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Effect of drinking water ozone treatment on select pharmaceuticals and personal care products (PPCPs) and endocrine disrupting compounds (EDCs)

Chaoyang Yue
University of Windsor

EFFECT OF DRINKING WATER OZONE TREATMENT ON SELECT PHARMACEUTICALS AND PERSONAL CARE PRODUCTS (PPCPs) AND ENDOCRINE DISRUPTING COMPOUNDS (EDCs)

By

Chaoyang Yue

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DECLARATION OF CO-AUTHORSHIP

This thesis incorporates the outcome of research undertaken in collaboration with the Applied Chromatography Section, Laboratory Services Branch, Ontario Ministry of the Environment (MOE), as part of a research project under the supervision of Dr. Rajesh Seth and Dr. Shahram Tabe. The collaboration related to research included preparation of native and surrogate PPCPs/EDCs spiking solutions, and analysis of PPCPs/EDCs after ozonation process, which were performed by the Applied Chromatography Section as detailed in Chapter 3 of this thesis.

I certify that, with the above qualification, this thesis, and the research to which it refers, are the product of my own work, and that any ideas or quotations from the work of other people, published or otherwise, are fully acknowledged in accordance with the standard referencing practices of the discipline. I acknowledge the helpful guidance and support of my supervisors, Dr. Rajesh Seth and Dr. Shahram Tabe.

ABSTRACT

The effect of five process variables on the transformation of 16 selected PPCP/EDCs during drinking water ozonation was systematically studied through 2^{5-1} fractional factorial designed experiments. Dissolved Organic Carbon (DOC) content, ozone dose, and their interaction were most significant for all 16 compounds, and accounted for 60-98% of the observed variability in the transformation efficiencies. Temperature was a significant factor for most of the fast-reacting compounds ($k_{O3} > 10^4$ $M^{-1}s^{-1}$), accounting for up to 20% of the change in transformation efficiency, but was not significant for the slow-reacting compounds ($k_{O3} < 10^3$ $M^{-1}s^{-1}$). Ozone exposure of > 1.0 mg L^{-1} min^{-1} resulted in > 80% transformation of all the 16 compounds at both low (5 °C) and high (23 °C) temperatures. However, this transformation is expected to be strongly dependent on the nature of the DOC for the slow-reacting compounds.

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LIST OF ABBREVIATIONS

Analysis of Variance	ANOVA
Advanced Oxidation Process	AOP
American Water Works Association	AWWA
Activated Carbon	AC
Collision Energy	CE
Chemical Oxygen Demand	COD
Product of disinfectant Concentration and Time	CT
Disinfection By-Product	DBP
Degree of Freedom	DF
Dissolved Organic Carbon	DOC
Dissolved Organic Matter	DOM
Drinking Water	DW
Endocrine Disrupting Compound	EDC
Ethoxyresorufin-O-Deethylase	EROD
Electrospray Ionization	ESI
Granular Activated Carbon	GAC
Hydrophilic-Lipophilic Balance	HLB
High Performance Liquid Chromatography	HPLC
Iodinated X-ray Contrast Media	ICM
Initial Ozone Demand	IOD
Acid Dissociation Constant	ka

Second-order rate constant of reaction between O_3 and a compound	k_{O3}
Second-order rate constant of reaction between •OH and a compound	k_{OH}
Liquid Chromatography	LC
Method Detect Limit	MDL
Ministry of the Environment, Ontario, Canada	MOE
Multiple Reaction Monitoring	MRM
Mass Spectrometry	MS
Model Water	MW
Natural Organic Carbon	NOM
Nephelometric Turbidity Units	NTU
Powder Activated Carbon	PAC
ρ-Chlorobenzoic Acid	pCBA
Particulate Organic Carbon	POC
Pharmaceutical and Personal Care Product	PPCP
Quality Control	QC
Sequential Sum of Squares	Seq. SS
Synthetic Organic Compound	SOC
Solid Phase Extraction	SPE
Sewage Treatment Plant	STP
Total Organic Carbon	TOC
Total Suspended Solid	TSS
Ultraviolet	UV
United States Environmental Protection Agency	USEPA

Water Treatment Plant	WTP
Waster Water Treatment Plant	WWTP

CHAPTER 1: INTRODUCTION

1.1 Environmental Side Effects Of PPCPs/EDCs- Current Status

The occurrence of endocrine-disrupting compounds (EDCs) as well as pharmaceuticals and personal care products (PPCPs) in the aquatic environment has raised growing concerns and research interests recently (Daughton et al., 1999; Heberer et al., 2002; Snyder et al., 2003). In the context of pollution, the United States Environmental Protection Agency defines pharmaceuticals and personal care products (PPCPs) as contamination from any product or its chemical constituents used by individuals for personal health or cosmetic reasons or used to enhance growth or health of livestock in the agribusiness (USEPA, 2008). Included in this list are thousands of chemical substances, including prescription and over-the-counter therapeutic drugs, veterinary drugs, fragrances, and cosmetics. Of particular concern is a sub-set of bioactive PPCPs, which are routinely detected in the environment, and are known or suspected to have toxic or other harmful side effects. In this context, chemicals that can cause the disruption of endocrine related processes, called endocrine disrupting chemicals (EDCs) are of particular concern in the aquatic environment. Chemicals in this group that are routinely detected in the aquatic environment include some PPCPs (e.g., 17α-ethinylestradiol), as well as others (e.g., metals, bisphenol A). Therefore, PPCPs/EDCs is used as a general term to represent all of these compounds in literature. With the development of advanced analytical instruments and methods, a variety of PPCPs/EDCs have been detected in wastewater effluents and drinking water supplies (Daughton et al., 2000; Kolpin et al., 2002), or even worse in drinking water, in the lower nanograms per litre range (Ternes et

al., 2001). Figure 1 shows various routes by which human and veterinary therapeutics are released to the environment.

Pharmaceutical compounds are designed either to be highly active and interact with receptors in humans and animals or to be toxic for a number of infectious organisms, including bacteria, fungi and parasites. Once released into the environment, pharmaceuticals are transported and distributed to air, water, soil or sediment. A wide range of subtle impacts has been reported on lower animals that have receptor systems similar to humans and animals used in agriculture, as well as infectious organisms that have a crucial role in the functioning of ecosystems, as listed in Table 1.1.

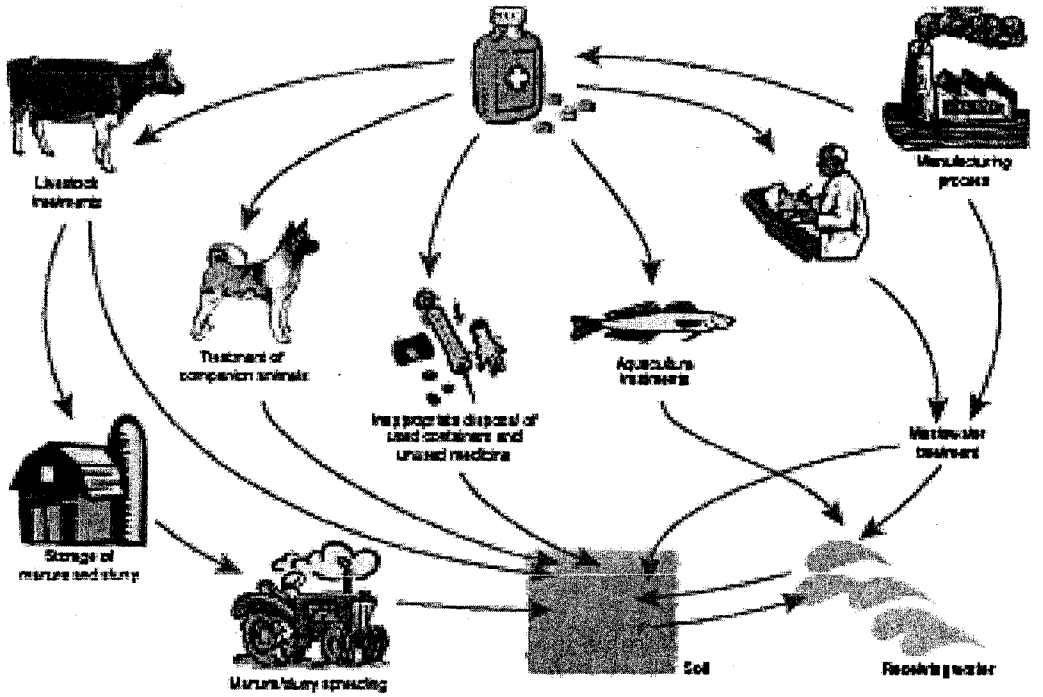


Figure 1.1 Routes of PPCPs/EDCs entering the environment (source: Boxall, 2004).

Although no harmful health effects on human have been reported due to PPCPs/EDCs contamination of the aquatic environment, effects from long-term exposure to individual

or a combination of several PPCPs/EDCs are not known. Applying the precautionary principle, the best strategy might be to minimize environmental contamination and removal of these compounds to the extent possible during drinking water treatment.

Table 1.1 Reported subtle effects of some selected PPCPs/EDCs detected in surface water (adapted from Boxall, 2004)

Compounds	Medicine Class	Reported Effects	Reference
Sulfamethoxazole	Antibiotic	Inhibition of basal ethoxyresorufin-*O*-deethylase (EROD) activity in cultures of rainbow trout hepatocytes	Laville et al., 2004
Carbamazepine	Anticonvulsant		
Tylosin	Antibiotic	Impacts on the structure of soil microbial communities	Westergaard et al., 2001
Ibuprofen	Anti-inflammatory	Stimulation of growth of cyanobacteria and inhibition of growth of aquatic plants	Pomati et al., 2004
Erythromycin	Antibiotic		
Tetracycline	Antibiotic		
17α-Ethinylestradiol	Contraceptive	Endocrine-disrupting effects on fish, reptiles and invertebrates	Young et al., 2002

1.2 Removal of PPCPs/EDCs by Different Treatments

Municipal wastewater treatment plants are a dominant source of release of PPCPs/EDCs to the aquatic environment. The residual concentration in drinking water is therefore governed by the efficiency of their removal by wastewater and water treatment processes. Conventional activated sludge municipal wastewater treatment has been shown to degrade several PPCPs/EDCs to varying extent, i.e., from complete to very poor, depending on their physicochemical properties (Joss et al., 2005; Göbel et al., 2007). Studies have demonstrated that traditional water treatment trains, mainly consisting of coagulation, flocculation, sedimentation, and filtration, are not capable of efficient

removal of PPCPs/EDCs (Zhang et al., 1999; Adams et al., 2002). Activated carbon adsorption, including granular activated carbon (GAC) and powder activated carbon (PAC) were effective in removal of some pharmaceuticals (Ternes et al., 2002; Westerhoff et al., 2005). However, the individual removal efficiency varies greatly and depends on the properties of the activated carbon sorbent (e.g. surface area, pore size distribution, surface charge, oxygen content), as well as the properties of the solute (e.g., shape, size, charge, hydrophobicity) (Ternes et al., 2002; Snyder et al., 2003). Amongst membrane filtration processes, reverse osmosis and nanofiltration have been shown to provide an excellent barrier for most PPCPs/EDCs. Polar and charged compounds, which interact with membrane surfaces, are better removed than less polar or neutral compounds (Snyder et al., 2003). However, membrane processes suffer from the disadvantage of producing waste concentrate or brine that must be disposed of. Chemical oxidation of PPCPs/EDCs by chlorine is selective, and in general not very effective (Westerhoff et al., 2005). Several studies have reported on the oxidation of PPCPs/EDCs by advanced oxidation processes (AOPs). These processes include the application of ozone, hydrogen peroxide, and ultraviolet light, either individually or in combination (Crittenden et al., 2005). The processes involve formation of highly reactive OH radicals (•OH), which is a very potent and non-selective oxidant. The reported oxidation efficiencies with ozone range from medium to high for many PPCPs/EDCs of concern depending on their chemical structures and functional groups (Zwiener and Frimmel, 2000; Acero et al., 2001; Ternes et al., 2002 and 2003; Westerhoff et al., 2005).

Treatment with ozone has been implemented or is being considered as an upgrade by several municipalities to improve the microbiological safety and reduce the formation of disinfection by-products during post-chlorination of the treated drinking water. The

transformation of PPCPs/EDCs and other organic contaminants during the process would therefore be an added benefit of the process. However, the efficiency of transformation of PPCPs/EDCs by ozonation is expected to be affected by several process variables, the effect of which has not been systematically or extensively studied.

1.3 Background- Occurrence of PPCPs/EDCs in Detroit River

Detroit River connects Lake St. Clair and Lake Erie, and is the source of drinking water for approximately 4.5 million residents of metropolitan Detroit, Michigan, USA and Windsor, Ontario, Canada (Jasim et al., 2006). Due to considerable loading of urban and agricultural runoff, sewage treatment plant discharges at the head of the river, and frequent combined sewer overflows, the sources, types and concentrations of PPCPs/EDCs in the river water are of ecological and human health concern.

The present study is a part of a larger project, sponsored in part by the American Water Works Association Research Foundation (AwwaRF), the Ontario Ministry of the Environment (MOE), and the Windsor Utilities Commission (WUC). In an earlier part of the study, the occurrence of 51 PPCPs and EDCs was examined over a 13-month period in the Detroit River Watershed. The sampling locations were chosen to follow the transport and fate of the target pollutants from the effluent of the Little River Sewage Treatment Plant (STP), Windsor, Ontario to the finished drinking water supplied to the Cities of Detroit and Windsor. Based on the results from this study (unpublished data), a set of 16 PPCPs/EDCs was selected for the current study. The selected substances are listed in Table 1.2. Thirteen compounds were selected in this study because they exhibited the highest frequencies of detection in the Detroit River Watershed. The remaining three chemicals (i.e., tetracycline, monensin and indomethacin) were selected

because they have only recently been added to MOE's list of monitored PPCPs/EDCs, and have not been widely monitored or reported.

Table 1. 2 Compounds to be studied in bench-scale experiments

No.	Compound Name	Description
1	Erythromycin	Antibiotic (macrolide)
2	Tylosin	Antibiotic (macrolide)
3	Lincomycin	Antibiotic (macrolide)
4	Sulfamethazine	Antibiotic (sulfonamide)
5	Sulfamethoxazole	Antibiotic (sulfonamide)
6	Sulfachloropyridazine	Antibiotic (sulfonamide)
7	Tetracycline	Antibiotic
8	Monensin	Antibiotic
9	Carbamazepine	Anticonvulsant
10	Ibuprofen	Anti-inflammatory
11	Naproxen	Anti-inflammatory
12	Indomethacin	Anti-inflammatory
13	Gemfibrozil	Lipid regulator
14	Bezafibrate	Lipid regulator
15	Clofibric Acid	Lipid regulator
16	Bisphenol A	Plasticizer

Among these selected PPCPs/EDCs, 8 compounds are antibiotics. Erythromycin and tylosin are macrolide antibiotics, which are similar in structure, mechanism of action, and spectrum. Erythromycin inhibits bacterial protein synthesis and is often used for people with allergy to penicillins. Tylosin is a veterinary drug for the treatment of disease in food producing animals. Lincomycin is a lincosamide antibiotic having an antibacterial spectrum similar to macrolides (Ikehata et al., 2006). Sulfachlorpyridazine, sulfamethazine and sulfamethoxazole are sulfonamide antibiotics and have a common

core chemical structure, i.e., para-aminobenzene (see Appendix C). Tetracycline inhibits bacterial protein synthesis by attacking the ribosome (Merck & Co., 1999). Monensin is an antibiotic blocking protein transport in side the cells and extensively used in beef and dairy cattle industries.

Carbamazepine is an anticonvulsant widely used to control generalized tonic-chronic seizures (Merck & Co., 1999), and was found to be highly resistant to biodegradation (Clara et al., 2004). Ibuprofen, naproxen and indomethacin are anti-inflammatory drugs to reduce pain and fever (Merck & Co., 1999). Gemfibrozil and bezafibrate are lipid regulators used for a range of metabolic disorders. Clofibric acid is a hydrolyzed metabolite of lipid regulator clofibrate. Bisphenol A is the only compound that is not a pharmaceutical. It is a plasticizer widely used in plastics manufacturing, for example, plastic bottles, food and beverage can linings and dental sealants. Identified as an endocrine-disrupting chemical, bisphenol A is able to duplicate, block or exaggerate hormonal responses.

1.4 Objectives of This Project

The objective of the current study is to examine the effect of process variables on the transformation of select PPCPs/EDCs of concern during ozone treatment of raw (untreated) source water. To ensure proper control of water quality parameters, the use of simulated raw water is envisaged. The present study is focused on conducting bench-scale experiments to include the following specific objectives:

- Select a suitable matrix for simulated raw water

- Select suitable ranges for five selected process variables (pH, DOC, temperature, ozone concentration, contact time) and a two-level fractional factorial design for the experiments
- Establish a protocol for spiking the 16 selected PPCPs /EDCs into the simulated raw water
- Conduct the 16 bench-scale experiments under the designed experimental conditions and monitor for several parameters including PPCP/EDC, DOC and ozone concentrations
- Examine kinetics of ozone decay under selected experimental conditions
- Statistically examine the results of the experiments to identify the importance of the selected process variables and their impact on PPCPs /EDCs transformation during the ozonation process.
- Develop recommendations for utilities regarding ozonation treatment for the transformation of PPCPs/ EDCs, based on the results of the current study.

