” in all experiments)
so that a reactor temperature of 260 °C is arrived at in approximately 30 minutes.

7. Reduce the applied current to the heating tape and allow the reactor to cool for approximately 30 minutes by itself.

8. After the 30-minute wait, provide an additional cooling to the reactor by pumping house air through the cooling tube.

9. Discharge the reacted liquid to a sample container and store until analyze by RPLC.

2.2.3 RPLC METHODS

To quantify the removal efficiency of TMP, a RPLC method with UV detection was used to measure the concentration of the analyte and other organic compounds before and after the oxidation process. An Agilent 1100 Series binary RPLC system with a multiple wavelength detector and auto-sampler was used for all separations (Agilent, Santa Clara, CA). Samples were injected without further treatment. At a flow rate of 0.6 ml/min, 5 µL sample volumes were separated isocratically with 80:20 (v/v) mobile phase A: B (mobile phase A: 1 mM ammonia acetate, 0.01% (v/v) glacial acetic acid and 10% (v/v) ACN water solution; mobile phase B: 100% ACN) on a X Bridge C-18 column (4.6 mm × 75 mm, 2.5 µm) (made in Ireland). UV detection was performed at a wavelength of 230 nm (Renew and Huang 2004). All quantifications were based upon peak areas integrated with the Agilent ChemStation® software and their corresponding concentrations.
calculated from the calibration curve constructed with the standards.

2.3 RESULT AND DISCUSSION
2.3.1 CHROMATOGRAPHY

Trimethoprim appears as a sharp peak at the retention time of 2.4 min in the chromatographic condition described above. Figure 2.3 shows the result of a representative injection of a 10 ppm standard trimethoprim sample with the sample area of 419.56 mAU*s.

2.3.2 STANDARD CURVE

At the same chromatographic conditions described above, all of the four standard samples were tested, and the resulting chromatograms presented in Figure 2.4 were obtained. From this figure, the peak shapes of the samples gradually become asymmetric with increasing concentrations. The main factors that influence peak symmetry depend upon retention, solvent effects, incompatibility of the solute with the mobile phase, or a development of an excessive void at the inlet of the column. In this work, the latter explanation could be eliminated since the column used for these studies was relatively new. In RPLC, adsorption phenomena due to the presence of residual silanol groups in the stationary phase may also lead to tailing (poor peak symmetry) (World Health Organization 2006). However, since this study was completed with only one compound, TMP, the asymmetry of
Figure 2.3 Chromatogram of 10 ppm standard sample of trimethoprim
Figure 2.4 Chromatogram of the five standard trimethoprim samples:
1 ppm (a); 5 ppm (b); 10 ppm (c); 20 ppm (d).
the chromatographic peak was not considered detrimental to the quantification of TMP.

According to the increased peak areas of these four standard samples, a calibration curve within the tested ranges of 1-20 ppm was found for trimethoprim (Figure 2.5). The calibration curve was linear within this range, and the correlation coefficient was 0.998, which indicates the regression line fits the data very well as demonstrated with the equation of the line reported on Figure 2.5. Hence, according to the equation ($y = 45.76x - 6.91$) and peak area results, it is possible to calculate the exact concentration of the sample. Because no physical quantity can be measured with perfect certainty and there are always experiment errors in any measurement, a minimum of three replicates, unless otherwise reported, were performed with each sample to provide an estimate of uncertainty.

2.3.3 OXIDATION REACTION

As reported in Chapter 1, wet-air oxidation systems remove organic contaminants and yield carbon dioxide, water and biodegradable short-chain organic acids. In order to see whether the WAO process could remove TMP successfully, TMP sample solutions were analyzed before and after WAO reaction; representative results are shown in Figure 2.6 from the reaction of a 10 ppm solution of TMP. The sample after reaction (AR) has a smaller peak at the retention time of TMP (2.6 min) compared with the sample before reaction (BR), which indicates most of the TMP has been oxidized. Two additional repeated trials
Figure 2.5 Regression curve for trimethoprim – standard sample

\[ y = 45.76x - 6.91 \]
\[ R^2 = 0.998 \]
Figure 2.6 Chromatogram results from the analysis of 10 ppm standard samples before (a) and after (b) the wet-air oxidation.
were conducted and the peak areas from all chromatogram results where used to
calculate the final concentrations from the calibration curve. The results indicated
that, in the case of the 10 ppm BR concentration, the AR concentrations were 1.42
ppm, 1.36 ppm and 1.41 ppm, respectively, resulting in a mean removal efficiency
of 85.4 ± 0.1 %.

Other peaks, besides TMP, associate with the elution of the products of the
oxidation reaction were also detected using the RPLC methods. Unfortunately,
these degradation products have not been determined at this time. Further research
using mass spectrometry and ion chromatography is planned in the near future to
determine the identity of these compounds.

2.3.4 SOLVENT ADJUSTMENT

As shown in Figure 2.6, two chromatographic peaks closely appear in the
time range of 2.4 – 3.0 min. One of the peaks represents the TMP and the other
peak belongs presumably to a degradation product. To increase the
chromatographic resolution between the two peaks, the 10 ppm reacted sample
was injected onto the column with three different mobile phase ratio to study the
effect of solvent to the final resolution and to try to separate these two peaks.
Figure 2.7 presents the chromatographic results of injected sample using the three
different solvent ratios. Since mobile phased A is 1mM ammonia acetate, 0.01%
glacial acetic acid and 10% ACN solution and mobile phase B is pure organic
ACN solvent, increasing the percentage of A means that mobile phase contains
Figure 2.7 Chromatograms of the separation of BF and AF using different mobile phase ratio: (a) A:B=85:15; (b) A:B=90:10; (c) A:B=95:5
more water and thus become a more polar, which increases retention times. This is because more polar solvent makes the affinity of the hydrophobic analyte to the hydrophobic stationary phase stronger relative to the now more hydrophilic mobile phase. Hence, these two peaks shift to the right and both have longer retention times. It is important to note that the TMP peak shifts from 2.44, to 2.96 and finally to 3.38 min, while the peak associated with a degradation product shifts from 2.67, to 3.30 to 5.40 min. Because of the shift differences, the compounds can be effectively separated. When using the mobile phase composition of A and B (90:10, v/v), the two close peaks can be baseline separated. For the chromatographic run using the mobile phase composition A:B at 95:5 (v/v), the sample analysis takes too much time for the second peak to elute. Thus, despite the complete separation of both compounds, the resulting long analysis time corresponds to a time and solvent waste for subsequent sample analyses. Thus, the mobile phase composition of 90:10 (A:B) was determined to be the most appropriate for analysis of TMP degradation products for this study.