CHAPTER 2: LITERATURE REVIEW- OZONATION

2.1 Selected Properties of Ozone and Its Applications in Water Treatment

Ozone, O_3, is a colorless and metastable gas at ambient temperatures with a pungent odour that can be detected at level as low as 0.01 to 0.05 ppm. Its density is 1.5 times that of oxygen and is 12.5 times more soluble in water (solubility in water 0.494 m^3/m^3 at 0 °C) (NCR, 1987). It is applied to water as a gas generated onsite by passing dry compressed air or pure oxygen across an electrode. Ozone is used as a strong oxidant/disinfectant in water treatment in a variety of applications, which include (1) disinfection, (2) oxidation of iron, manganese and sulfides, (3) oxidation of taste and odour compounds, (4) oxidation of micropollutants, (5) removal of color, (6) control of disinfection by-products (DBP) precursor and (8) reduction of chlorine demand (Crittenden et al., 2005).

2.2 Ozone Decomposition Mechanisms and Kinetics

2.2.1 Ozone Reactions and Decomposition

Ozone can react with compounds in aqueous solutions (e.g., water) by two types of reactions: direct reaction by molecular ozone and indirect reaction by hydroxyl radical species that form when ozone decomposes in water (Hoigné et al., 1976). Molecular ozone directly oxidizes inorganic species (e.g., Fe^{2+}, Mn^{2+}, Br^- and NH_3) in water matrix, also selectively attacks the electron-rich bonds contained in specific functional groups in organics (e.g., aromatics, olefins and amines) (Hoigné et al., 1983). In comparison, the indirect reaction has a much less selectivity but a quick reaction rate by hydroxyl radicals,

which possesses a higher oxidizing potential than molecular ozone (2.8 V vs 2.07 V) (Ku et al., 1996; Hoigné, 1997). However, the formation of free radicals from ozone is affected by either the solution pH or the presence of some scavengers in the water to be treated. The following diagram illustrates these two general reactions of ozone in water, where Si represents all compounds in water (Langlais et al., 1991).

$$O_3 + Si \rightarrow Products$$

$$O_3 + OH^- \rightarrow \bullet OH \text{ (radical)} + Si \rightarrow Products$$

Although the two reactions proceed simultaneously and compete for substrate, they may be differentiated by using radical scavengers (e.g., carbonate and bicarbonate) to inhibit indirect free oxidation but without affecting the direct oxidation reaction (Chiang et al., 2006).

Ozone decomposition in aqueous solution plays a very important role in the application of ozonation processes and has been studied for several decades (Ku et al., 1996). Kinetic studies have shown that the decay of ozone in natural waters can be generally expressed as a two-stage first-order kinetic reaction. The first stage, i.e. the initial ozone demand phase, is marked by a sudden depletion of ozone that occurs within the first seconds of introduction, and is considered to be caused by those substances readily oxidized by ozone, such as organic and inorganic compounds (Urfer et al., 1999). The second stage is a slower radical chain reaction, which behaves according to first-order kinetics. This reaction is first-order in ozone concentration, and the decomposition rate can be measured at a given pH and in presence of excess radical scavengers, which prevent secondary reactions (Langlais et al., 1991; Urfer et al., 1999).

HSB model, proposed by Hoigné, Staehelin, and Bader, is often cited in the literature to describe the spontaneous decomposition of ozone (Langlais et al., 1991; Westhoff et al.,

1997). This radical chain process is believed to be initiated, promoted, and inhibited by many compounds in the raw water source. Langlais et al. (1991) defined initiators of the free-radical reaction as "compounds capable of inducing the formation of a superoxide ion (O_2^-) from an ozone molecule", which include hydroxide ion (OH^-), H_2O_2/HO_2^-, Fe^{2+}, formate, humics, as well as ultraviolet radiation at 253.7nm. In pure water, where no other initiators exist, the self-decomposition of ozone is initiated by reaction with the hydroxide ion (OH^-). Promoters are "all organic and inorganic compounds capable of regenerating the O_2^- superoxide anion from the hydroxyl radical". The rate constant of the $O_2^{\bullet-}$ formed with ozone is very high ($1.1\times10^9\ M^{-1}s^{-1}$). Therefore, the conversion of less ozone-selective OH radicals into the highly selective $O_2^{\bullet-}$ promotes the chain reaction (Pi et al., 2005). Common promoters include O_3, humic acids, aryl groups, formic acid, glyoxylic acid, primary alcohols and phosphates. Inhibitors are "compounds capable of consuming the OH radicals without regenerating the superoxde anion O_2^-". Bicarbonate and carbonate ions, alkyl groups, tertiary alcohols, and humic substances are within this group. Some important decomposition reactions initiated by hydroxide ions are given as follow (von Gunten, 2003a; Crittenden et al., 2005):

$$O_3 + OH^- \rightarrow HO_2^- + O_2 \qquad k_1 = 70\ M^{-1}s^{-1} \qquad (2.1)$$

$$O_3 + HO_2^- \rightarrow O_3^{\bullet-} + HO_2^{\bullet} \qquad k_2 = 2.8\times10^6\ M^{-1}s^{-1} \qquad (2.2)$$

$$HO_2^{\bullet} \leftrightarrow O_2^{\bullet-} + H^+ \qquad Ka = 1.6\times10^{-5}\ 25°C \qquad (2.3)$$

$$O_3 + O_2^{\bullet-} \rightarrow O_3^{\bullet-} + O_2 \qquad k_3 = 1.1\times10^9\ M^{-1}s^{-1} \qquad (2.4)$$

$$O_3^{\bullet-} + H^+ \rightarrow HO_3^{\bullet} \qquad k_4 = 5.2\times10^{10}\ M^{-1}s^{-1} \qquad (2.5)$$

$$HO_3^{\bullet} \rightarrow {\bullet}OH + O_2 \qquad k_5 = 1.4\times10^5\ s^{-1} \qquad (2.6)$$

Among these elementary reactions, step (2.1) is the initiation reaction of ozone self-decomposition, which is only fast at high pH. While increasing pH can be costly in realistic water treatment, addition of hydrogen peroxide (therefore dissociating to HO_2^-)

represents a cheap solution (reaction 2.2), and this leads to an advanced oxidation process (AOP). The overall stoichiometry of these reactions is given as following reaction, which shows that 1.5 moles of ozone is needed to produce 1 mole of •OH.

$$3O_3 + OH^- + H^+ \rightarrow 4O_2 + 2{\bullet}OH \qquad (2.7)$$

2.2.2 Parameters Affecting Ozone Decay

Because of the powerful oxidizing capability and high instability of ozone, the decomposition mechanism is considered to be very complicated and is greatly affected by water quality and process parameters such as temperature, pH, alkalinity, DOC, ozone dosage, and UV intensity. The effects of some very important parameters on ozone decomposition are described as following:

Temperature

Temperature affects the solubility of ozone in water and its reaction rates causing ozone to decomposition, i.e., direct reaction and indirect reaction of ozone (Hoigné, 1994; Urfer et al., 1999). Higher temperature results in less soluble and less stable ozone in water, but the reaction rate with the substrate increases (Langlais et al., 1991). Mizuno et al. (2007) developed an ozone self-decomposition model based on a second-order in ozone concentration, and calculated that 2.2 times enhancement of rate constant with each 5 °C increase of temperature in the range of 15 – 30 °C. Elovitz et al. (2000) studied the effect of varying reaction temperatures on the rate of ozone depletion at an initial dose of 1.0 mg/L and pH 8.0 and found 7-fold increase in the rate constants of secondary phase, i.e., first-order kinetic phase, with increasing temperatures from 5 to 25 °C. Interestingly,

temperature has limited effects on hydroxyl radical reactions since •OH reaction have activation energies typically on the order of 5 – 10 kJ/mol.

pH

The stability of ozone is strongly affected by the pH value of the water. The direct effects on ozone decomposition can be seen from the initiation reaction between ozone and hydroxide anions (OH^-) (reaction 2.1 in Section 2.2.1). Therefore, lowering the pH decreases the concentration of OH^- thus producing a stabilizing effect on molecular ozone, which in turn favours direct reaction pathway. Whereas high pH values accelerate ozone decomposition, consequently favouring the indirect reaction pathway. Mizuno et al. (2007) also calculated 5-times enhancement of decomposition rate constant with increase of one pH unit based on their model. Elovitz et al. (2000) also reported 34-fold increase in the rate of ozone depletion with increasing pH from 6.0 to 9.0. In addition to the hydroxide-initiated ozone decomposition reaction, as pH increases, O_3 would be more reactive with deprotonated acid and phenol moieties in the dissolved organic matter (DOM) thus increasing the rates of direct electrophilic attack of O_3 with DOM. Changes in pH value can also affect the rate of ozone consumption through pH-dependent reactions in the O_3 decomposition chain cycle involving reaction intermediates such as HO^- and $O_3•^-$. These concomitant effects make it difficult to construct a mechanistic interpretation of the effect of reaction pH on the O_3 kinetics. Similarly to temperature, pH has limited effect on oxidation reactions involving •OH (Elovitz et al., 2000).

Alkalinity

In most natural waters with pH values of 6 to 9, alkalinity is the combined concentration of bicarbonate ions (HCO_3^-) and carbonate ions (CO_3^{2-}) (Davis et al. 1998). HCO_3^- and CO_3^{2-} species act as inhibitors in the O_3 decomposition cycle by scavenging chain carrier •OH radicals, but not generating superoxide (O^{2-}) or other species that accelerate the decomposition of O_3 (Urfer et al., 1999; Hoigné, 1994). Increased carbonate alkalinity therefore enhances the stability of the ozone molecules, but an apparent levelling off effect was observed with increasing HCO_3^- / CO_3^{2-} concentration (Formi et al., 1982; Staehelin et al., 1982; Tomiyasu et al., 1985; Elovitz et al., 2000). The reason for the levelling phenomenon is still unclear. Elovitz et al. (2000) showed a two-fold decrease in the rate of zone depletion when the carbonate alkalinity was increased from 0 – 1.5 mM. The chain termination reactions by carbonate alkalinity can be expressed by following equations (von Gunten, 2003a):

$$\bullet OH + CO_3^{2-} \rightarrow CO_3^{\bullet -} + OH^-, \quad k = 3.9\times10^8\ M^{-1}s^{-1} \qquad (2.8)$$

$$\bullet OH + HCO_3^- \rightarrow CO_3^{\bullet -} + H_2O, \quad k = 8.5\times10^6\ M^{-1}s^{-1} \qquad (2.9)$$

Ozone Dose

Ozone dose is a key control parameter in full-scale ozonation plants. Therefore, it is important to understand its effect on observed ozone decomposition kinetics. Different research groups have demonstrated that the rate of ozone decay varies with the applied ozone concentration in surface water, ground water and wastewater (Park et al., 1999; Sladic, 2001; Buffle et al., 2006a). Buffle et al. (2006a) reported that, in ozonation of wastewater, ozone consumption prior to 350 ms increases with increasing dose, but the rate of ozone decomposition decreases. Park and co-workers showed that decay rate

constant, k, decreased exponentially with an increase of ozone dose from 1 to 6 mg/L (Park et al., 1999). The peculiarity of kinetics raises the importance to test different levels of ozone doses covering the range of interest for the treatment process at certain temperature.

Organics

Organics in water are naturally occurring or from human sources (Langlais et al., 1991). Natural organic matter (NOM) is the term used to describe the complex matrix of organic chemicals originating form natural sources that are present in all water bodies (Crittenden et al., 2005). NOM is measured most commonly using total organic carbon (TOC) as a surrogate measure. TOC is composed primarily of two fractions: dissolved organic carbon (DOC), which can pass through a 0.45 μm filter, and particulate organic carbon (POC), those retained on the filter (Crittenden et al., 2005). DOC seems to be the water quality parameter that has a stronger influence on the efficiency of the ozonation process. NOM can affect the ozone stability in two ways: it can either directly react with ozone or indirectly affect its stability through scavenging of OH radicals (von Gunten, 2003a). Direct reactions cause an instantaneous ozone demand that are generally attributed to double bonds, activated aromatic systems, amines and sulfides (von Gunten, 2003a). Schulze et al. (1999) showed that a raw water with TOC = 3.9 mg/L had an ozone demand 2 to 4 times higher than a settled water sample with TOC = 1.5 mg/L. Scavenging OH radicals by NOM can either inhibit or accelerate the chain reaction of ozone decomposition depending on if there is formation of superoxide radicals ($O_2^{\cdot-}$). Previous studies have also shown that the effects of NOM on ozonation are dependent of the nature and concentration of organic compounds. Rechhow et al. (1992) performed

ozonation experiments on various fractions of DOM and observed that humic and fulvic acid fractions were responsible for most of the ozone consumption. Pi et al. (2005) found that some aromatic compounds (e.g., benzoate) tremendously accelerated ozone decomposition in buffered water although their direct reactions with ozone are very low (i.e., very low $k_{O3,}$). Based on their findings and detection of H_2O_2 as an intermediate, they proposed a new reaction pathway, which is different from HSB model. Elovitz et al. (2000) studied six waters having moderate and similar DOC concentration and alkalinity, and found a three-fold difference in O_3 depletion rates. They also concluded that the large-scale biogeochemical factors (e.g., limestone, temperature climate) rather than local environmental factors (e.g., local run-off, point-source pollution) dictate the behavior of the water towards ozonation. Buffle and co-workers studied ozone decomposition in wastewater, and found that ozone was quickly consumed within 350 ms, and no residual ozone could be measured beyond 20 seconds. In addition, ozone decomposition seemed not to follow apparent first-order kinetics as it would during the second phase of natural water ozonation (Buffle et al., 2006a). The effects of NOM on ozone decomposition can be elucidated from following equations (von Gunten, 2003a):

Direct reactions with O_3

$$O_3 + NOM1 \rightarrow NOM1ox \quad (2.10)$$
$$O_3 + NOM2 \rightarrow NOM2^{+\bullet} + O_3^{\bullet -} \quad (2.11)$$

Propagation reactions to produce $O_2^{\bullet -}$

$$\bullet OH + NOM3 \rightarrow NOM3 + H_2O \text{ or } NOM3\bullet + OH^- \quad (2.12)$$
$$NOM3\bullet + O_2 \rightarrow NOM3\text{-}O_2^{\bullet} \rightarrow NOM3^+ + O_2^{\bullet -} \quad (2.13)$$

Chain termination reactions

$$\bullet OH + NOM4 \rightarrow NOM4 + H_2O \quad (2.14)$$
$$NOM4\bullet + O_2 \rightarrow NOM4\text{-}O_2^{\bullet} \rightarrow \text{no } O_2^{\bullet -} \text{formation} \quad (2.15)$$

Other parameters that have an influence on ozone decomposition include UV light intensity and anion species in aqueous solution. Increasing UV intensity resulted in increased decomposition rate of ozone, but this effect seemed to be dominating only in acidic solution; whereas the decomposition of ozone by the reaction with OH^- could be the predominant reaction in alkaline solutions (Ku et al., 1996). Sotelo et al. (1989) studied that effect of anions on the self-decomposition rate in aqueous solution and found the decomposition rate of ozone was highly dependent on the type of anions dissolved in solutions. Anions in aqueous solutions could scavenge hydroxyl radicals generated from O_3/OH^- therefore inhibiting the degradation rate of dissolved organic matter. However, different scavenging abilities of these anions have been suggested based on a wide range of the rate constant values (e.g., $10^5 - 10^{10}\ M^{-1}s^{-1}$) between hydroxyl radical reaction with various anions (Ku et al., 1996). Table 2.1 shows the summary of selected factors that influence stability of ozone in aqueous solutions.

Table 2.1 Factors that influence stability of aqueous ozone residuals

Increases stability	**Reduces Stability**
Low pH	High pH
High alkalinity	Low alkalinity
Low TOC	High TOC
Low temperature	High temperature

2.3 Removal of PPCPs/EDCs by Ozone Oxidation

2.3.1 Removal of PPCPs/EDCs from Pure, Simulated and Natural Source Waters

Ozonation of selected PPCPs/EDCs has been studied by many different research groups. Since the biggest concern over the occurrence of these chemicals is their presence in drinking water sources, which can directly impact human health, most studies have

focused on their removal from drinking water sources. Zwiener and Frimmel (2000) selected clofibric acid, ibuprofen, and diclofenac as target chemicals, and examined their removal by ozone in Milli-Q ultra-pure water. Although diclofenac was well removed (97%), removal efficiencies for ibuprofen (12%) and clofibric acid (8%) were low. They concluded that ozone reacts as a selective oxidant, and the substituted aminogroup in diclofenac is a possible center for the readily reaction with ozone. No comments on the low reactivity of ibuprofen and clofibric acid were provided. In 2002, Ternes and co-workers investigated the elimination of bezafibrate, clofibric acid, carbamazepine and diclofenac during drinking water treatment processes under laboratory conditions and at two full-scale water treatment plants in Germany (Ternes et al., 2002). Within varying ranges of temperature (9.9 – 23 ^{o}C) and dissolved organic carbon (DOC) concentrations (1.3 - 2.4 mg/L), carbamazepine and diclofenac were well removed (>97%) even with the low applied ozone dose of 0.5 mg/L. Intermediate to high removals (50 - 80%) were observed for bezafibrate with increased ozone doses of 1.5 – 3 mg/L. However, only a reduction of ≤40% was achieved for clofibric acid even at the high ozone dose of 3.0 mg/L. The authors stated that deprotonated secondary aromatic amines in diclofenac and nonaromatic double bonds in carbamazepine were responsible for the high reactivity with ozone. The medium reactivity of bezafibrate was attributed to its more slowly reactive disubstituted benzene rings; and missing active sites susceptible to direct ozone attack was deemed to be responsible for very slow reaction of clofibric acid.

Adams et al. (2002) reported rapid and efficient conversions (>95%) of sulfachlorpyridazine and sulfamethazine by ozonation in pre-filtered Missouri River water samples. More than 95% of initial concentration of 50 μg/L was transformed for both compounds in < 2 minutes with an applied ozone dose of 0.3 mg/L. Reactions

occurred even faster in distilled/deionized water systems. More recently, Westerhoff and co-workers conducted series of bench-scale experiments to examine the fate of 62 different PPCPs/EDCs during simulated drinking water treatment processes (Westerhoff et al., 2005). Three drinking water suppliers and one model water were used with initial PPCPs/EDCs concentrations ranging from 10-250 ng/L. The DOC ranged from 3.0 to 4.0mg/L, ozone dosage used was 2.5-4.0mg/L, and contact time was 3.0 minutes. An average removal of 80% was observed for ibuprofen, 88% for sulfamethoxazole, 98% for gemfibrozil, 91% for naproxen and 99% for carbamazepine.

2.3.2 Removal of PPCPs/EDCs from Wastewater

Occurrence of PPCPs and EDCs in effluent from municipal sewage treatment plants (STPs) or wastewater treatment plants (WWTPs) also raised many concerns since some of these treated wastewaters are discharged into receiving waters, others may used in agricultural fields, and therefore become the major source of pharmaceuticals in the aquatic environment (Ternes, 1998; Kolpin et al., 2002). Effluents from STPs or WWTPs usually have much high amount of DOC, COD, and total suspended solid (TSS), which will require higher O_3 dosage (e.g., 5 - 15 mg/L) than that applied in water treatment. Two pilot studies on removal of PPCPs/EDCs from wastewater were performed by the Ternes and Huber groups, respectively (Ternes et al., 2003; Huber et al., 2005). In their experiment, Ternes and co-workers demonstrated that sulfamethoxazole, erythromycin, carbamazepine can be well removed (>92 - 98%) at O_3 dosage of 5 mg/L (contact time 18 min.); ibuprofen and clofibric acid were only half removed (48 - 50%). Increasing O_3 dosage to 10 or 15 mg/L only increased removal of ibuprofen and clofibric acid to >62% and >59%, respectively. However, certain compounds in iodinated X-ray contrast media

(ICM) group, for example diatrizoate, only exhibited removal efficiencies for not higher than 14% even at highest O_3 dosage (Ternes et al., 2003).

Huber and co-workers investigated the influence of suspended solids on the oxidation of 24 pharmaceuticals in an effluent of conventional activated sludge treatment (CAS) (Huber et al., 2005). Their results showed that suspended solids have only a minor influence on the oxidation efficiency of nonsorbing micropllutants. Estimation of O_3 absorption by sludge particles based on film theory proved that only 0.4% of the O_3 transferred into the bulk solution is consumed by sludge particles. This also explains why oxidation by •OH is relatively unaffected by suspended solids. Because the highest share of O_3 reacts in the bulk liquid, •OH is formed in the bulk liquid as well and does not come into contact with sludge particles due to its extremely short lifetime. However, the negative impact of suspended solids cannot be neglected because once micropollutants, especially microorganisms, are sorbed to sludge particles or floc, oxidation and disinfection efficiency will be difficult to achieve because they will only experience a relatively low O_3 exposure (Huber et al., 2005).

2.3.3 Kinetics of Oxidation with Ozone

In the case of ozonation, kinetics of oxidation of PPCPs/EDCs can be represented by the second-order rate constant for the reactions of selected PPCPs/ EDCs with ozone (k_{O3}) and OH radical (k_{OH}). It has been shown that the second-order rate constants determined in pure aqueous solution could be applied to predict the behavior of pharmaceuticals (i.e. removal efficiency) in natural waters (Huber et al., 2003). Determination of k_{O3} usually relies on three methods: ozone in excess, pharmaceuticals in excess, and competition kinetics. While the first two methods are usually limited to rate constants that are lower

than about $1000 M^{-1}s^{-1}$, competition kinetics is suitable for compounds with high rate constants (Huber et al., 2003). Determination of rate constants is therefore case specific, and dependent on temperature and pH value.

Because of the non-selective and fast reactive properties of hydroxyl radical OH, k_{OH} can only be determined by competition kinetics. In the experiments determining k_{OH}, *p*-chlorobenzoic acid (*p*CBA) has been selected as reference exhibiting a rate constant of $k_{OH} = 5\times10^9\ m^{-1}s^{-1}$ (Buxton et al., 1988). OH radicals were generated either by photolysis of H_2O_2 at 313 nm if the compound is photo-stable, or with γ-radiolysis if compounds undergo direct photolysis. The data were evaluated based on Equation 2.16, where $k_{OH}(R)$ and $k_{OH}(M)$ are the rate constants for the reference (R) and target compound (M), respectively. The irradiation time is represented by *t*. k_{OH} values for most of important micropollutants ranged from $3.0\text{-}10 \times 10^9\ M^{-1}s^{-1}$ (Huber et al., 2003; Dodd et al., 2006).

$$\ln\left(\frac{[M(t)]}{[M(0)]}\right) = \ln\left(\frac{[R(t)]}{[R(0)]}\right)\frac{k_{OH}(M)}{k_{OH}(R)} \qquad (2.16)$$

2.3.4 Prediction of Oxidation of PPCPs/EDCs

Most of our understanding of oxidation rate determination and by-product identification comes from empirical laboratory studies. Because the ozonation is selective and case-specific, this approach for discovering the behavior of contaminants is time-consuming, expensive, relies upon advanced measurement techniques, and often requires synthesis of by-products that are not commercially available. Therefore, good prediction of oxidation of PPCPs/EDCs becomes very important.

Chemical Structure-Reactivity Linkage - Qualitative

Qualitative prediction for reactivity of some PPCPs/EDCs with ozone can made by examining the existence of certain functional group(s) in their chemical structures. Since ozone is a strong oxidant, it reacts well at sites of high electron density, such as activated aromatic ring, hydroxyl or amine functionalities, or double bonds (Zwiener and Frimmel, 2000; Ternes et al., 2002; Westerhoff et al., 2005). Consequently, deprotonated species are more active than protonated analogues. Electron-donating (e.g., hydroxyl, amine) or electron-withdrawing (e.g., carboxyl) functional groups lead to increasing and decreasing reactivity, respectively. In addition, Hammett-based correlations have previously related organic compound structures to their reactivity with common drinking water disinfectants, but such correlations have been limited to single aromatic-ring analogues (Gallard et al., 2002).

Prediction Based on Second-order Rate Constant – Quantitative

Oxidation of micropollutants during ozone treatment involves primary oxidant ozone molecules and secondary oxidant hydroxyl radicals •OH formed during ozone decomposition. The oxidation of micropollutant C during an ozonation process therefore consists of two oxidation pathways, and can be formulated according to a rate law such as Equation (2.17) and quantified by using integrated forms of Equation (2.18) or (2.19) (von Gunten, 2003a):

$$-d[C]/dt=k_{O3}[C][O_3] + k_{OH}[C][\bullet OH] \quad (2.17)$$

$$\ln[C(t)/ C(0)]= -(\int[O_3]dt)\, kO_3 -(\int[\bullet OH]dt)\, k_{OH} \quad (2.18)$$

$$\ln[C(t)/ C(0)]= -(\int[O_3]dt)(\, kO_3 + k_{OH}R_{ct}) \quad (2.19)$$

where $\int[O_3]dt$ is called O_3-exposure and can be determined by integrating the measured O_3 concentrations over time during ozone decomposition. $\int[\bullet OH]dt$ is called •OH-exposure, which can be calculated either with help of R_{ct} value; or simply by use of a probe compound that has a known k_{OH} and that does not react with O_3, i.e., using Equation (2.20) and letting kO_3 equal to 0 (zero). The R_{ct} concept was developed by Elovitz and von Gunten (1999), and equals the ratio of the •OH-exposure to the O_3-exposure. It compared the potential for oxidation by •OH to the potential for oxidation by O_3. R_{ct} values for a given water matrix and ozonation condition can be experimentally determined from the experimentally measured decrease in concentration of an ozone-resistant compound (e.g., *p*-chlorobenzoic acid) and ozone (Haag and Yao, 1993; Elovitz and von Gunten, 1999).

R_{ct} values during both the initial and the second phase of ozone decomposition are highly dependent on the nature and content of organic matter, but decrease exponentially during the initial phase before reaching a constant value in the second phase (Buffle et al., 2006b). von Gunten (2003a) reported that typical range of R_{ct} value 10^{-9}~10^{-7} for the secondary phase of ozonation in natural waters and > 10^{-7} during the initial phase or throughout an advanced oxidation proess. In many natural water applications, the initial phase may not be distinguishable and the R_{ct} value may be calculated based on the second phase. In case it is distinguishable and significant, separate R_{ct} values may be calculated for the two phases and the expected transformation of the micropollutant quantified using Equation (2.19). Equation (2.19) shows that for a micropollutant with a $k_{.OH}$ value of 5×10^{9} $M^{-1}s^{-1}$, an R_{ct} value of 3.6×10^{-7} will be required for 90% transformation at an ozone exposure of 1 mg/L.min (assume kO_3 is very low).

This cited model was believed to work reasonably well for some compounds that exhibit a low reactivity to O_3 such as clofibric acid and iopromide, but failed for predicting the residuals of fast-reacting compounds with O_3 during ozonation of municipal wastewater effluents (Huber et al., 2005). The authors attributed the observed strong deviations to the complexity of ozonation process in the presence of sludge particles or colloids. Despite of the prediction failure, oxidation by •OH can always be calculated even for compounds that react fast with O_3. Consequently, the comparison of the predicted oxidation by •OH with the measured residual (C_m) allows for assessing the relevance of the two oxidation pathways for a selected compound according to the following Equation 2.20 (von Gunten, 2003a; Huber et al., 2005), where ibuprofen (IBU) was used as a probe compound to determine •OH-exposure.

$$f(^{\bullet}OH) = \frac{\frac{1}{k_{OH,IBU}} \ln\left[\frac{C_{IBU}(\tau)}{C_{IBU}(0)}\right] k_{OH,P}}{\ln\left[\frac{C_{P,m}(\tau)}{C_{P,m}(0)}\right]} \qquad (2.20)$$

where f(•OH) designates the fraction of oxidation by •OH , and 1-f(•OH), the fraction of oxidation by O_3. The knowledge of these values is important for predicting different products formed depending on different oxidation pathways.

2.4 Oxidation of PPCPs/EDCs by Advanced Oxidation Processes (AOPs)

Some water supplies may contain toxic synthetic organic compounds (SOCs) that must be removed or destroyed to protect public health. As mentioned in Chapter 1, advanced oxidation processes involve highly reactive hydroxyl radicals, which have rate constants usually 3 - 4 orders of magnitude greater than other oxidants such as chlorine and ozone.

Therefore AOP is a viable option to oxidize the SOCs completely into carbon dioxide, water, and mineral acids (e.g., HCl).

Two most extensively studied ozone-based AOPs for the treatment of PPCPs/EDCs are O_3/H_2O_2 and O_3/UV (Zwiener and Frimmel, 2000; Huber et al., 2003; Ternes et al., 2003; von Gunten, 2003a). In the O_3/UV system, photolysis of ozone in aqueous solutions was found to lead to the production of hydrogen peroxide and oxygen molecules after a sequence of reactions. Then the hydrogen peroxide either reacts with O_3 or is split by UV to produce hydroxyl radicals •OH (Peyton et al., 1983; Reisz et al., 2003; Crittenden et al., 2005).

$$O_3 + H_2O_{(l)} + \text{UV light} \rightarrow H_2O_2 + O_2 \quad (2.21)$$
$$H_2O_2 + \text{UV light} \rightarrow 2OH\bullet \quad (2.22)$$
$$2O_3 + H_2O_2 \rightarrow 2OH\bullet + 3O_2 \quad (2.23)$$

The combination of ozone with hydrogen peroxide is the most commonly applied AOP. The elementary reactions that are involved in the production of •OH from H_2O_2/O_3 are similar to ozone self- decomposition except that the initiation occurs through hydrogen peroxide dissociation. Reaction (2.1) in section 2.2.1 therefore is replaced by following reaction:

$$H_2O_2 \leftrightarrow HO_2^- + H^+ \qquad K_a = 1.6\times10^{-12} \quad (2.24)$$

However, determining and maintaining a proper ratio of H_2O_2/O_3 may not be easy in reality. There are several issues that affect the proper dosages of H_2O_2 and O_3. Since ozone tends to be more reactive with background organic matter and inorganic species than H_2O_2, the applied ozone dosage will have to be higher than estimated from stoichiometry. However, an excess O_3 dosage has the potential of wasting O_3 and scavenging •OH through following reaction:

$$\bullet OH + O_3 \rightarrow HO_2^{\bullet} + O_2, \qquad k = 1.0\times10^8 \sim 2.0\times10^9 M^{-1}s^{-1} \quad (2.25)$$

This reaction is fast and important since it consumes both ozone and hydroxyl radicals, therefore lowers the oxidation capacity of the system. On the other hand, if hydrogen peroxide is over-dosed, the excessive H_2O_2 is not easily removed, and not only raises health concern, but also consumes chlorine and interferes with disinfection (Crittenden et al., 2005). It may also scavenge •OH via the following reactions:

$$\bullet OH + HO_2^- \rightarrow HO_2^\bullet + OH^- \qquad k = 7.5\times10^9\ M^{-1}s^{-1} \qquad (2.26)$$

$$\bullet OH + H_2O_2 \rightarrow HO_2^\bullet + H_2O \qquad k = 2.7\times10^7\ M^{-1}s^{-1} \qquad (2.27)$$

It is no surprise that many efforts were made to determine the optimal concentrations of these two oxidants, as well as the proper ratio for the treatment. Huber et al reported that by applying 0.7mg/L H_2O_2 and 2.0mg/L O_3 (i.e. ratio of H_2O_2/O_3=0.35), oxidation of the ozone-resisting compound ibuprofen was increased from 40% to over 80% for a contact time of 10 min (Huber et al. 2003). In a separate study, Zwiener and Frimmel (2000) achieved about 15-30% degradation of both clofibric acid and ibuprofen at a concentration of 0.4mg/L H_2O_2 and 1.0mg/L O_3 (i.e. ratio 0.40), and more than 90% at an increased oxidant concentration of 1.4mg/L H_2O_2 and 3.7mg/L O_3 (i.e. ratio 0.38).

It is worthy to note that the efficiency of an AOP also strongly depends on the OH radical scavenging capacity of the water matrix by scavengers such as HCO_3^-, CO_3^{2-} and DOC (Langlais et al., 1991; Huber et al., 2003), as shown in equation (2.28):

$$\bullet OH \text{ scavenging capacity} = k_{OH,\,DOC} \times [DOC] + k_{OH,\,HCO_3^-} \times [HCO_3^-] + k_{OH,\,CO_3^{2-}} \times [CO_3^{2-}] \qquad (2.28)$$

where $k_{OH,\,DOC}$, $k_{OH,\,HCO_3^-}$ and $k_{OH,\,CO_3^{2-}}$ are the second-order rate constants for the reaction of natural organic matter, bicarbonate, carbonate with •OH radicals, respectively. It was demonstrated that the main advantage of the AOPs lies in the acceleration of the ozone transformation process, and the same oxidation degree can be achieved in a much

shorter contact time (Acero et al., 2001). Comparison of these two O_3-based AOPs is given in Table 2.2.

Table 2.2 Advantages & disadvantages of O_3-based AOPs (adapted from Crittenden et al., 2005)

Selected AOPs	Advantages	Disadvantages
O_3/H_2O_2	• Waters with poor UV light transmission may be treated • Special reactors not required	•O_3 production can be expensive & inefficient process • Gaseous O_3 in off-gas must be removed • Maintaining & determining proper O_3/H_2O_2 dosage may be difficult • Low pH is detrimental
O_3/UV	• No need to maintain precise O_3/H_2O_2 dosage • Residual O_3 degrade rapidly • O_3 absorbs more UV light than equivalent H_2O_2	• Use O_3 & UV to produce H_2O_2 - very inefficient compared to adding H_2O_2 • Special reactors required • Ozone in off-gas must be removed • Volatile compounds will be stripped

CHAPTER 3: METHODOLOGY

3.1 Selection of Variables

The impact of ozone treatment is largely influenced by variables such as pH, temperature, DOC content, ozone concentration and contact time. The range for these parameters, as listed in Table 3.1, was selected based on typical values in surface drinking water source literature. The high and low values for each of the parameters were chosen for the two-level fractional factorial design of the experiments. Ozone is very reactive and unstable, with its reactivity affected by several variables including pH, temperature, and DOC content.