2.3.5 REMOVAL EFFICIENCY

Several factors are capable of influencing the effectiveness of the WAO reaction. The optimal combination of all these factors allows one to obtain the best degradation yield. In Section 2.3.3, the removal efficiency of 10 ppm standard TMP sample was 85.4 ± 0.1 % as shown in Figure 2.6. To determine this best combination of other operational parameters and thus achieve a higher removal
percentage of this contaminant, a series of experiments were conducted to
investigate the effect of individual factors for oxidation of the antibiotic, including
the time the reaction is held at the high temperature, the initial TMP concentration
and the volume of sample charged to the laboratory VTR.

A. Residence Time

Temperature is always one of the most important factors that impact the
degree of oxidation in WAO processes. To investigate the effectiveness of the test
conditions for the TMP degradation studies, three control trials were conducted.
Since the laboratory VTR simulates the flow of wastewater through a vertical tube,
instead of increasing the reaction temperature, the temperature was held at the
highest point investigated to study the influence of the residence time to the final
removal result. This effectively simulates a slower flow of wastewater through the
full-scale VTR.. The only difference between these trials was to increase the
residence time at 260 °C an addition 15 and 30 minutes. The entire time-
temperature profile for the laboratory VTR is showed in Figure 2.8, which again,
represents the simulation time of the waste spending in a full-scale VTR.

Three trials for each sample condition were performed. The effect of
increased reaction time on TMP oxidation by WAO is shown in Figure 2.9;
summaries are also presented in Table 2.1 along with all other experimental results
from the optimization study.

The results show that the reaction time has a markedly progressive effect,
Figure 2.8 Time profile of the wet-air oxidation process
Figure 2.9 Degradation of TMP: Variation of the residence time at 260 °C
most notably when the reaction time was increased from 0 min to 15 min. This additional 15 minutes resulted in the removal efficiency increasing from 85.4 ± 0.1 % to 90.2 ± 0.4 %, resulting in almost 5 % removal improvement. However, this effect was not as pronounced when the time was increased into 30 min, because the additional 15-minute time increase only achieves a 2 % additional improvement. This means that there is a significant yield variation between the reaction time of 0 -15 min, and in experiments conducted at 30 min, there is smaller difference for oxidation. In other words, the second 15 min difference does not have the same marked effect as the first 15 min .

The wet-air oxidation is known to follow a free radical mechanism (Li, Chen and Gloyna 1991). The breaking of the chemical bonds breaking is under the direct influence of the temperature and the reaction time. Longer reaction time will provide enough energy for the bond breaking and fulfill a more complete oxidation reaction. The more the reaction time is retained, the more the necessary energy for this breakage is sufficient.

While the time differences between the increase from 15 and 30 minutes are not easily explained, the impact of increased reaction time, in general, can be explained by what is known about mechanisms associated with the WAO process. The wet-air oxidation is known to follow a free radical mechanism (Li, Chen and Gloyna 1991). The breaking of the chemical bonds breaking is under the direct influence of the temperature and the reaction time. Thus, a longer reaction time will provide more net energy for the bond breaking and will result in a more
complete oxidation reaction. Therefore, the longer the reaction was held at the higher temperature, the more the necessary energy required for radical formation and bond breakage was supplied to the reaction mixture.

B. Initial target Concentration

The efficiency of pollutants removal by WAO has been reported by some researchers to be impacted by the characteristics of wastewater; in particular, some researchers have reported the initial concentration of the pollutants impact removal efficiency (Lei, et al. 2007). Others, however, have reported that the initial concentration of wastewater had little influence on the removal efficiency while others argued that higher initial concentration favored the wastewater treatment (Fu, Chen and Liang 2005).

In this study, the experiments completed at identical reaction time, but with various initial TMP concentrations were found to have a measureable effect on the removals of TMP by WAO. The samples with different initial concentrations (0.5, 1, 5 and 10 ppm) were oxidized under identical reaction conditions (the same reaction time and temperature). After the reactions and analysis of each sample, the mean percentage of TMP oxidation as a function of the initial concentration of TMP was plotted and evaluated. These results are summarized in Figure 2.10. All samples were analyzed in triplicate with the exception of the lowest sample (500 ppb), which was only analyzed twice.
Figure 2.10 Result of trimethoprim oxidation at initial concentrations of #1: 0.5 ppm, #2: 1 ppm, #3: 5 ppm and #4: 10 ppm
As shown in Figure 2.10, it was observed that with the decrease in the concentration of the TMP solution, the measured degradation of TMP decreases slightly from 91.9 to 86.6% between 10 ppm and 0.5 ppm. Since the differences between these samples are little (within the range of 5.5%), the starting TMP concentration has almost none effect for the removal efficiency. In addition, for the trial of sample #1 (0.5 ppm) the concentration of the treated sample was below the detection limit of the UV detector even after the sample injection volume was increased from 5 to 40 µL. Thus, it is difficult to predict precisely what the removal efficiency of TMP solutions at lower concentrations (ppb) will be. However, for the purposes of the evaluation of WAO as feasible wastewater treatment option, the measured decrease indicated that the initial concentration of TMP did not have a pronounced impact of the degradation efficiency for the ppm concentration range.