Table 3.1 Values for the 2-levels of the five variables selected for bench-scale experiments

Variables	pH	DOC content (mg/L)	O_3 Dose (mg/L)	Contact Time (min.)	Temperature (°C)
Level 1	6.8	0.8	1.0	2	5
Level 2	8.1	4.5	3.0	6	23

3.2 Experimental Design

A one-half fractional factorial (2^{5-1}) experimental design was performed using Minitab to obtain the experimental conditions for the 16 designed experiments with five variables. The experiments were selected in a random order, and each experiment was conducted in triplicate. Factorial designs have several advantages. They are more efficient than one-factor-at-a-time experiments. Furthermore, a factorial design is necessary when interactions may be present to avoid misleading conclusions. Finally, factorial designs

allow the effects of a factor to be estimated at several-levels of the other factors, yielding conclusions that are valid over a range of experimental conditions (Montgomery, 2005).

3.3 Preparation of Simulated Water

The simulated water was prepared from ultrapure water (>18 MΩ) produced by the Milli-Q water purification system. A DOC stock solution of ~100 mg.C/L made from Suwannee River natural organic matter (SR-NOM, reverse osmosis isolation, purchased from International Humic Substances Society) was used to achieve the desired DOC content. This stock solution was prepared by dissolving 0.25g SR-NOM in 1-L Milli-Q water and filtering through 1.5μm membrane filter. 1 M $NaHCO_3$ solution was used to adjust pH values of all samples. A 20 ft^3 VWR incubator was employed for temperature control.

3.4 Spiking Procedure

To avoid the problem of precipitation of the target chemicals, the stock spiking solution for the target substances was prepared in pure methanol at the MOE laboratory. The final concentrations for the spiked contaminants in simulated water ranged between 200 and 1600 ng/L. These levels of concentrations are at least 30 times the method detection limits (MDLs)(see Table 3.2), and within a factor of five of their maximum detected concentrations in the Detroit River watershed for all the target contaminants. Prior to adding the stock spiking solution into simulated water, methanol evaporation by pure N_2 gas was performed. This procedure minimized addition of organic carbon from methanol but without causing the losses of PPCPs/EDCs spiked.

Table 3.2 Initial spiked concentrations of PPCPs/EDCs prior to ozonation and their method detection limits (MDL)

Compound Names	**Conc. (ng/L)**	**MDL (ng/L)**	**MDL/Conc.**
Erythromycin	1470.0	16	92
Tylosin	1010.0	20	51
Lincomycin	336.3	0.86	391
Sulfamethazine	318.9	2.3	139
Sulfachloropyridazine	630.0	4.6	136
Sulfamethoxazole	349.2	1.7	204
Tetracycline	1554.0	26	60
Monensin	805.0	23	35
Carbamazepine	226.2	1.0	226
Ibuprofen	1000.0	32	31
Naproxen	348.0	2.1	166
Indomethacin	1100.0	29	38
Gemfibrozil	180.0	1.4	128
Bezafibrate	242.0	2.7	90
Clofibric acid	375.0	9.4	40
Bisphenol A	1414.0	48	29
Carbamazepine-d10	118.5	1.0	118
Ibuprofen-d3	433.0	32	13.4
Gemfibrozil-d6	182.3	1.4	130
Clofibric acid-d4	139.5	9.4	14.8
Bisphenol A-d16	951.0	48	19.8

3.5 Ozone Treatment

Ozone was generated using a laboratory-scale ozone generator (Ozonia North America, NJ). Fresh stock liquid ozone solution (~30 mg O_3/L) was prepared by bubbling an oxygen carrier gas into refrigerated distilled water for about 30 minutes. The decay of ozone in the stock solution was minimized through the use of an ice bath. After a quick measurement of ozone concentration in the stock solution, determined aliquots of the stock solution were transferred to 2-L silanized glass reactors containing the water sample. A stopwatch was immediately started to record the time. After ozonation, a 5% (w/w) $Na_2S_2O_3$ solution was used to quench ozone residual.

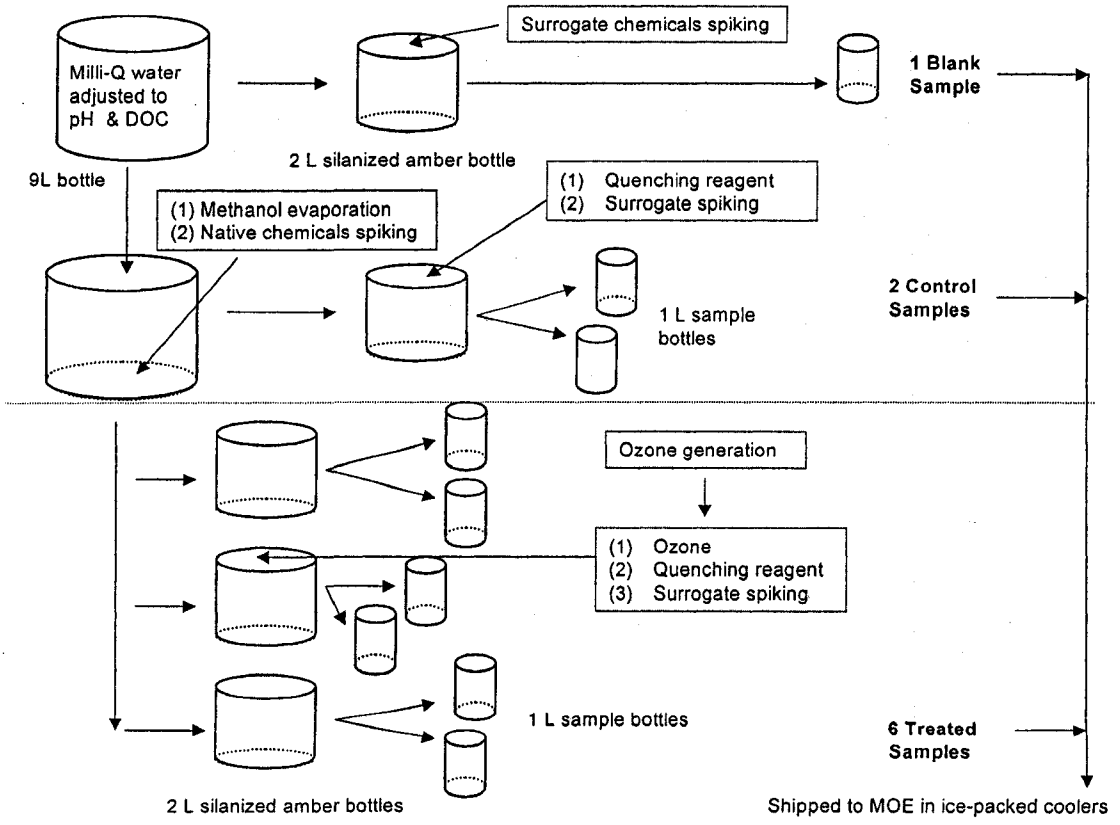


Figure 3.1 General procedures of bench-scale experiments.

A general procedure of bench-scale experiment is given in Figure 3.1. Important steps included water matrix simulation (i.e., pH and DOC adjustment), methanol evaporation and 16 target chemicals spiking, ozone generation and ozone treatment. Deuterated forms of five of these chemicals, i.e., gemfibrozil-d6, ibuprofen-d3, clofibric acid-d4, bisphenol A-d16 and carbamazepine-d10, were also added as surrogates after the experiments to correct for recovery. For the remaining eleven chemicals, the deuterated forms were either unavailable or cost-prohibitive. All samples were then stored in a refrigerator at 4 °C, and shipped for PPCP/ EDC analyses to the Laboratory Services Branch, MOE in ice-packed coolers by overnight courier within 24 – 48 hrs of collection.

3.6 Ozone Decay Study and Exposure Determination

Ozone decay experiments were performed using the simulated water matrix without addition of target PPCPs/EDCs. For each study listed in Table 3.3, a control experiment was run in parallel under the same conditions but without the addition of DOC. At the higher temperature (23 °C), samples were collected for analyses at 0.5, 1.0, 1.5, and 2.0 minutes, and each minute after until the 12th minute. At the lower temperature of 5 °C, the sample collection was continued until the 22nd minute.

Table 3.3 Operating conditions of ozone decay studies

No.	Temperature (°C)	DOC content (mg/L)	Starting ozone concentration (mg/L)	pH
1	5	4.5	3	6.8
2	23	4.5	3	6.8
3	5	0.8	3	6.8
4	23	0.8	3	6.8
5	23	0.8	3	8.1

Ozone exposures of the experiments (up to 2 minutes) were determined based on two methods. For the experiments under the same conditions where ozone decay studies were performed, ozone exposures were determined by integrating the measured ozone concentrations over time, i.e., the areas under ozone decay curves. These experiments included those conducted with O_3 dosage of 3.0 mg/L. Similar results were also obtained for these experiments by fitting an exponential model (when DOC = 4.5 mg/L) or linear model (DOC = 0.8 mg/L) based on 2-point measurement (i.e., ozone residuals before and after treatment). Therefore for remaining experiments with a low O_3 dosage, 1.0 mg/L, and without receiving decay studies, ozone exposures were determined in a same manner, i.e., assuming an exponential model or linear model were also applicable to O_3 dosage 1.0 mg/L when DOC content was high and low, respectively.

3.7 Analytical Methods

3.7.1 Parameters Analysis at University of Windsor

Ozone Residual

Ozone concentrations of stock solutions, and ozone residuals after each experiment, were measured using a Spectronic 20D+ spectrophotometer (600nm wavelength) following the Standard Methods (4500-O_3)/Indigo Colorimetric Method (APHA, 1998).

Dissloved Organic Carbon (DOC)

DOC contents in stock solution and simulated water were analyzed using a Shimadzu TOC-V_{CSH} total organic carbon analyzer, according to the Standard High-Temperature Combustion Method (5310B) (APHA, 1998). Prior to each measurement, fresh Milli-Q

water samples (>18 MΩ) were run at least three times to clean the sample injection system. Laboratory control samples were also regularly analyzed to confirm the performance of the instrument.

pH

The pH values were measured on a VWR meter (Model 8100; VWR, Canada), which was calibrated prior to each use. During each experiment, samples were collected before and after ozone treatment for pH measurement.

3.7.2 PPCPs/EDCs Analysis at MOE

PPCPs/EDCs extraction and analyses were conducted at the Applied Chromatography Section, Laboratory Services Branch, Ontario Ministry of the Environment (MOE). The procedure used, as provided by the Applied Chromatography Section follows.

Sample Preparation

Laboratory QC samples (one pure water blank and two pure water spikes) and bench-scale samples, each of 800 mL, were prepared for solid phase extraction using Waters (Millford, MA, USA) HLB cartridges (6 mL, 200 mg).

To the blank sample, only isotope-labeled surrogates were added, while both native PPCPs/EDCs and isotope-labeled surrogates were spiked into two pure water spike samples. After adding 4 g of ethylenediaminetetraacetic acid disodium salt (Na_2EDTA), laboratory QC and bench-scale samples were homogenized on a laboratory roller (Wheaton Science, NJ, USA) for 10 min, followed by addition of 20 mL of 0.25 M

aqueous ammonium acetate solution. The pH value of each sample was adjusted to 6.95±0.05 using 50% (w/v) NaOH, 10% (w/v) NaOH and 10% (v/v) H_2SO_4 solution. The Hydrophilic-Lipophilic Balance (HLB) cartridges were sequentially conditioned with 5 mL each of methanol and water before the Solid Phase Extraction (SPE). Following extraction, the HLB cartridges were rinsed with 5 mL of 5% (v/v) methanol-water, dried by air, and the target compounds eluted from the SPE cartridges with 5 mL methanol. 1 mL of the eluate from each sample was evaporated to dryness with N_2 at 30 °C on Dionex SE 500 Evaporator, and reconstituted by using 0.1 mL of internal standard solution. Calibration standards were also prepared along with each batch of samples for instrumental analysis.

Instrumentation

Analyses were performed using an Agilent 1100 LC (Mississauga, Ontario, Canada) coupled with an Applied Biosystems API 4000 Q-trap mass spectrometer (Foster City, CA, USA) using an ESI interface. Multiple reaction monitoring (MRM) data were acquired and processed for all compounds in either positive or negative ion mode. An LC column (Thermo Electron, Bellefonte, PA, USA, Hypersil Gold, C-18, 100 × 2.1 mm, 3 μm) was used in two separate chromatographic runs with acidic and neutral mobile phases, respectively (Table 3.4 and Table 3.5). The column was maintained at room temperature and the injection volume 20 μL. Curtain, collision, nebulizer, and auxiliary gases of the MS-MS were set at 10, 5, 35 and 45, respectively. Source temperature was kept at 500°C for positive mode and 400°C for negative mode. Ion spray voltage, declustering potential, entrance potential, and collision cell exit potential used were 5200,

60, 10 and 10 V for the positive and -4200, -80, -10 and -3 V for the negative Electrospray Ionization (ESI), respectively. Multiple reaction monitoring parameters were optimized by direct infusion of individual target compound using a syringe pump. The most intense ion pair for target analytes and their respective optimized parameters were chosen for the analysis. Values of collision energy (CE) are listed in Table 3.6.

Table 3.4 LC gradient condition for ESI positive mode analysis. A, 0.03% HFBA (heptafluorobutyric acid) in water, B, acetonitrile

Total Time (min)	Flow Rate (µl/min)	A (%)	B (%)
0.0	200	85	15
13	200	0	100
15	200	0	100
17	200	85	15
28	200	85	15

Table 3.5 LC gradient condition for ESI negative mode analysis. A, 10 mM ammonium acetate in water; B, acetonitrile

Total Time (min)	Flow Rate (µl/min)	A (%)	B (%)
0	200	90	10
15	200	15	85
17	200	90	10
27	200	90	10

Table 3.6 Mass spectrometry parameters

Compound name	MRM transition	Collision energy (eV)
ESI positive mode detection		
Carbamazepine	237/194	20
Erythromycin	734/158	32
Ibuprofen	207/161	15
Lincomycin	407/126	32
Monensin	694/676	40
Naproxen	231/185	20
Sulfachloropyridazine	285/156	20
Sulfamethazine	279/186	23
Sulfamethoxazole	254/156	21
Tetracycline	445/410	22
Tylosin	916/174	50
D_{10}-Carbamazepine	247/204	25
D_3-Ibuprofen	210/164	15
$^{13}C_6$-Sulfamethazine (IS)	285/186	25
$^{13}C_3$-Ibuprofen (IS)	210/163	15
ESI negative mode detection		
Bezafibrate	360/274	-25
Bisphenol A	227/133	-35
Clofibric acid	213/127	-20
Gemfibrozil	249/121	-15
Ibuprofen	205/161	-10
Indomethacin	356/312	-15
D_{16}-Bisphenol A	241/142	-40
D_3-Clofibric acid	217/131	-15
D_6-Gemfibrozil	255/121	-15
D_3-Ibuprofen	208/164	-10
$^{13}C_3$-Ibuprofen (IS)	208/163	-10

3.8 Analytical Data Processing

Results from two bench-scale experiments, Experiment10 and 7 (referred herein as Expt. A and B, respectively) are discussed below to elucidate the procedure used for data analyses. The results (Tables 3.7 and 3.8) showed that the varying sample matrix for different experiments had an effect on chemical recoveries. The effect is particularly prominent for five of the 16 target chemicals including monensin, tetracycline, lincomycin, erythromycin, and tylosin.

Several observations can be made from the results presented for the two experiments. Comparing the results of recoveries for the five chemicals with deuterated surrogates, the data (before correction with surrogate) showed that the recoveries for these chemicals were affected by the experimental conditions (or the sample matrix). For example, the recoveries for the native carbamazepine and its deuterated form ranged between 77 – 93%, 59 – 77%, and 56 – 68% in the laboratory spikes, Experiment A, and Experiment B respectively. However, within the same experiment, the recoveries were more consistent and agreed within ± 10%, except for clofibric acid where the agreement was within ± 20%. After correcting for deuterated form surrogate recovery, the recoveries for native carbamazepine were much more consistent and ranged between 107 – 119% for the laboratory spikes and the controls from the two experiments. The results also showed that the variability between the two duplicates for all samples was typically within ±10%. This suggests that although the data for the remaining eleven chemicals cannot be corrected using surrogate recoveries to calculate absolute concentrations, it may still be possible to compare the relative levels of each chemical between the control and treatments within the same experimental run (or with the same background matrix).