C. Sample Volume

The effect of sample volume of the aqueous solution on TMP removal is shown in Table 2.1. In this experiment, solutions, consisting of 10 ppm TMP, were treated with a 30-min hold time at 260 °C. Solutions were prepared in volumes of 500 and 300 ml solution. As shown in Table 2.1, the 300 ml solution results in a TMP mean removal of approximately 88.7%, which is lower than the 91.9% of 500 ml experiment. Even though this proved that 500 ml volume was optimal for the reactor configuration, the differences vary only 3% after increasing the sample
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<th>AF (ppm)</th>
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<th>STDEV</th>
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Table 2.1 Influence of various operation factors on TMP oxidation by WAO

*For the trial of 0.5 ppm, the concentration is too low to be detected by UV and there are experimental errors existing. Thus, it has a higher deviation than others. I assumed that the second trial of 0.5 ppm represented the result because its initial concentration was closes to 0.5 ppm.
volume. Therefore, sample volume has a relatively small effect on TMP removal when compared to the other parameters that were varied.

2.4 CONCLUSIONS

In this chapter, the wet-air oxidation process was tested as an alternative technology for the removal of TMP. The WAO process is indeed a promising technology for degradation of this persistent pharmaceutical because it is capable of reducing the concentration of TMP in water solutions with the removal efficiency ranging from 85.4 % to 91.9 %, which has equal or higher removal efficiency when compared with other previously reported removal methods that were described in section 1.3.2.

In addition, a RPLC method was optimized for the determination of trimethoprim in water solutions. Using this developed method, the peak areas obtained from RPLC chromatographs provide a linear relationship between the concentration of TMP and chromatograph peak area.

In the last section of this chapter, experiments under common WAO conditions (260 °C, 300 psi of breathing air pressure) were carried out to study the effect of the operation parameters to TMP removal. Results showed that reaction time was the most important factor for wet-air oxidation of the antibiotic. A longer reaction time help remove TMP from 85.4 % (without hold at 260 °C) to 90.2 % (15 min hold at 260 °C). For the initial target concentration, only a slight decrease in degradation efficiency was observed when the initial concentration of TMP was
reduced. Finally, for the test using the laboratory VTR system, the results from the sample volume study showed that no significant gains in oxidation efficiency for TMP could be made by altering the volume of the sample to be treated.
CHAPTER 3 GEMFIBROZIL

3.1 INTRODUCTION

Gemfibrozil is an emerging contaminant that has received noticeable attention over the past few years. This is because it has been detected in trace quantities in both groundwater and surface waters that are used for drinking water supplies. Some concerns have been raised over the potential risk to human health from exposure to this pharmaceutical residue via drinking water, although it should be noted that no health concerns have been raised yet associate with the detection of the gemfibrozil in these waters. However, continual development of advanced instrumentation and the improved analytical methods have made possible the detection of the pharmaceuticals at low levels (ppb to ppt) in different environmental matrices.

In this chapter, the application of wet-air oxidation to the removal of gemfibrozil (GEM) in water solutions is studied. As the Chapter 2, a surrogate wastewater is used instead of actual wastewater so that only one type of contaminant (GEM) is being treated, thus avoiding any unknown effects of other
environmental factors. The aim of this work was to explore and optimize for the best removal efficiency of GEM in wastewater. In comparison to Chapter 2, this chapter mainly discussed the effect of additional surfactant and organic matter on the final removal efficiency of WAO by using the best operation parameters of the oxidation process found in the previous chapter. Furthermore, the impact of drug loss in the transfer piping of the laboratory VT (and thus not effectively treated) on overall WAO efficiency was study by quantifying the quantity of drug residue that remained in the reactor tubing.

3.2 MATERIAL / EXPERIMENT DESIGN

3.2.1 CHEMICALS

Gemfibrozil (purity = 99.5%) were purchased from Sigma (St. Louis, MO). Acetonitrile (ACN) of RPLC grade was supplied by Sigma, and phosphoric acid (85%) was purchased from Sigma (St. Louis, MO). RPLC grade water was obtained from a Thermo Scientific water purification system. A 10,000 mg/L stock solution of GEM was prepared by dissolving 0.5 g of TMP in the methanol and diluting to 50 mL. The solution was stored in stoppered flasks in the dark until needed. A 10,000 mg/L stock solution of Triton X-100 (TX-100) was made by dissolving 4.76 ml of Triton in 500 ml water and was stored in flasks at dark until needed.
3.2.2 WET-AIR OXIDATION

To achieve the required concentrations (5, 10, 20, 25, 40, 50 ppm, respectively) of standards and samples, the GEM stock solution was diluted with water. To study the effect of surfactant to the water solubility and removal efficiency of GEM, an additional volume of TX-100 stock solution (50, 100 ml) were added to the 500 ml sample to increase the concentration of surfactant (1,000, 2,000 ppm, respectively) of the aqueous system. To study the impact of other forms of organic matter on the WAO process, varying amounts of formic acid and sucrose were added in the experiments in an attempt to achieve higher oxidation efficiencies.

After mixing all of additional compounds, the volume of all final experiments was 500 ml. Then, the samples were ready for treatment using the WAO. All WAO operation procedures were the same as the TMP, except with the initial pressure of breathing air was 350 psi and fixed reaction time (10 min) at 260 °C.