Table 3.7 Analytical results for bench-scale Experiments A and B, PPCPs/EDCs ESI+

	Monensin	Tetracycline	Lincomycin	Erythromycin	Sulfamethazine	Sulfachloropyridazine	Sulfamethoxazole	Carbamazepine	Tylosin	Naproxen	Ibuprofen	Carbamazepine D10	Ibuprofen D3	Carbamazepine	Ibuprofen
QC samples at MOE															
Blank	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	86%	108%	ND	ND
Spike 1	84%	180%	117%	173%	103%	101%	107%	82%	102%	85%	102%	77%	100%	107%	101%
Spike 2	118%	195%	123%	198%	108%	104%	109%	93%	159%	89%	109%	78%	103%	119%	106%
Experiment A (Apr30/07); Conditions: pH=6.8, DOC=0.8mg/L, Ozone conc.=3.0mg/L, Contact time= 6 min., Temperature=23C															
Wash	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Blank	ND	ND	1%	ND	ND	ND	ND	ND	ND	ND	ND	65%	105%	ND	ND
Treated 1 Sample 1	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	82%	94%	0%	0%
Treated 1 Sample 2	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	82%	107%	0%	0%
Treated 2 Sample 1	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	75%	94%	0%	0%
Treated 2 Sample 2	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	90%	111%	0%	0%
Treated 3 Sample 1	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	83%	103%	0%	0%
Treated 3 Sample 2	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	82%	95%	0%	0%
Control Sample 1	130%	261%	318%	324%	112%	124%	134%	77%	281%	103%	102%	65%	95%	118%	107%
Control Sample 2	139%	253%	299%	272%	97%	110%	118%	72%	282%	97%	109%	59%	104%	121%	104%
Experiment B (May01/07); Conditions: pH=8.1, DOC=4.5mg/L, Ozone conc.=1.0mg/L, Contact time= 2 min., Temperature=23C															
Wash	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Blank	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	46%	88%	ND	ND
Treated 1 Sample 1	135%	62%	133%	94%	30%	39%	40%	21%	62%	34%	39%	46%	72%	46%	54%
Treated 1 Sample 2	188%	67%	141%	103%	31%	42%	45%	27%	70%	37%	55%	55%	85%	49%	64%
Treated 2 Sample 1	178%	82%	164%	89%	38%	47%	48%	26%	73%	41%	47%	53%	88%	49%	53%
Treated 2 Sample 2	227%	97%	155%	77%	37%	46%	45%	34%	83%	54%	55%	65%	97%	52%	57%
Treated 3 Sample 1	170%	87%	161%	54%	36%	37%	39%	27%	84%	43%	43%	65%	84%	50%	51%
Treated 3 Sample 2	189%	94%	166%	67%	37%	39%	43%	30%	75%	48%	59%	89%	94%	51%	63%
Control Sample 1	377%	235%	465%	67%	112%	91%	83%	68%	261%	100%	104%	57%	103%	119%	101%
Control Sample 2	307%	233%	476%	78%	122%	90%	86%	65%	238%	102%	96%	56%	96%	116%	99%

Remarks: The values shown in this table are expressed as a percentage of the expected response based on the initial spiked concentration (see Table 3.2).

Table 3.8 Analytical results for bench-scale Experiments A and B, PPCPs/EDCs ESI-

	Gemfibrozil	Ibuprofen	Bezafibrate	Indomethacin	Clofibric acid	Bishpenol A	Gemfibrozil D6	Ibuprofen D3	Clofibric acid D4	Bisphenol A D16	Gemfibrozil	Ibuprofen	Clofibric acid	Bishpenol A
QC samples at MOE														
Blank	ND	ND	ND	ND	ND	ND	118%	99%	97%	95%	ND	ND	ND	ND
Spike 1	123%	94%	98%	70%	96%	97%	122%	101%	95%	108%	100%	93%	102%	90%
Spike 2	120%	103%	90%	61%	89%	94%	112%	97%	81%	92%	107%	105%	110%	102%
Experiment A (Apr30/07); Conditions: pH=6.8, DOC=0.8mg/L, Ozone conc.=3.0mg/L, Contact time= 6 min., Temperature=23C														
Wash	ND	ND	ND	ND	ND	2%	ND	ND	ND	ND	ND	ND	ND	2%
Blank	ND	ND	ND	ND	ND	2%	99%	94%	112%	90%	ND	ND	ND	2%
Treated 1 Sample 1	0%	0%	0%	0%	0%	0%	126%	101%	99%	102%	0%	0%	0%	0%
Treated 1 Sample 2	0%	0%	0%	0%	0%	0%	121%	98%	101%	101%	0%	0%	0%	0%
Treated 2 Sample 1	0%	0%	0%	0%	0%	0%	111%	90%	93%	94%	0%	0%	0%	0%
Treated 2 Sample 2	0%	0%	0%	0%	0%	0%	132%	103%	96%	110%	0%	0%	0%	0%
Treated 3 Sample 1	0%	0%	0%	0%	0%	0%	115%	103%	98%	97%	0%	0%	0%	0%
Treated 3 Sample 2	0%	0%	0%	0%	0%	0%	119%	101%	105%	104%	0%	0%	0%	0%
Control Sample 1	105%	93%	92%	86%	151%	97%	95%	93%	116%	86%	110%	100%	130%	113%
Control Sample 2	106%	97%	95%	84%	147%	100%	97%	93%	112%	91%	109%	104%	131%	110%
Experiment B (May01/07); Conditions: pH=8.1, DOC=4.5mg/L, Ozone conc.=1.0mg/L, Contact time= 2 min., Temperature=23C														
Wash	ND	ND	ND	ND	ND	1%	ND	ND	ND	ND	ND	ND	ND	1%
Blank	ND	ND	ND	ND	ND	6%	61%	82%	70%	61%	ND	ND	ND	6%
Treated 1 Sample 1	33%	46%	32%	20%	83%	19%	63%	79%	94%	61%	52%	58%	89%	32%
Treated 1 Sample 2	35%	49%	32%	21%	80%	20%	67%	81%	94%	63%	52%	61%	85%	32%
Treated 2 Sample 1	34%	49%	30%	23%	79%	26%	63%	73%	88%	64%	54%	67%	90%	40%
Treated 2 Sample 2	41%	58%	38%	26%	86%	31%	75%	96%	95%	74%	54%	60%	91%	42%
Treated 3 Sample 1	36%	54%	35%	25%	89%	28%	67%	82%	96%	69%	53%	66%	93%	40%
Treated 3 Sample 2	35%	55%	35%	25%	87%	28%	66%	86%	98%	68%	54%	64%	89%	41%
Control Sample 1	67%	91%	54%	54%	118%	91%	66%	87%	85%	70%	102%	105%	139%	129%
Control Sample 2	69%	95%	54%	54%	121%	89%	65%	90%	86%	70%	106%	105%	142%	128%

Remarks: The values shown in this table are expressed as a percentage of the expected response based on the initial spiked concentration (see Table 3.2).

3.9 Statistical Analysis

Statistical analyses were conducted to determine factors having significant effects and possible interactions between them by using statistical analysis software Minitab14. According to Montgomery (2005), the effect of a factor is defined to be the change in response produced by a change in the level of the factor. The interaction occurs if the difference in response between the levels of one factor is not the same at all levels of the other factors. Significant factors and interactions can be well illustrated with normal probability plot of effects, main effects plot and interaction plot. These plots of 16 selected PPCPs/EDCs were constructed directly from Minitab and given in Chapter 4, Section 4.1 and Appendix B.

In the normal probability plot of the effects, points that do not fall near the line usually signal important effects. Important effects are larger and further from the fitted line than unimportant effects. Unimportant effects tend to be smaller and centered around zero. If there is no error term, Minitab uses Lenth's method (Lenth, 1989) to identify important effects. If there is an error term, Minitab uses the corresponding p-values shown in the Session window to identify important effects. This plot also distinguishes positive effects from negative effects. A main effects plot is a plot of the means at each level of a factor. A main effect occurs when the mean response changes across the levels of a factor. Main effects plots can be used to compare the relative strength of the effects across factors. A more extreme slope indicates a more significant effect on response. An interaction plot is a plot of means for each level of a factor with the level of a second factor held constant.

Once the significant factors have been determined, contribution table of each target PPCP/EDC was obtained based on analysis of variance (ANOVA) of these factors by using General Linear Model. The contribution percent of each factor to the variation in

removal efficiency (response) therefore was determined by dividing individual sequential sum of squares (Seq. SS) to total Seq. SS. The R-square (R^2) term indicated the percentage of variation in removal all these significant factors explain. The error term (i.e. combination of insignificant effects) was not included in the R-sq value.

Linear regression model obtained from Minitab was also used to fit ozone decay kinetics, the second phase (i.e. semi-log plot of ozone residual versus time). The slope of the linear regression model therefore was taken as the first-order ozone decay rate constant k. A confidence limit for this regression coefficient under certain conditions was constructed based on the method of least squares (Johnson, 2005), and compared with others to determine whether these ks are statistically significantly different based on 90% confidence limits ($\alpha = 0.1$). More details are given in Chapter 4, Section 4.3 and Appendix D.

CHAPTER 4: RESULTS AND DISCUSSION

4.1 Experimental Results and Statistical Analysis

The operating conditions for the 16 bench-scale experiments based on a 2-level fractional factorial design are presented in Table 4.1.

4.1 Five-Factor Fractional Factorial Design for Bench-Scale Experiments

Experiment	Variables				
	pH	DOC (mg/L)	O_3 Dose (mg/L)	Contact Time (min.)	Temp. (°C)
1	6.8	4.5	1	6	23
2	6.8	4.5	3	6	5
3	8.1	0.8	1	6	23
4	6.8	0.8	1	2	23
5	8.1	0.8	3	6	5
6	6.8	0.8	3	2	5
7	8.1	4.5	1	2	23
8	8.1	0.8	1	2	5
9	6.8	0.8	1	6	5
10	6.8	0.8	3	6	23
11	6.8	4.5	3	2	23
12	6.8	4.5	1	2	5
13	8.1	4.5	3	6	23
14	8.1	0.8	3	2	23
15	8.1	4.5	1	6	5
16	8.1	4.5	3	2	5

It is generally accepted that ozone reacts with compounds in aqueous solutions (e.g., water) by two types of reactions, i.e. direct reaction with molecular ozone and indirect reaction by hydroxyl radical species that form when ozone decomposes in water (Hoigné et al., 1976). The reactivity of different compounds upon direct ozone attack is well represented by their second-order rate constants (k_{O3}). The k_{O3} values available from the literature were presented in Table 4.2. Before discussing the results, compounds with k_{O3} values > 5×10^4 $M^{-1}s^{-1}$ (i. e., bisphenol A, carbamazepine, naproxen, sulfamethoxazole, tylosin, lincomycin and tetracycline) are considered fast reacting with ozone (Dodd et al., 2006) and were put in Group A (Table 4.3). Compounds with k_{O3} values < 5×10^4 $M^{-1}s^{-1}$ (i. e. bezafibrate, ibuprofen and clofibric acid) were put in Group B. The remaining compounds (i. e., sulfamethazine, sulfachloropyridazine, gemfibrozil, indomethacin and erythromycin and monensin) were put in either Group A or B (Table 4.3) based on the similarity of their behavior to the compounds already assigned to Group A or B.

A summary of the results obtained from 16 experiments is presented in Table 4.4 on the basis of different groups. The individual analytical results for the 16 selected PPCPs/EDCs for all the 16 experiments are presented in Appendix A. The results show that >90% transformation of all chemicals (Groups A and B) were achieved under the conditions of higher O_3 dose (3.0 mg/L) and lower DOC content (0.8 mg/L) (Expts. 5, 6, 10, and 14), whereas lower transformation (< 70% for Group A and < 40 % for Group B) were observed at the lower ozone dose (1.0 mg/L) and higher DOC content (4.5 mg/L) (Expts. 1, 7, 12, 15).

Table 4.2 Available second-order rate constants for the selected PPCPs/EDCs

Compounds	**pKa**	**k_{O3}, at 20 °C, ($M^{-1}s^{-1}$)**	**k_{OH}, 25 °C, pH=7, ($M^{-1}s^{-1}$)**	**Reference**
Bisphenol A		$(1\text{-}10) \times 10^6$		Huber et al., 2003
Carbamazepine		$\sim 3\times 10^5$, pH=7	$(8.8\pm1.2)\times10^9$	
Naproxen	4.5	$2\text{x}10^5$	$(9.6\pm0.5)\times10^9$	
Sulfamethoxazole	1.6, 5.7	$\sim 2.5\times 10^6$, pH=7	$(5.5\pm0.7)\times10^9$	
Tylosin	7.7	5.1×10^5, pH=7 1.4×10^6, pH=7.7		Dodd et al., 2006
Lincomycin	7.8	6.7×10^5, pH=7 1.4×10^6, pH=7.7		
Tetracycline	3.3, 7.7, 9.7	1.9×10^6, pH=7 3.2×10^6, pH=7.7		
Sulfamethazine	2.6, 8		5.0×10^9	Ikehata et al., 2006
Sulfachlorpyridazine	2, 5.9		4.4×10^9	
Bezafibrate	3.6	590 ± 50, pH=6	$(7.4\pm1.2)\times10^9$	Huber et al., 2003
Ibuprofen	4.9	9.6 ± 1, pH=6	$(7.4\pm1.2)\times10^9$	
Clofibric acid		<20	$(4.7\pm0.3)\times10^9$	

Table 4.3 Compound grouping

Group A	**Group B**
Bisphenol A	Ibuprofen
Lincomycin	Clofibric acid
Tylosin	Bezafibrate
Tetracycline	Monensin
Naproxen	
Carbamazepine	
Sulfamethoxazole	
Sulfamethazine	
Sulfachloropyridazine	
Erythromycin	
Indomethacin	
Gemfibrozil	

Table 4.4 Summary of experimental results

O_3 dose (mg/L)	DOC (mg/L)	Experiment No.	Transformation efficiency	O_3 residual (mg/L)	
				2 min.	6 min.
3.0	0.8	5, 6, 10, 14	Both Group A & B: > 90%	1.4 – 2.3	0.82 – 1.5
1.0	0.8	3, 4, 8, 9	Group A: > 90% Group B: > 90% in exp. 3,4,9 70 - 90% in exp. 8	0.07 – 0.38	0.07 – 0.25
3.0	4.5	2, 11, 13, 16	Group A: >90% Group B: 80 - 90%	0.09 – 0.11	0.08 – 0.10
1.0	4.5	1, 7, 12, 15	Group A: 50 - 70% Group B: 30 - 40%	0.07 – 0.09	0.07 – 0.08

To identify the relative importance of each process parameter, statistical analysis was performed for each target compound by using the statistical software MINITAB 14 at 90% confidence level ($\alpha = 0.1$). Results of the statistical analysis are presented in Figures 4.1 – 4.3 for bisphenol A as an example for Group A compounds and in Figures 4.4 – 4.6 for ibuprofen as an example for Group B compounds. Due to analytical problems with clofibric acid for one experiment (Expt. 1) and erythromycin for two experiments (Expts. 7 and 12), the statistical analysis could not be conducted for these two chemicals. For the remaining 13 chemicals, the results are included in Appendix B.

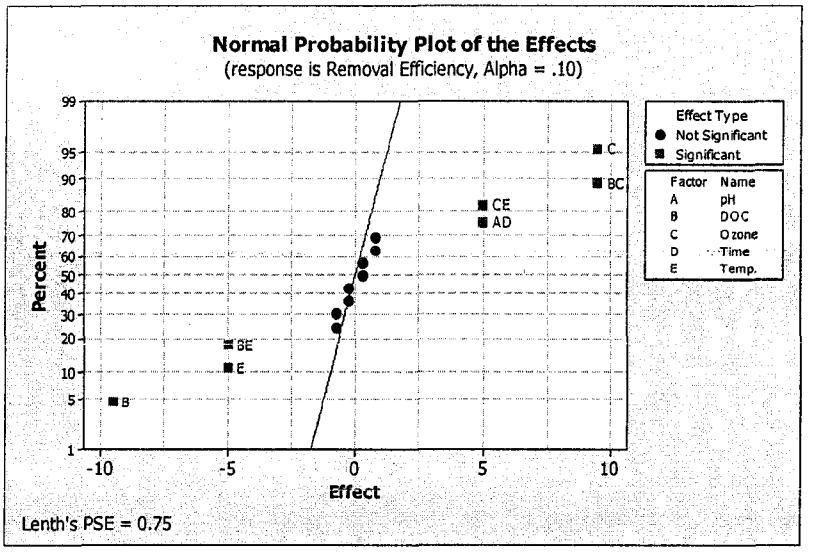


Figure 4.1 Normal probability plot for the effect of process variables on the oxidation of bisphenol A.

Figure 4.1 is the normal probability plot for bisphenol A (Group A). The results show that from the five variables (designated as A = pH, B = DOC content, C = ozone dose, D = contact time, and E = temperature) and all possible two-way interactions, the effects of DOC content, ozone dose, temperature and their two-way interactions were significant for the oxidation of bisphenol A at 90% confidence level. The effect is positive for factor C (ozone dose) and its interactions with both factors B (DOC content) and E (temperature) (i.e., transformation increases with increase in value). In addition, 2-way interaction between factors A (pH) and D (contact time) also has a significantly positive effect. However this effect may actually be due to the 3-way interaction of DOC content, ozone dose, and temperature which confounds with the 2-way interaction of pH and contact time in the statistical analysis of the 2-level fractional factorial design (Box et al., 1978), which will be discussed later. Figure 4.1 further shows that the effects of factors B (DOC content) and E (temperature) and their two-way interaction B*E exert significantly negative impacts, i.e., transformation decreases with increase in value. The main effects

of the variables (DOC content, ozone dose, and temperature) are plotted in Figure 4.2, and their interactions effects are plotted in Figure 4.3. The statistical results obtained were similar for the other ten Group A compounds (Appendix B) except that temperature (and its interactions) were statistically significant for seven of the ten compounds.

The relative significance of the effects was determined by ANOVA (analysis of variance) using Minitab, and the results are presented in Table 4.5. The results show that ozone dose, DOC content and their interaction were the dominant factors affecting the transformation of bisphenol A in the current study, and accounted for about 73% of the observed variability. Temperature and its interactions with DOC content and ozone dose accounted for about 20% of the change in transformation efficiency.

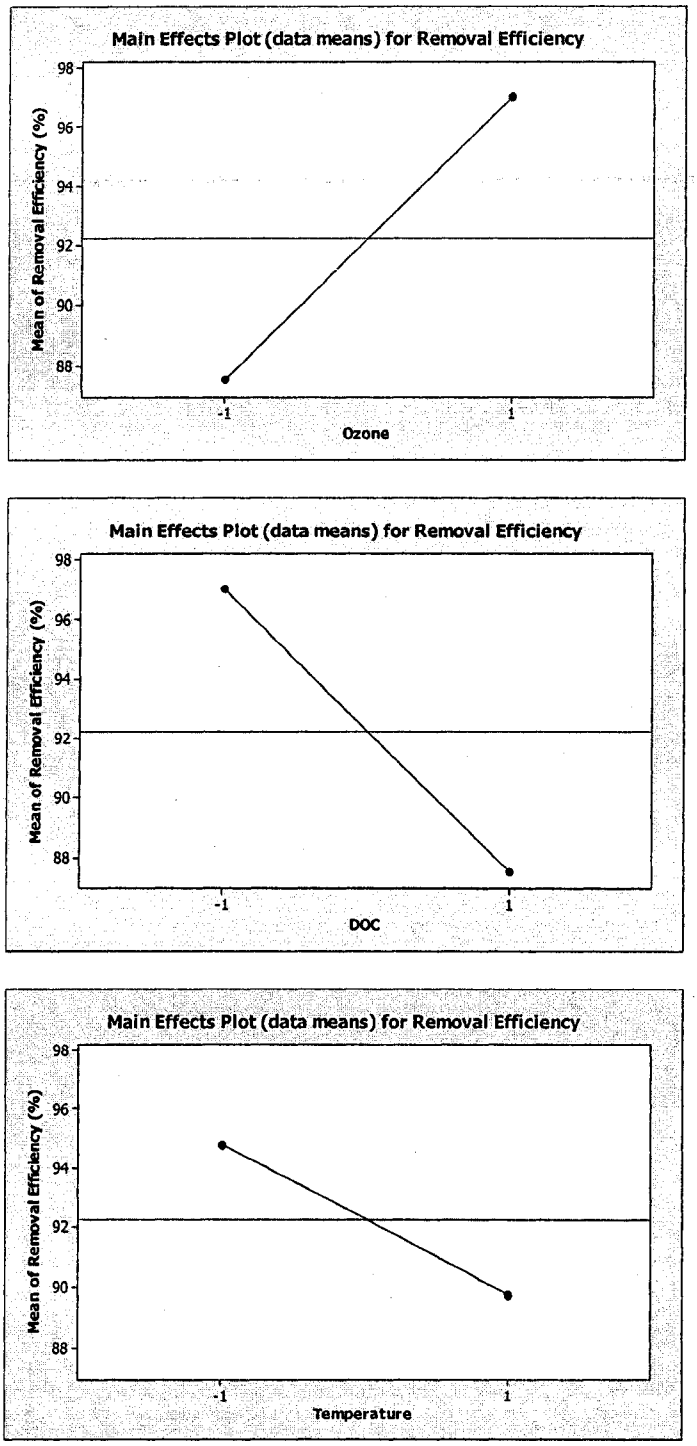


Figure 4.2 The effect of DOC content, ozone dose, and temperature on the oxidation of bisphenol A ($\alpha = 0.1$). For each factor, lower level = -1 and higher level = 1.

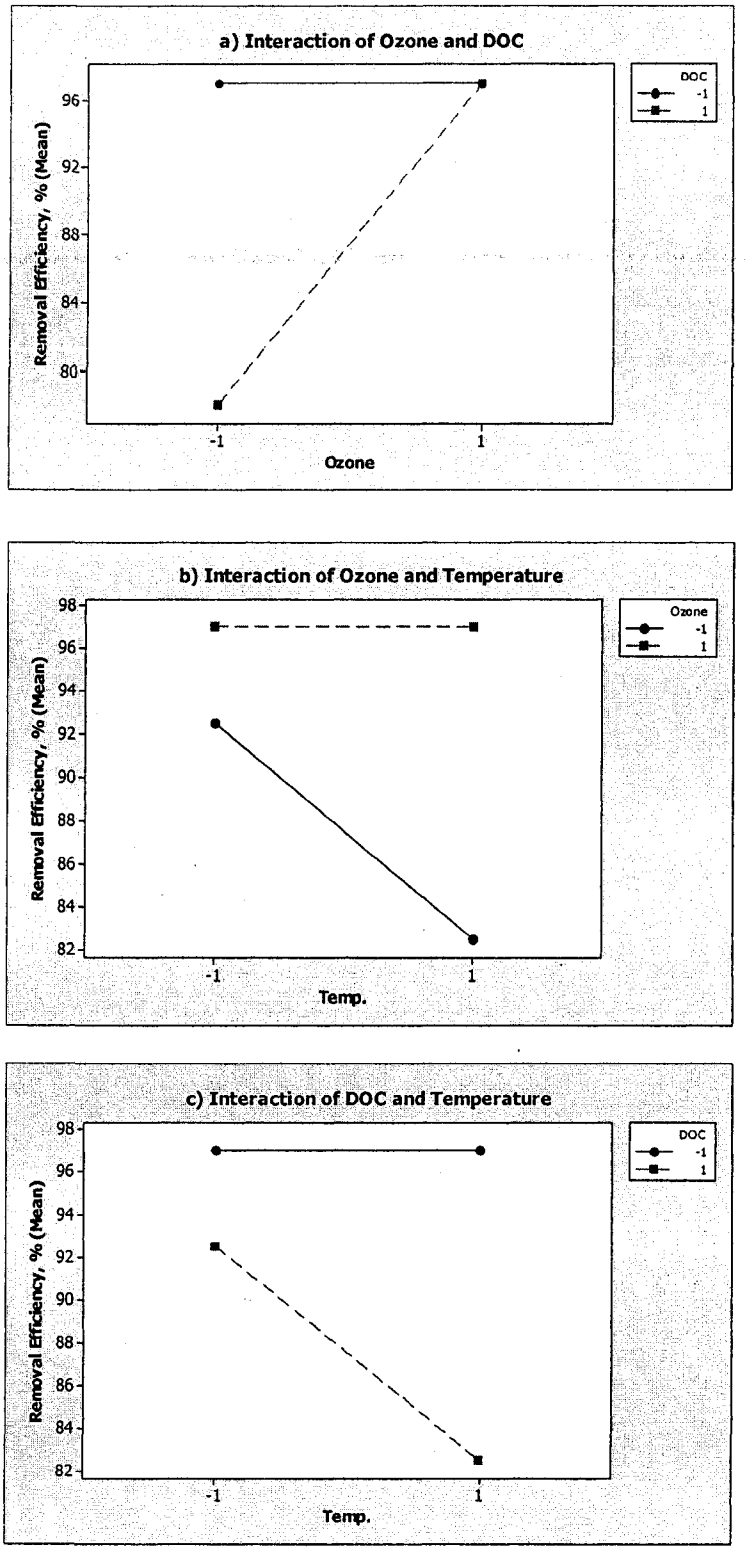


Figure 4.3 Plots for significant 2-way interactions between DOC content, ozone dose, and temperature for bisphenol A.

Table 4.5 Contributions of significant factors towards oxidation of bisphenol A at 90% confidence level based on ANOVA analysis

Source	DF [a]	Seq SS [b]	Contribution (%)
B	1	361.0	24.2 [c]
C	1	361.0	24.2
E	1	100.0	6.7
B*C	1	361.0	24.2
A*D	1	100.0	6.7
B*E	1	100.0	6.7
C*E	1	100.0	6.7
Error	8	10.0	0.6
Total	15	1493.0	
R-Square (R^2) =99.4 %			

A- pH; B- DOC; C- O_3 dose; D- contact time; E- temperature; B*C- interaction between B and C

[a] DF-degree of freedom; [b] Seq SS- sequential sum of squares

[c] Contribution 24.2%=361.0/1493.0

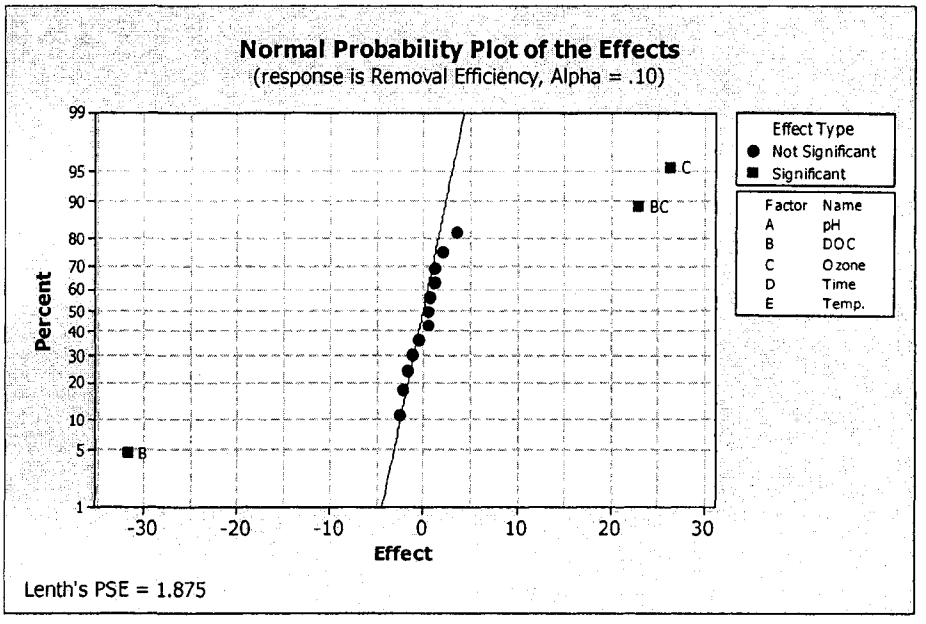


Figure 4.4 Normal probability plot for the effect of process variables on the oxidation of ibuprofen.

Figure 4.4 is the normal probability plot for ibuprofen (Group B). The results show that from the five variables (designated as A = pH, B = DOC content, C = ozone dose, D = contact time, and E = temperature) and all possible two-way interactions, the effects of DOC content, ozone dose, and their two-way interactions were significant for the oxidation of ibuprofen at 90% confidence level. Unlike bisphenol A, temperature or its interactions were not statistically significant for the transformation of ibuprofen. The effect is positive for factor C (ozone dose) and its interactions with factor B (DOC content) (i.e. transformation increases with increase in value). Figure 4.4 further shows that factor B (DOC content) exerts a significant negative impact, i.e., transformation decreases with increase in value. The main effects of the variables (DOC content and ozone dose, and temperature) are plotted in Figure 4.5, and their interactions effects are plotted in Figure 4.6. The statistical results obtained were similar for the other two compounds in Group B (Appendix B).

The relative significance of the effects was determined by ANOVA (analysis of variance) using Minitab, and the results are presented in Table 4.6. The results show that ozone dose, DOC content and their interaction are the dominant factors affecting the oxidation of ibuprofen in the current study, and account for about 98% of the observed variability in transformation efficiency.

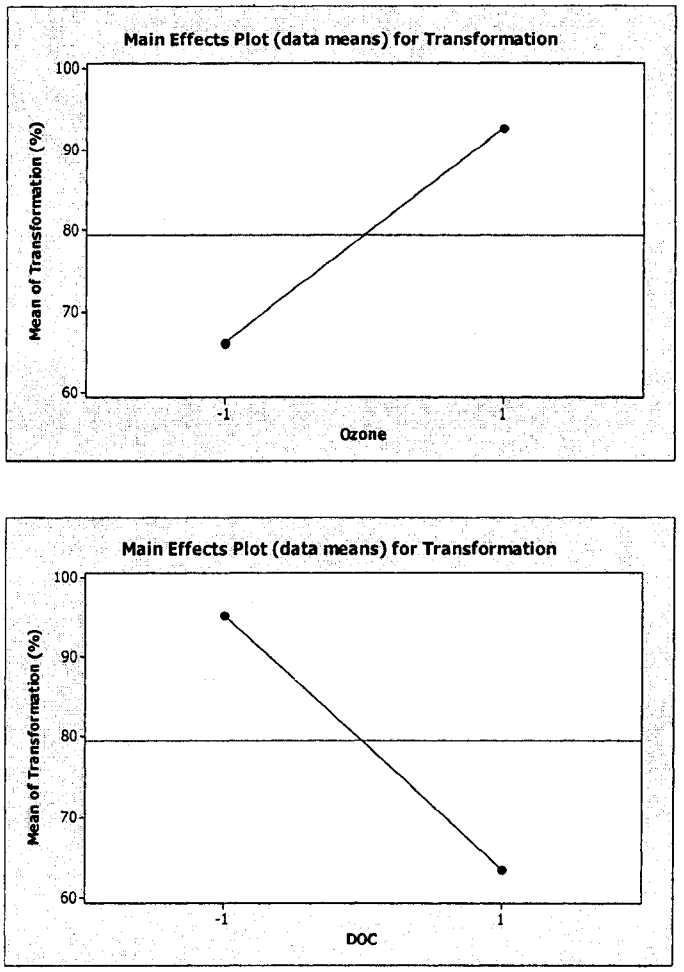


Figure 4.5 The effect of DOC content and ozone dose on the oxidation of ibuprofen ($\alpha = 0.1$). For each factor, lower level = -1 and higher level = 1.

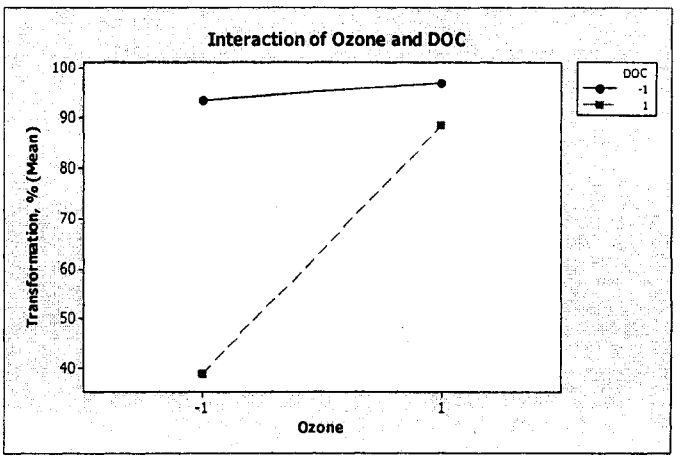


Figure 4.6 Plots for significant 2-way interactions between DOC content and ozone dose for ibuprofen.

Table 4.6 Contributions of significant factors towards oxidation of ibuprofen at 90% confidence level based on ANOVA analysis

Source	DF [a]	Seq SS [b]	Contribution (%)
B	1	4032.3	44.3 [c]
C	1	2809.0	30.9
B*C	1	2116.0	23.2
Error	12	146.5	1.6
Total	15	9103.7	
R-Square (R^2) = 98.4 %			

B- DOC; C- O_3 dose; B*C- interaction between B and C
[a] DF-degree of freedom; [b] Seq SS- sequential sum of squares
[c] Contribution 44.3%=4032.3/9103.7

Table 4.7 Summary of contributions of significant factors affecting the oxidation of target chemicals studied at 90% confidence level based on ANOVA analysis

Compound	Contribution (%)							
	C	B	B*C	E	C*E	B*E	A*D	Error
Bisphenol A	24.2	24.2	24.2	6.7	6.7	6.7	6.7	0.6
Sulfamethazine	29.9	29.9	29.9	2.5	2.5	2.5	2.5	0.3
Sulfamethoxazole	31.6	31.6	31.6	1.2	1.2	1.2	1.2	0.4
Sulfachloropyridazine	29.2	29.2	29.2	2.9	2.9	2.9	2.9	1.0
Lincomycin	20.3	20.3	20.3	9.0	9.0	9.0	9.0	3.1
Indomethacin	23.1	23.1	23.1	7.4	7.4	7.4	7.4	1.1
Naproxen	31.1	31.1	31.1	1.5	1.5	1.5	1.5	0.7
Gemfibrozil	33.0	33.0	33.0	-	-	-	-	1.0
Carbamazepine	29.1	29.1	29.1	-	-	-	-	12.7
Tylosin	31.8	32.9	30.7	-	-	-	-	4.6
Tetracycline*	27.7	42.3	24.2	-	-	-	-	5.8
Ibuprofen	30.9	44.3	23.2	-	-	-	-	1.6
Bezafibrate	31.7	42.1	22.9	-	-	-	-	3.3
Monensin	34.2	40.3	18.8	-	-	-	-	6.6

A- pH; B- DOC; C- O_3 dose; D- Contact time; E- Temperature
* Contribution of pH =2.4%

A summary of the contributions of significant factors for all the chemicals (excluding clofibric acid and erythromycin) based on ANOVA analysis at 90 % confidence level is presented in Table 4.7.