3.2.3 RPLC METHODS

The concentration of GEM was determined by RPLC-UV detector (Agilent Technologies, series 1100) equipped with a X Bridge C-18 column (4.6 mm × 75 mm, 2.5 µm) (made in Ireland). The detection wavelength was 230 nm, and all analyses were conducted at room temperature. Separations were conducted using a mobile phases of (A) pH 2.5 phosphoric acid solution and (B) acetonitrile. With
the constant ratio 40:60 (v/v) of mobile phase A:B, GEM was eluted at 3.86 min 
(METHOD 1) (Kublin, et al. 2010). When an additional TX-100s were added in 
the system and in order to separate the TX-100 and GEM whose retention times 
were both around 3.5-5 min, a gradient chromatographic elution was needed. It 
was obtained by initially running 60% A, decrease to 50% from 4 to 5 min then 
followed by a return of mobile phase A back to 60% in 1 min from 20 to 21 min. 
The last 4 min of the gradient was held so that the column would re-equilibrate 
prior to the next analysis. Thus, the overall run was completed in 25 min 
(METHOD 2). The timetable for the mobile-phase gradient program is shown in 
Figure 3.1. The overall the flow rate was set at 1 mL/min and all injection volumes 
were 20 µL.

To quantify the formic acid production during WAO experiments with 
GEM, the Phenomenex Synergi 4u Hydro-RP 80R column (4.6 mm × 250 mm, 4 
µm) was used. The concentration of the acidic analytes was measured before and 
after the oxidation process (METHOD 3). The detection wavelength was 230 nm 
with the mobile phase of pH 2.5 phosphoric acid solution. The flow was set at 0.7 
ml/min, injection volume was 20 µL, and the run was completed in 8 min. All 
quantifications were based upon peak areas integrated with the Agilent 
ChemStation® software and their correspond concentrations on the standard 
calibration curve.
Figure 3.1 The timetable of solvent for the RPLC METHOD 2
3.3 RESULT AND DISCUSSION

3.3.1 CHROMATOGRAPHY

In the chromatographic analysis, a 40 ppm sample of gemfibrozil appears as a sharp peak at the retention time of 3.86 min with the width of 0.09 min, the peak height of 193.61 mAU and a peak area of 1111.82 mAU*s in the chromatographic condition described above (METHOD 1). Figure 3.2 shows a representative RPLC result of the 40 ppm standard gemfibrozil sample.

3.3.2 STANDARD CURVE

At the same chromatographic conditions described above (METHOD 1), all of six standard samples were tested; increased peak areas of correlated with increased sample injections, and the relationship was determined to be linear within the tested ranges of 5-50 ppm for gemfibrozil. The calibration curve is presented in Figure 3.3. The calibration curve was linear within this range and the correlation coefficient was 0.999, which indicates the regression line fits the data very well in accordance with the straight line in Figure 3.3. Hence, according to the equation \( y = 27.66x + 4.50 \) and peak area results, it is possible to calculate the concentration of the samples, both before and after treatment by WAO.
Figure 3.2 Chromatogram of 40 ppm standard sample of gemfibrozil
Figure 3.3 Regression curve for GEM – standard sample

\[ y = 27.89x - 0.01 \]

\[ R^2 = 0.999 \]
3.3.3 OXIDATION REACTION

As with TMP, wet-air oxidation system removes organic contaminants and yields carbon dioxide, water and biodegradable short-chain organic acids. In order to see whether this process could remove GEM successfully, samples before and after WAO reaction were compared, and the results were shown in Figure 3.4. As is Chapter 2, three trials were performed for each sample and the AR sample had smaller peak than the BR sample. This indicated most of the GEM had been oxidized. According to the calibration curve, the mean concentration of ARs was 11.27 ppm. Hence, the mean removal efficiency was calculated to be 71.6 ± 3.6%.

To study the some of the products of this oxidation, a Hydro-RP 80R column was used to determine which acids were produced (METHOD 3). Figure 3.5 shows the results of BR and AR by using the Hydro-RP 80R column. The AR had an apparent peak at 4.8 min, which didn’t exist in the BR result. This peak belongs to the formic acid according to the formic acid standard sample, which corresponds with the previous researches and findings that formic acid was one of the major products of wet-air oxidation.

3.3.4 REMOVAL EFFICIENCY

Section 3.3.3 reported the removal efficiency of 40 ppm standard GEM sample was 71.6 ± 3.6 %. In this section, to achieve a higher removal percentage of GEM, the effect of additional organic materials including a non-ionic surfactant, formic acid and sucrose on the final degradation and conversion into subsequent
Figure 3.4 Chromatogram results from the analysis of 40 ppm samples before (a) and after (b) the wet-air oxidation.
Figure 3.5 Chromatogram results from the analysis of acidic production of 40 ppm samples before (a) and after (b) the wet-air oxidation
intermediates such as organic acids, was investigated. The optimum WAO conditions for the laboratory VTR that was determined from Chapter 2 for TMP were used for these experiments.

A. Surfactant effect

Gemfibrozil is a hydrophobic, lipid-lowering drug with poor water solubility, around 0.01 mg/mL (Kasim, et al. 2004), which might limit the ability of the compound to be transported into the reactor for oxidation effectively. Due to the hydrophobicity of the drug, the possibility of the drug sticking to the surfaces of the transfer tubing of the laboratory reactor was a concern for this portion of the research. Thus, this is the major reason why introducing a surfactant into the GEM system was studied. One of the most important properties of surfactants is that is they form micelles in solutions. This makes surfactants have particular significance in pharmacy because of their ability to increase the solubility of sparingly soluble substances in water (Mall, Buckton and Rawlins 1996). When surfactant molecules are dissolved in water at concentrations above the critical micelle concentration (cmc), they form aggregates called micelles (Rangel-Yagui, Pessoa-Jr and Tavares 2005). Micelles are commonly used as drug delivery devices to solubilize hydrophobic drug molecules.

In this thesis, the nonionic surfactant, Triton X-100 (Figure 3.6), was selected and dissolved in water at concentration of 1,000 and 2,000 ppm, which is above the cmc (0.22-0.24 mM, 137.5-150 ppm) for Triton X-100. Based on the
presence of Triton X-100 micelles, GEM could have an increased solubility in the aqueous system. This part aimed to study the effect of triton micelle on the GEM removal efficiency.

![Chemical structure of Triton X-100](image)

Due to the presence of the micelles, a new RPLC method needed to be developed. Thus, in order to have a better selectivity, *METHOD 2* was developed to analyze the mixture sample of 40 ppm GEM and 1,000 ppm TX-100. The results are summarized in Figure 3.8(a). Gemfibrozil shifted and displayed a peak at 12.48 min, and TX-100 had multiple peaks ranging from 15 to 18 min. Both of the two components eluted at different retention times. A clear separation of them was achieved at 230 mm wavelength and no interference between the eluting peaks was observed. Therefore, a combined solution of GEM and TX-100 was directly used for the quantitation studies of these two individual components.

At the *METHOD 2* chromatographic conditions, all of the six standard samples were tested within the ranges of 50 – 1,000 ppm for TX-100. The calibration curve is presented in Figure 3.7.
Figure 3.7 Regression curve for TX-100 – standard sample

\[ y = 11.62x - 28.34 \]
\[ R^2 = 0.999 \]
To study the GEM removal efficiency, the peak areas for both GEM and TX-100 were determined for each sample. Figure 3.8 provides a representative example of samples before and after the WAO reaction. Using the peak area intensity and the calibration curve, the GEM and TX-100 concentration of BR and AR is 40.03 ppm and 1005.63 ppm, 8.75 ppm and 675.86 ppm, respectively. Thus, the final removal of GEM is 78.2 % and of TX-100 is 32.8 %.

Table 3.1 shows the variation of initial GEM, TX-100 and breathing air pressure in the WAO oxidation when the drug and surfactant are varied. Higher oxidation efficiency could be achieved if the surfactant was introduced into the system (#1 and #3, 71.60 to 79.9 %), but too high of a surfactant concentration in the solution did not help achieve the goal of increased oxidation efficiency (#1 and #6, 71.6 to 71.3). This is because the WAO process is not necessarily selective for each type of organic matter; rather the process oxidizes all of the various forms of organic material in the solution, which includes both the GEM and TX-100. From the results of trial #1 and #2, the removals of individual GEM and TX-100 are 71.6 % and 90.1 %, respectively. Within certain amounts of TX-100, the surfactant could help increase the solubility of GEM, thus have higher removal efficiency. However, the presence of 2,000 ppm TX-100s is so concentrated that parts of the energy (and oxygen from the breathing air that was used to pressurize the system) would be used for removal the TX-100, which is not what was originally expected.

To test the previous conclusion in Chapter 2, specifically that higher removal efficiencies were obtained the longer the reaction was held time at 260°C,
Figure 3.8 Chromatogram results from the analysis of the 40 ppm samples with 1,000 ppm TX-100 before (a) and after (b) the wet-air oxidation
trials #4 and #5 were conducted. Comparing the result of trial #3 to trial #4, the mean GEM oxidation results did increase from 79.9 % to 90.2 %, which proved again that temperature was a very important factor for the VTR reaction.

For the study of the initial oxygen concentration effect, unlike the Lei’s study (Lei, et al. 2007), there was a measurable difference of GEM removal between the observed results according to the trials #3 and #5. [Note. In all reactions in this thesis, the laboratory VTR was pressurize with breathing air that served as the source of oxygen for the WAO process.] While there is a 2% decrease in oxidation of GEM, it is not clear what factor in the WAO process contributed to this observed decrease.

<table>
<thead>
<tr>
<th>Trial</th>
<th>GEM (ppm)</th>
<th>TX-100 (ppm)</th>
<th>Time (min)</th>
<th>Oxygen (psi)</th>
<th>Mean GEM Oxidation %</th>
<th>Mean TX-100 Oxidation %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40</td>
<td>-</td>
<td>10</td>
<td>350</td>
<td>71.6</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>1,000</td>
<td>10</td>
<td>350</td>
<td>-</td>
<td>90.1</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>1,000</td>
<td>10</td>
<td>350</td>
<td>79.9</td>
<td>32.8</td>
</tr>
<tr>
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<td>1,000</td>
<td>30</td>
<td>350</td>
<td>90.2</td>
<td>40.4</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
<td>1,000</td>
<td>10</td>
<td>400</td>
<td>77.8</td>
<td>32.3</td>
</tr>
<tr>
<td>6</td>
<td>40</td>
<td>2,000</td>
<td>10</td>
<td>350</td>
<td>71.4</td>
<td>37.5</td>
</tr>
</tbody>
</table>

Table 3.1 Influence of the oxidation result of the gemfibrozil and surfactant on pre-concentration factor, retention time (Rt) and initial oxygen pressure

**B. Formic acid**

The WAO process would ideally produce carbon dioxide and water as final products after complete oxidation of organic matter. However, in sub-critical
WAO systems, the reaction produces some organic by-products, which are resistant to some extent to further oxidation, like small molecular weight acids (acetic, formic, oxalic acids) (Zalouk, et al. 2009). Recall in section 3.3.3 that the results had also shown that formic acid was one of the acidic products. In this section, a study to evaluate the effect of additional formic acid added prior to the WAO process is described.

Aqueous GEM samples, without the presence of surfactant, precipitated when the formic acid was added into this system. This is because GEM has a very low solubility in acid solution (0.0019 %), and when formic acid was added to the solutions, the pH of the solution dropped below the pKa of GEM resulting in the formation of the unionized (and thus most hydrophobic) form of GEM. Micelles formed by surfactant could then solubilize the GEM in these acidic environmental conditions. Hence, in order to introduce formic acids into the system, all the experiments in this portion of the research were performed in the presence of Triton X-100 (1,000 ppm).