The table shows that the relative effects of the process variables studied on the oxidation of the target compounds within each group as well as between Groups A and B were similar. As observed for bisphenol A and discussed earlier, the table also shows that DOC content, ozone dose and their interaction had the most significant impacts on the transformation efficiencies of the other compounds in Group A, and accounted for 60 to 95% of the observed variability in their transformation. Temperature was observed to be significant for the transformation of seven of eleven Group A chemicals including bisphenol A, sulfamethazine, sulfamethoxazole, sulfachloropyridazine, lincomycin, naproxen, and indomethacin. Furthermore, the interactions of temperature with DOC content and ozone dose accounted for 3.6 to 27% of the observed variability in transformation. The relatively small (1.2 to 9%) but significant effect of the 2-way interaction of pH and contact time on the transformation of these same seven Group A chemicals may actually be due to the 3-way interaction of DOC content, ozone dose, and temperature which confounds with the 2-way interaction of pH (factor A) and contact time (factor D) in the statistical analysis of the 2-level fractional factorial design (Box et al., 1978). This argument is further strengthened by the fact that the effect of pH and contact time interaction was only significant for the chemicals for which temperature and its interactions with DOC content and ozone dose were significant. The pH (factor A) was found to be significant only for tetracycline. However, the estimated effect of the factor on its transformation is small (<3%). Similarly, for compounds of Group B including ibuprofen, bezafibrate, and monensin, DOC content, ozone dose and their

interaction had the most significant impact, accounting for 93 to 98% of the observed variability in the transformation. Temperature and its interactions were not significant for any of the Group B compounds.

The interaction plots for both Groups A and B compounds, as shown in Figure 4.3 for bisphenol A, Figure 4.6 for ibuprofen and included in Appendix B for the remaining, are interesting. The results show that although both DOC content and ozone dose had a major influence on the transformation of the compounds (Table 4.7), the effect was most significant when the DOC content was high (4.5 mg/L) and the ozone dose was low (1.0 mg/L), as is evident from Figures 4.7 - 4.8 for Group A compounds and Figures 4.9 – 4.10 for Group B compounds.

Figure 4.7 shows that the transformations of all compounds in Group A were >97% with one exception at an ozone dose of 3.0 mg/L at both low and high DOC contents. The exception was tetracycline at a DOC of 4.5 mg/L, which was 92%. At the lower ozone dose of 1.0 mg/L (Figure 4.8), the transformation was >97% at the lower DOC content (0.8 mg/L) but reduced to between 50 to 80% at the higher DOC level (4.5 mg/L).

For compounds of Group B, similar effects were observed, as shown in Figures 4.9 and 4.10. At an ozone dose of 3.0 mg/L, the transformations of all compounds of Group B were close to 100% at lower DOC loading of 0.8 mg/L and >80% at higher DOC loading of 4.5 mg/L as shown in Figure 4.9. At the lower ozone dose of 1.0 mg/L (Figure 4.10), the transformation was >90% at the lower DOC content of 0.8 mg/L, but reduced to between 30 to 40% at the higher DOC level of 4.5 mg/L.

The effect of temperature on the transformation of the compounds of Group A was similarly influenced by the DOC content and ozone dose, as shown in Figures 4.11 and 4.12. Figure 4.11 shows that the transformation of Group A compounds exceeded 95% at

both low (4 °C) and high (23 °C) temperatures and both low and high DOC contents when the ozone dose was high (3.0 mg/L), and also at the low ozone dose of 1.0 mg/L when the DOC content was low (0.8 mg/L). At both high DOC content (4.5 mg/L) and low ozone dose (1.0 mg/L), increase in temperature significantly reduced the transformation efficiency for eight of the eleven Group A compounds statistically analyzed, the reductions were estimated to be between 6 – 28%. For tetracycline, the effect was opposite to that observed for the other compounds but was not statistically significant. The effect of temperature was not statistically significant for any of the compounds of Group B.

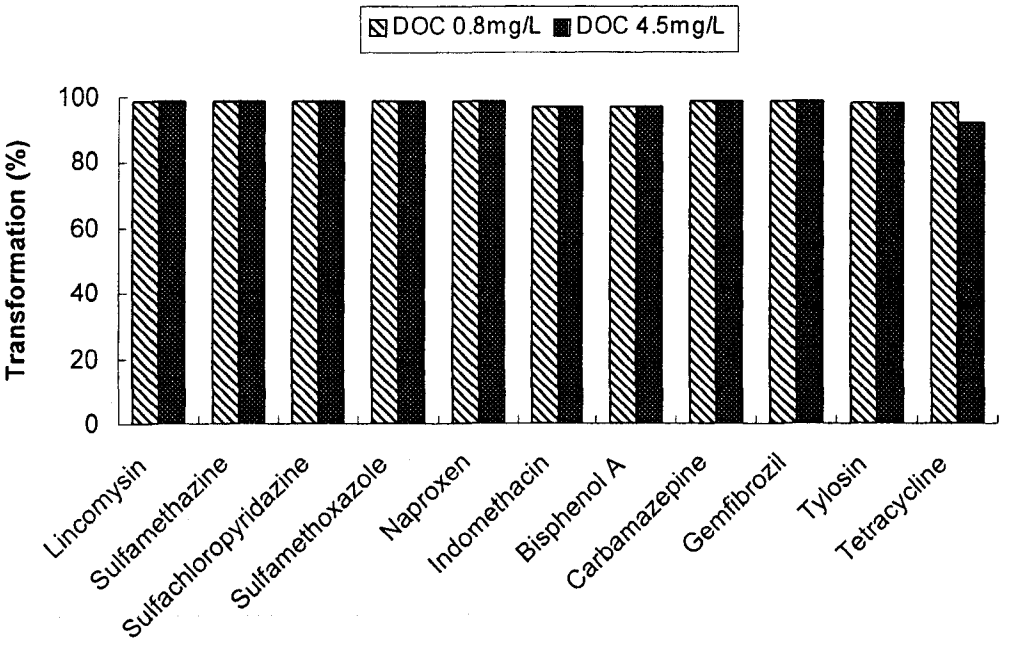


Figure 4.7 Effect of DOC on transformation efficiency for compounds in Group A (O_3=3.0 mg/L).

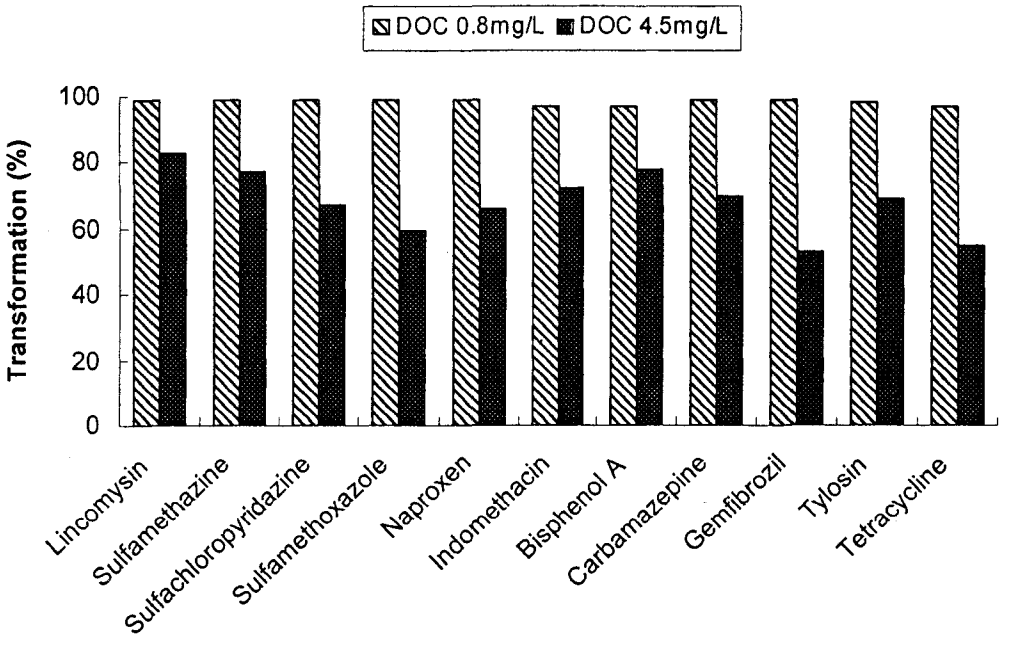


Figure 4.8 Effect of DOC on transformation efficiency for compounds in Group A (O_3=1.0 mg/L).

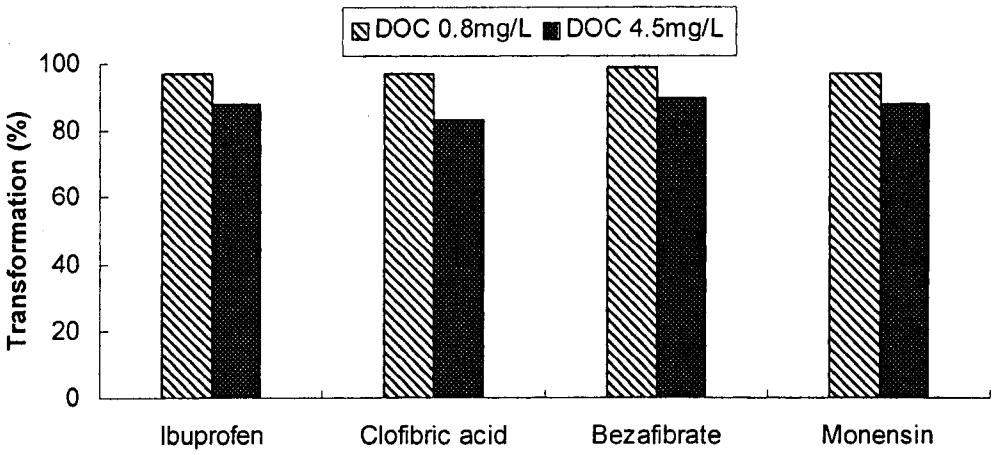


Figure 4.9 Effect of DOC on transformation efficiency for compounds in group B (O_3=3.0 mg/L).

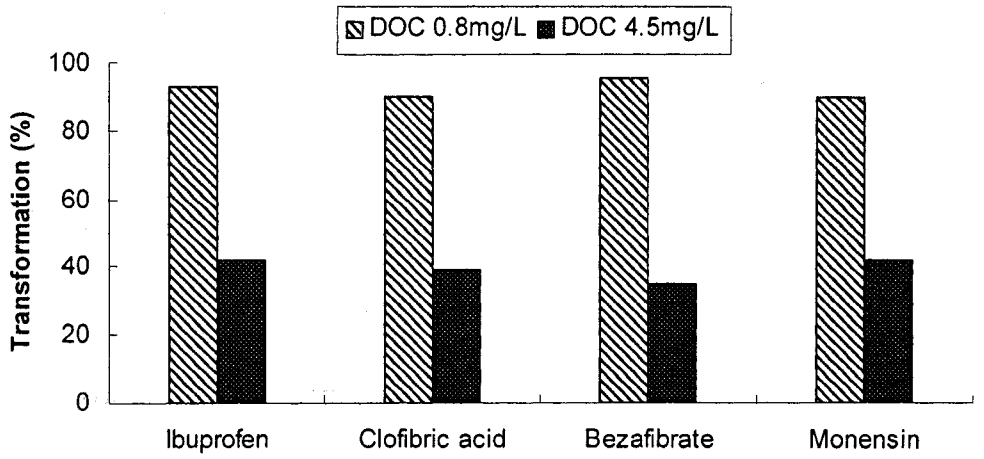


Figure 4.10 Effect of DOC on transformation efficiency for compounds in group B (O_3=1.0 mg/L).

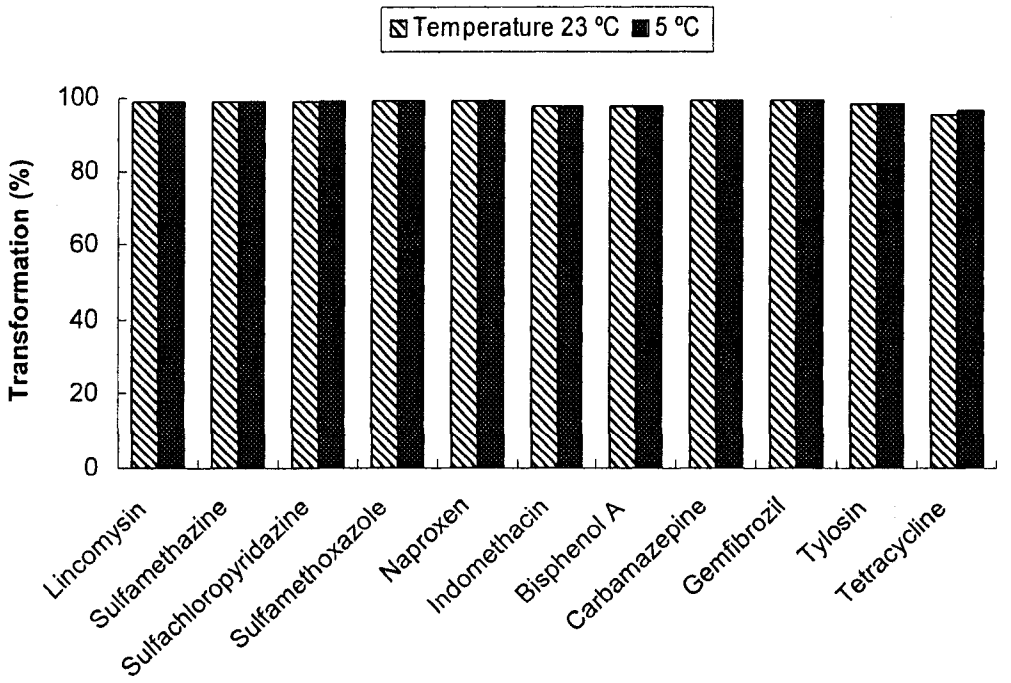


Figure 4.11 Effect of temperature on the transformation of Group A compounds (excluding experiments with both high DOC content and low ozone dose).

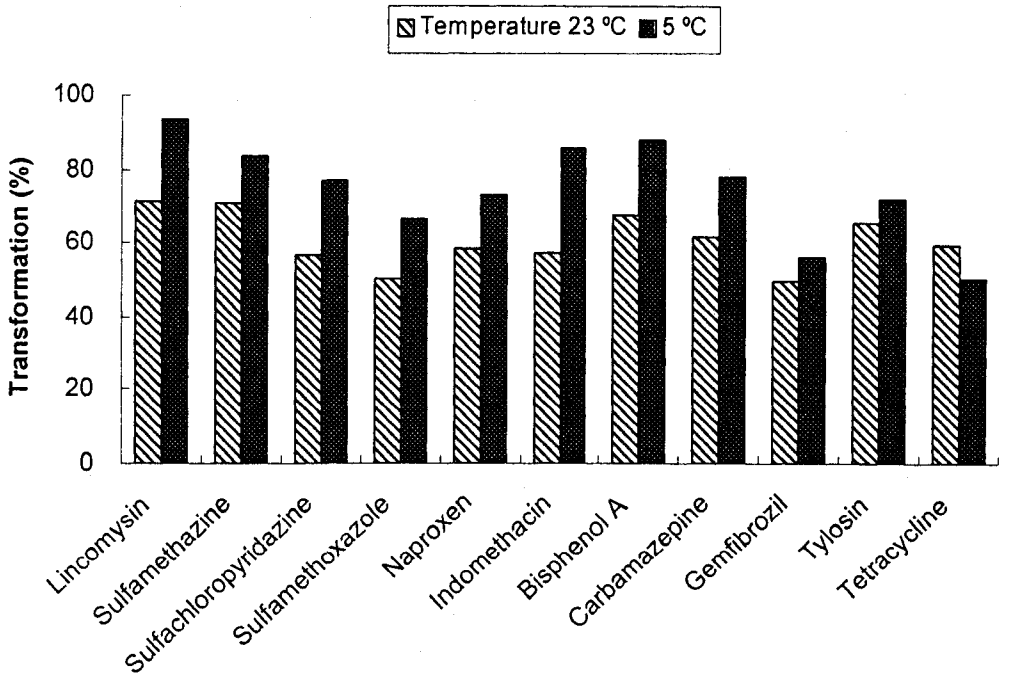


Figure 4.12 Effect of temperature on the transformation of Group A compounds at both high DOC content (4.5 mg/L) and low ozone level (1.0 mg/L).