Triton present in the solution was analyzed after oxidation of each sample. Figure 3.9 shows that the origin sample without any acid produced 0.26 mM formic acid after the WAO, which supported the research reported by others that formic acid was indeed one of the organic by-products of WAO. Notice that the two low values of formic acid concentration (0.63, 0.77mM) corresponded to the samples containing the high proportion of formic acid (1.6, 2.6 mM), which could be interpreted that most of the formic acids were reacted by the oxidation process.
To study whether the reacted formic acids were used for the removal of GEM, the GEM removal results were compared between samples with and without adding formic acid into the system. As shown in Table 3.2, the removal results are 79.9, 65.2, 61.6 and 74.4 % for the presence 0, 1.6, 2.6 and 5.2 mM of formic acid, respectively. Instead of achieving a better removal result, there is a decrease in removal efficiency after adding the formic acid into system. Hence, even through the added formic acids were consumed by WAO, it doesn’t help improve the GEM removal efficiency. It should be noted that at the highest formic acid concentration (5.2 mM), the removal efficiency of GEM has increased with respect to the other formic acid solutions, although it is still lower than the GEM solution without any formic acid. No clear explanation for these observations can be made; thus, further research is needed to determine why these observations were found.

<table>
<thead>
<tr>
<th>#</th>
<th>GEM (ppm)</th>
<th>TX-100 (ppm)</th>
<th>Formic Acid (mM)</th>
<th>Mean Gem Oxidation %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40</td>
<td>-</td>
<td>1.6</td>
<td>Precipitated</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>1,000</td>
<td>-</td>
<td>79.9</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>1,000</td>
<td>1.6</td>
<td>65.2</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>1,000</td>
<td>2.6</td>
<td>61.6</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
<td>1,000</td>
<td>5.2</td>
<td>74.4</td>
</tr>
</tbody>
</table>

Table 3.2 Influence of formic acid on the gemfibrozil oxidation result
Figure 3.9 RPLC analysis of formic acid production of 40 ppm GEM with 1,000 ppm TX-100 before and after the wet-air oxidation.
C. Sucrose

Generally, organics degradation by WAO were recognized as a free-radical mechanism (Li, Chen and Gloyna 1991), and hydroxyl radical is an extremely potent oxidizing agent with a short life which is able to oxidize organic compounds and generate other free radicals in the presence of organic compounds. Thus, in the WAO system, the reaction intermediates, especially the organic radicals increased, accelerate the speed of the reaction with the help of dissolved oxygen (Lei, et al. 2007). In other words, additional organic matters could help increase the rate of oxidation reaction. The study reported in this section evaluates the impact of adding sucrose as one type of organic matter to the 40 ppm GEM original solution system to explore whether sucrose could help GEM removal. All the experiments completed in the sucrose studies were performed at identical temperature, reaction time and breathing air pressure; the only difference in these tests was an increasing amount of sucrose was added to the samples. All tests were performed in triplicate. The GEM removal results with different amount of sucrose are presented in Figure 3.10. From the starting point, the sample without any added sucrose has a removal efficiency of 71.6 %. For the samples with 500, 1,000, 2,000 and 4,500 ppm concentration of sucrose, the GEM removal efficiency increased to 85.5, 90.6, 95.0 and 95.5 %, respectively. The results also show that the removal efficiencies for GEM removal are quite similar for the 2,000 and 4,500 ppm samples. The oxidation did not improve significantly after adding more
Figure 3.10 Additional sucrose dependence of the GEM removal during WAO of the 40 ppm standard solution (T=260 °C, P=350 psi, Rt=10min)
than 2 grams of sucrose, possibly indicating that no more oxidizable organic matter remained in the reactor or that the added oxidant (oxygen from the breathing air) was either depleted or not at a sufficient enough concentration for the WAO to proceed. The addition of sucrose to the gemfibrozil solution, however, does significantly influence the GEM oxidative efficiency by producing certain intermediates presumably, thus increasing the speed of the reaction.

All of the BR and AR samples in this study were run by METHOD 3 to determine the qualitative and quantitative properties of acids that were produced by wet-air oxidation. One of the major products found was formic acid, and the concentration was quantified by using a formic acid calibration curve. These results are presented in Figure 3.11. In general, the more sucrose that was added into the solution, the more formic acid was produced. This resulted in a higher removal efficiency for the WAO process. Based on these formic acid studies and those studies reported in the previous section, an intermediate formic acid was found to be advantageous for treating the GEM wastewater, however, adding the formic acid directly into wastewater may not be a good help for removal reaction since GEM will precipitate. Hence, formic acid is one of the important acidic products by WAO that has the significant effect to the degradation of organic matters. Further research about its reaction mechanism is planned.
Figure 3.11 The sucrose dependence of the formic acid production of the 40 ppm sample
(#1 Sample with no sucrose; #2 Sample with 500 ppm sucrose; #3 with 1,000 ppm
sucrose; #4 with 2,000 ppm sucrose; #5 with 4,500 ppm sucrose)
3.3.5 RESIDUE STUDY

The design of the test reactor for the WAO process makes it susceptible to sample loss, especially when samples are sparingly soluble and present at low concentrations (ppm and below). Residual liquids can adhere in many portions of the piping systems in the laboratory VTR. While these low-flow areas would most likely be engineered correctly in a full-scale version of the VTR, these areas can potential skew the results from the WAO test using the laboratory VTR. All of the removal results discussed in the previous sections were based on the differences between the BR and AR, without taking into account portions of the drugs that might have stuck to the transfer piping and resided in unreacted liquids that stick or do not make it to the reactor vessel for treatment after entering the sample flask. To obtain the most accurate removal efficiency of the GEM, this section describes the procedure developed to quantify any unreacted compounds.

The first experiment of this residue study aims to determine whether there is drug residue in the system after discharging the reacted sample from the reactor. Methanol (200 ml) was slowly poured into the sample vessel and pumped into the reactor instead of cleaning the reactor using water. Methanol was used because the organic solubility of GEM is much higher in methanol than in water; thus the methanol would help dissolve the adherent GEM on the surfaces in the test reactor. Once the methanol was added, the reactor was operated with the rotation of reactor for 10 min to sufficiently rinse the inside. After discharging and collecting the
methanol, the same RPLC method was performed to quantify the mass of GEM residue.

Assuming that GEM does not stick on the surface of the system and has been discharged without any residue, the concentration of GEM in the methanol should be zero. However, the analysis showed that the methanol sample concentration was 2.68 ppm (for the sample of 40 ppm GEM) and 3.47 ppm (for 40 ppm GEM with surfactant micelle) concentration of GEM. In other words, the average GEM residues were 6.7% (40 ppm GEM) and 8.7% (40 ppm GEM with surfactant micelle). Hence, some drugs did adhere on surface of the entering pipe and the reactor.

The second experiment was conducted to determine the location where the 6.7% of GEM residues mainly adhering to the surfaces of the laboratory reactor. There are two possible situations: the transfer piping and/or the reactor. The regular 40 ppm GEM sample was charged into the VTR system with the same procedures as above. However, the difference of this trial was to rotate the vertical tube for 6 min without heating after charging 350 psi breathing air pressure into the reactor. Table 3.3 shows the analysis results of BR and AR samples. For all of these trials, ARs have lower concentration than BRs (37.40 < 35.57; 37.86 < 35.57; 38.37 < 36.41), which means that 5.4% of drug was lost when the sample was pumped into the reactor. Since the total GEM loss is 6.7%, the residues in the transfer piping were concluded to be the main source of drug loss.
<table>
<thead>
<tr>
<th>Trial</th>
<th>Sample Before</th>
<th>Sample After</th>
<th>GEM Loss</th>
<th>GEM Average Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Peak Area mAU*s</td>
<td>Concentration ppm</td>
<td>Peak Area mAU*s</td>
<td>Concentration ppm</td>
</tr>
<tr>
<td>1</td>
<td>1043.14</td>
<td>37.40</td>
<td>991.92</td>
<td>35.57</td>
</tr>
<tr>
<td>2</td>
<td>1055.87</td>
<td>37.86</td>
<td>992.18</td>
<td>35.57</td>
</tr>
<tr>
<td>3</td>
<td>1070.26</td>
<td>38.37</td>
<td>1015.52</td>
<td>36.41</td>
</tr>
</tbody>
</table>

Table 3.3 GEM concentrations before and after going through the VTR system

The final part of residue study is to prove the result of the second experiment that the transfer piping is the main source that results in the drug loss. First, a 40 ppm GEM sample was processed with the procedure described in section 3.2.2. When discharging the sample from the reactor, instead of collecting one AR sample, the effluent liquid was separated into four parts, in approximately the portion shown in Figure 3.12. The first two samples are both small portions (AR1 and AR2), followed by the largest portion (AR3), and the end part came out with mixed pressure (AR4). Table 3.4 shows the results of GEM removal of different portion of the effluent liquid. AR1, AR2 and AR3 had almost the same removal rate, but for the AR4, there was an obvious removal efficiency result that was very low (13.05 %). The effluent sample came at the end represents the particles that adhered on the transfer piping, as shown in the blue circle in Figure 3.12. This experiment also proved that most of the GEM loss occurred on surfaces associated with the transfer piping between the sample flask and the reactor vessel.
Figure 3.12 Approximate portion of effluent liquid
Because of the 5.4 % GEM loss in the transfer piping, all of the results obtained above should be altered. In the results of sucrose study, for example, all of the BR samples were named as “40 ppm sample”. Since the experimental error, the real concentrations of BR samples made were between 37.79 to 40.03 ppm (see Table 3.5). After the 5.4 % GEM loss caused by pumping, the concentrations of BR samples that in the reactor decreased to the range of 35.56 – 37.87 ppm. Thus, the corrected GEM removal efficiencies, taking in account the residue effect, were calculated, and the results are listed in Table 3.5. By adding the corrected GEM removal efficiencies to the Figure 3.10, a new Figure 3.13 was shown. From the Figure 3.13, the differences (within 2 %) that caused by residue effect were not significant in the GEM studies at these concentrations (40 ppm). However, these effects must be carefully considered when the test concentrations of compounds are lowered in future studies.

<table>
<thead>
<tr>
<th></th>
<th>GEM Removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>AR1</td>
<td>79.0%</td>
</tr>
<tr>
<td>AR2</td>
<td>77.9%</td>
</tr>
<tr>
<td>AR3</td>
<td>75.6%</td>
</tr>
<tr>
<td>AR4</td>
<td>13.1%</td>
</tr>
</tbody>
</table>

Table 3.4 The GEM removal of different portion of the effluent liquid
Table 3.5 Concentration of BR with its removal efficiency by the consideration of residue effect

<table>
<thead>
<tr>
<th>Trial</th>
<th>BR Concentration ppm</th>
<th>GEM Removal %</th>
<th>BR Concentration ppm</th>
<th>GEM Removal %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40.03</td>
<td>71.6</td>
<td>37.87</td>
<td>70.0</td>
</tr>
<tr>
<td>2</td>
<td>37.59</td>
<td>85.5</td>
<td>35.56</td>
<td>84.7</td>
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<tr>
<td>3</td>
<td>37.79</td>
<td>90.6</td>
<td>35.75</td>
<td>90.0</td>
</tr>
<tr>
<td>4</td>
<td>39.82</td>
<td>95.0</td>
<td>37.67</td>
<td>94.7</td>
</tr>
<tr>
<td>5</td>
<td>37.91</td>
<td>95.5</td>
<td>35.86</td>
<td>95.2</td>
</tr>
</tbody>
</table>

Figure 3.13 Additional sucrose dependence of the GEM removal of the 40 ppm standard solution with respect of residue effect
3.4 CONCLUSIONS

Wet-air oxidation is capable of removing the concentration of 40 ppm GEM in pure water (solutions with minimal added organic matter) with a removal efficiency of 71.6%. To achieve better removal efficiencies, this chapter describes the impact of adding additional organic matter to the solution system prior to the treatment. The non-ionic surfactant, TX-100, helped to increase the solubility of GEM in pure water, thus improving the efficiency of VTR reaction. The additional of formic acid, both alone and in combination with TX-100, did not give any obvious differences for the final removal results even though it is one of the major products of WAO. During all these studies of organic matters, sucrose was the organic matter source that demonstrated an increase in the reaction efficiency. The highest removal efficiency (95.5%) is achieved when adding more that sucrose concentration in the solution was 4,500 mg/L.

This chapter also discussed the drug residue effect on the calculate removal efficiency from the laboratory test reactor. It was determined that, due to the interaction of GEM with the reactor piping system, most of the GEM loss occurs do to when the house air is pumping the sample into the reactor. However, this loss could be accounted for with blank samples, and the overall removal efficiency GEM by WAO can be corrected.
CHAPTER 4 CONCLUSIONS AND FUTURE DIRECTIONS

The use of wet-air oxidation system for the pharmaceutical removal has proven to be effective degraded representative drugs in surrogate wastewaters. Specifically, the WAO process has a removal efficiency of 91.0 % for TMP and 95.5 % for GEM. The higher efficiencies were obtained when certain forms of organic matter (sucrose) were used in the reaction process, and when reaction time and temperature of the WAO process were optimized. Tables 4.1 and 4.2 summarized the TMP and GEM removal efficiencies of WAO compared with the reported results from other previous chemical and biological techniques. The results summarized here demonstrate that wet-air oxidation can achieve equal or even higher removal efficiencies in the removal of the test compounds when compared with the other wastewater treatment techniques. Thus, wet-air oxidation can be the promising technology to remove the persistent pharmaceutical pollutants from wastewaters.
<table>
<thead>
<tr>
<th>Treatment Technology</th>
<th>Removal %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biological</td>
<td></td>
</tr>
<tr>
<td>Membrane bioreactor</td>
<td>55-86&lt;sup&gt;[1]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Montmorillonite KSF &amp; K10</td>
<td>20-25&lt;sup&gt;[2-3]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Carbon black</td>
<td>16&lt;sup&gt;[4]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ozonation</td>
<td>90&lt;sup&gt;[5]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ferrate(VI)</td>
<td>100&lt;sup&gt;[6]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mn(VII)</td>
<td>74-80&lt;sup&gt;[7]&lt;/sup&gt;</td>
</tr>
<tr>
<td>TiO&lt;sub&gt;2&lt;/sub&gt;/UV</td>
<td>80&lt;sup&gt;[8]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Wet air oxidation</td>
<td>85-92</td>
</tr>
</tbody>
</table>

Table 4.1 Removal results of TMP by WAO compared with previous techniques

2. Bekçi, Seki and Yurdakoc 2006
3. Bekçi, Seki and Yurdakoc 2007
4. Dominguez-Vargas and Carrillo-Perez 2012
5. Dodd, Kohler and Gunten 2009
7. Hu, Martin and Strathmann 2010
8. Ryan, Tan and Arnold 2011

<table>
<thead>
<tr>
<th>Treatment Technology</th>
<th>Removal %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biological</td>
<td></td>
</tr>
<tr>
<td>Australia STPs</td>
<td>15-90&lt;sup&gt;[9]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Swedish WWTPs</td>
<td>32&lt;sup&gt;[10]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Bacterial community</td>
<td>36&lt;sup&gt;[11]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Chemical</td>
<td></td>
</tr>
<tr>
<td>Peracetic acid</td>
<td>&lt; 75&lt;sup&gt;[12]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Chlorine dioxide</td>
<td>90&lt;sup&gt;[12]&lt;/sup&gt;</td>
</tr>
<tr>
<td>Wet air oxidation</td>
<td>72-96</td>
</tr>
</tbody>
</table>

Table 4.2 Removal results of GEM by WAO compared with previous techniques

9. Ying, Kookanab and Kolpin 2009
Since this work represents a simulation of the treatment of residual pharmaceuticals in wastewater, however, further work must be accomplished to determine whether this treatment technology is effective under actual conditions. Thus, future work in this research area is needed. Specific experiments that are needed are detailed below.

First, the degradation of the pharmaceuticals in the real aquatic ecosystems depends on a variety of factors, including not only the compound's properties, but also other environmental factors, the presence of natural microbial communities (Gros, Petrović and Barceló 2007, Onesios, Yu and Bouwer 2009). All of these environmental factors should be considered as important removal effects. More importantly, the removal of these compounds should be accomplished using actual sewage to determine the effectiveness of the WAO process under operation conditions as close as possible to the proposed use of this technology.

Second, a broader evaluation of the impact of the type of organic matter used in the WAO process needs to be conducted. Preliminary results from other members of the research group indicate that certain compounds produce higher percentages of formic acid per carbon atom. Based on the results presented in Chapter 3, formic acid appears to have a positive correlation to the degradation of these drugs.

Third, it is necessary to better understand the degradation mechanisms of these two pharmaceuticals so that to develop the most optimal operation. Formic acid, as one of the key products of WAO, plays an important role in the entire
removal reaction. How does it work and what is its mechanism during the entire reaction? The subsequent analysis of mass spectrometry and ion chromatography would be probably helpful to solve these questions.

Finally, while the degradation of the target pharmaceuticals has been demonstrated in this work, degradation products, in addition to the simple organic acids like formic and acetic acid were produced. Presently, the chemical identity of these compounds is not known. Thus, future experiments must also focus on determining the identity of the degradation products.
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