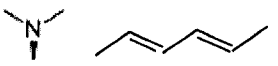
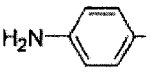
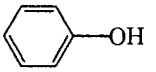
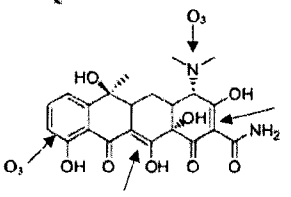
4.2 Discussion

The experimental results demonstrate that ozone oxidation is an effective process for the transformation of all the 16 PPCPs/EDCs included in the current study. Transformation exceeding 90% was observed for all the compounds in Group A in 12 of the 16 experiments, with lower transformation efficiencies of 50 – 70% only under conditions of high DOC and low ozone dose (Table 4.4). The results observed are consistent with those observed in the literature where ozone alone was used. For example, Synder et al. (2007) reported >90% transformation for carbamazepine, erythromycin, gemfibrozil, and naproxen from surface water from three natural sources, at ozone dose of 2.5 – 7 mg/L and a contact time of 5 minutes. Adams et al. (2002) reported rapid and efficient conversions (>95%) of sulfachlorpyridazine and sulfamethazine by ozonation in pre-filtered Missouri River water samples in < 2 minutes with an applied ozone dose of 0.3 mg/L. Several of the compounds in this Group including bisphenol A, carbamazepine, naproxen, sulfamethoxazole, tylosin, lincomycin and tetracycline have reported k_{O3} larger than 5×10^4 $M^{-1}s^{-1}$ (Table 4.2). Their high activities with ozone were attributed to the presence of an amino group, an activated aromatic system or a double bond. The presence of sulphidic groups also results in a fast reaction with ozone (von Gunten, 2003a). The proposed active sites of these compounds upon ozone attack are given in Table 4.8. Their chemical structures and schematic illustration of ozone attack are given in Appendix C.

Group B compounds were more sensitive to the variables studied in the current study than Group A compounds. Transformation exceeding 90% was observed in seven out of eight experiments at low DOC concentration with both low and high ozone doses (Table 4.4). Oxidation was affected at high DOC content, particularly at the low ozone dose of 1 mg/L

when transformation was reduced to between 30 – 40% for all compounds in the Group (Table 4.4). With reported $k_{O3} < 10^3$ $M^{-1}s^{-1}$, Group B compounds are regarded as medium or slow-reacting with molecular ozone, and their relatively lower reactivity are considered due to lack of active functional groups (e.g., monensin), or only possessing weakly activated aromatic rings (e.g., ibuprofen), or having electron-withdrawing substituent (e.g., clofibric acid) (see Appendix C).

Table 4.8 Suggested active sites upon ozone attack for group A compounds (adapted from Huber et al., 2003; Dodd et al., 2006; Ikehata et al., 2006)

Group A compounds	Suggested reactive site/group	Diagram
Erythromycin Lincomycin Tylosin	Tertiary amine Tertiary amine & sulfur atom Tertiary amine and conjugated diene	
Sulfamethazine Sulfamethoxazole Sulfachloropyridazine	Aromatic amine Aromatic amine Aromatic amine	
Bisphenol A	Phenol	
Carbamazepine	Non-aromatic C=C double bond	
Tetracycline	Phenolic structure, olefinic bonds and tertiary amine	
Naproxen Gemfibrozil Indomethacin	Oxy-activated aromatic ring	see Appendix C

4.2.1 Effect of ozone dose and DOC - Group A Compounds

Due to their high reactivity with ozone, direct oxidation with molecular ozone is expected to be the main oxidation pathway for the transformation of Group A compounds in typical drinking water sources ozonation process. Due to a strong interaction between DOC

content and ozone, some studies have used specific ozone consumption or DOC-normalised O_3 dose (mg O_3/mg DOC) to evaluate oxidation efficiency (Bahr et al., 2007; Buffle et al., 2006; Vieno et al., 2007). Zwiener and Frimmel (2000) also concluded that for a sufficient degradation of the pharmaceuticals (>90%) the ozone concentration should equal to DOC value, but no source water and the compounds studied were specified. Therefore, this ratio is expected to change due to the difference in the nature of NOM from one source water to another. Since ozone exposure, expressed as a product of concentration and contact time or CT value with units of mg/L.min, is expected to be directly correlated to oxidation by ozone and is also the parameter used for controlling the ozonation process, the relationship between ozone exposure and transformation of Group A compounds was examined in the current study. Ozone exposure (CT values) were calculated for the 16 experiments, and the transformation efficiencies observed for all the Group A compounds have been plotted against the calculated exposure values at 5 and 23 ^{o}C in Figures 4.13 (a) and 4.13 (b) respectively. The figures show that at both the low and high temperatures, transformation efficiencies for all Group A compounds exceeded 97% when the ozone exposure values were > 1.0 mg/L.min. In experiments with high DOC content and low ozone dose, ozone exposure values were <1.0 mg/L.min, and the transformation efficiencies were reduced to between 50 – 70%.

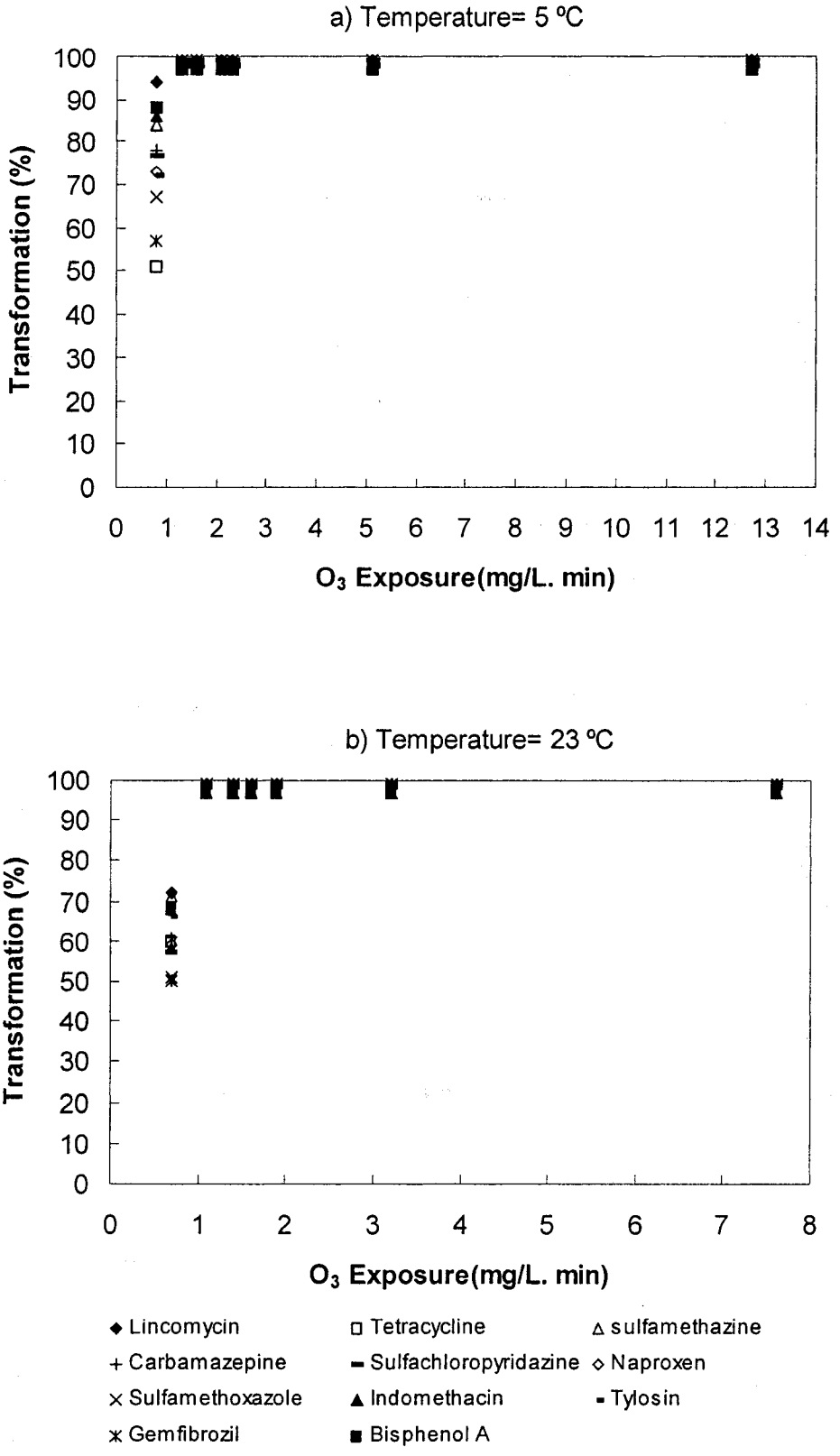


Figure 4.13 Transformation of Group A compounds as function of ozone exposure, a) T= 5 °C; b) T= 23 °C.

4.2.2 Effect of ozone dose and DOC- Group B Compounds

Although excellent transformation efficiencies for Group B compounds were observed in the present study, the results need to be interpreted with caution. Group A compounds have high reaction rate constants with ozone and based on the results of this and previous studies, their transformation is expected to be relatively insensitive to water matrix properties provided an adequate ozone exposure is ensured. Group B compounds with low reactivity with ozone are dependent on the secondary oxidant hydroxyl radicals (•OH) for their transformation. Hydroxyl radicals are the strongest oxidants formed in water during ozone decomposition. Unlike ozone that is a very selective oxidant, •OH radicals are nonselective and react with a large array of both inorganic and organic compounds with rate constants ranging between 10^8 to 10^{10} $M^{-1}s^{-1}$ (Haag and Yao, 1993). However the concentration of •OH radicals, and thus the resulting exposure and transformation of Group B compounds, is strongly influenced by its reactivity with various components of the water matrix, for example, organic matter, alkalinity, temperature and pH (von Gunten, 2003a). Amongst them, organic matter has the greatest influence as specific organic compounds can participate in the initiation, promotion or inhibition reactions during ozone decomposition, which significantly influence •OH exposure. In addition, certain organic compounds can directly react with ozone without the formation of •OH (i.e., non-initiation). Therefore the extent and nature of the impact of organic matter on •OH radical concentration and exposure depends on both its type and content. Detailed discussions of these factors affecting ozone decomposition can be found in Chapter 2, Section 2.2.

Table 4.9 Comparison of selected PPCPs/EDCs ozonation (in DW sources) from literature and current study

Compounds	Water Description	O_3 dose (mg/L)	DOC (mg/L)	Oxidation (%)	Ref.
Ibuprofen	Pure water	1.0	0	12	2
	3 DW supplies & 1 MW	2.5 - 4.0	3.0 - 4.0	80 (avg.)	1
	Lake water; well water	2.0	0.8 - 3.7	40 - 77	3
	Simulated water	1.0 - 3.0	0.8, 4.5	31 - >97	*
Bezafibrate	Flocculated natural water	1.5	1.3	~ 50	4
	Flocculated natural water	3.0	1.3	~ 80	4
	Lake water	0.1 - 2.0	1.3, 3.7	<5 - >97	3
	Simulated water	1.0, 3.0	0.8, 4.5	37 - >99	*
Clofibric Acid	Pure water	1.0	0	8	2
	Simulated water	1.2	2.4	57±17	4
	Flocculated natural water	2.5 ~ 3.0	1.3	<40	4
	Simulated water	1.0, 3.0	0.8, 4.5	35 - >97	*
Monensin	Simulated water	1.0, 3.0	0.8, 4.5	28 - >97	*

Note: DW- drinking water; MW- model water; Ref: 1.Westerhoff et al., 2005; 2. Zwiener and Frimmel, 2000; 3. Huber et al., 2003; 4. Ternes et al., 2002; * this study

Due to the strong influence of •OH exposure on the transformation of Group B compounds, their oxidation is expected to be strongly influenced by the characteristics of the source water, especially the content and nature of DOC. Relating the transformation to ozone exposure alone would thus be misleading. Zwiener and Frimmel (2000) observed only 8% and 12 % transformation for clofibric acid and ibuprofen in pure water with ozone dosage of 1.0 mg/L and contact time of 10 minutes (Table 4.9). Although ozone exposure is significant in this case, ozone decomposition is initiated only through hydroxide ions (OH^-) in pure water and •OH exposure is expected to be very low. The results obtained in the current study are compared against a few other studies reported in

literature in Table 4.9. No studies reporting the transformation of monensin were identified.

In general, the results show that the transformations of Group B compounds were accelerated in the presence of organic matter. For ibuprofen, bezafibrate, and chlorfibric acid, the range of transformation efficiencies observed in the current study largely overlapped that reported in the literature. The highest transformation efficiency observed in the current study is somewhat higher than previously reported. However, the reported efficiencies vary considerably, which might be due to the influence of the content and nature of organic matter.

To determine the expected transformation of any micropollutant due to •OH exposure, Elovitz and von Gunten (1999) introduced the concept of R_{ct}, which was defined as the ratio of •OH exposure to ozone exposure. R_{ct} values for a given water matrix and ozonation condition can be experimentally determined from the experimentally measured decrease in concentration of an ozone-resistant compound (e.g. *p*-chlorobenzoic acid, ibuprofen) and ozone (Haag and Yao, 1993; Elovitz and von Gunten, 1999). Knowing the second-order rate constant for the reaction of a micropollutant P with •OH (k_{OH}) and ozone (k_{O3}) , the expected transformation of P due to both •OH and ozone exposures over a given time "t" can be estimated using the ozone exposure by the following equation (Acero and von Gunten, 2001):

$$\ln[C(t)/C(0)] = -(\int[O_3]dt)(k_{OH}R_{ct} + k_{O3}) \qquad (4.1)$$

It has been shown that R_{ct} values are very high and variable during the initial ozonation period. During the first 200 s R_{ct} values were observed to decrease by two orders of magnitude from 2×10^{-6} to 3×10^{-8} for Lake Zurich water studied by Buffle et al. (2006b).

These values are comparable to or higher than those observed with ozone-hydrogen peroxide advanced oxidation process (Acero and von Gunten, 2001). R_{ct} values then became more or less constant in the minute range (Elovitz and von Gunten, 1999; Elovitz et al., 2000). R_{ct} values during the second (constant) phase in natural waters have been reported to be in range of 10^{-8} or lower, which could be enhanced with the addition of H_2O_2 (Acero and von Gunten, 2001).

For an ozone resistant compound such as ibuprofen (low k_{O3}), Equation (4.1) reduces to the following:

$$\ln[C_{IBU}(t)/C_{IBU}(0)] = -(\int[O_3]dt)(k_{OH,IBU}R_{ct}) \qquad (4.2)$$

Using Equation (4.2), ozone exposure values calculated for the eight experiments with ozone contact time of 2 min, and measured transformation efficiencies for ibuprofen in these experiments, average R_{ct} values during the first 2 min were calculated as also shown in Table 4.10.

Table 4.10 Summary of O_3-exposure, •OH-exposure and R_{ct} value in current study

Exp.	Experimental Conditions	O_3 exposure (mole/L. sec)/ (mg/L.min)	OH exposure (mole/L. sec)	R_{ct}
7	8.1; 4.5 mg/L; 1 mg/L; 2 min; 23 °C	8.8×10^{-4}/0.7	7.5×10^{-11}	8.5×10^{-8}
12	6.8; 4.5 mg/L; 1 mg/L; 2 min; 5 °C	9.6×10^{-4}/0.8	5.9×10^{-11}	6.1×10^{-8}
4	6.8; 0.8 mg/L; 1 mg/L; 2 min; 23 °C	1.4×10^{-3}/1.1	4.7×10^{-10}	3.5×10^{-7}
8	8.1; 0.8 mg/L; 1 mg/L; 2 min; 5 °C	1.6×10^{-3}/1.3	2.5×10^{-10}	1.6×10^{-7}
11	6.8; 4.5 mg/L; 3 mg/L; 2 min; 23 °C	2.0×10^{-3}/1.6	3.1×10^{-10}	1.6×10^{-7}
16	8.1; 4.5 mg/L; 3 mg/L; 2 min; 5 °C	2.0×10^{-3}/1.6	2.5×10^{-10}	1.3×10^{-7}
14	8.1; 0.8 mg/L; 3 mg/L; 2 min; 23 °C	4.0×10^{-3}/3.2	4.7×10^{-10}	1.2×10^{-7}
6	6.8; 0.8 mg/L; 3 mg/L; 2 min; 5 °C	6.4×10^{-3}/5.1	4.7×10^{-10}	7.3×10^{-8}

The calculated average R_{ct} values range between 3.5×10^{-7} – 6.1×10^{-8}. These high values are within the range of R_{ct} values reported for Lake Zurich water during the initial phase of ozone decomposition and higher than those observed with ozone-hydrogen peroxide advanced oxidation process (Acero and von Gunten, 2001). The high values suggest that Suwannee River NOM isolate used to adjust DOC levels in this study may contain a higher fraction of DOC (e.g. phenols, amines) that initiate a rapid decomposition of ozone to produce •OH radicals. This may also explain the higher maximum oxidation for Group B compounds observed in the current study as compared to those cited in Table 4.9. The high reactivity of Suwannee River NOM has also been reported in the study by Synder et al. (2007), where a rapid and at least a three-fold higher ozone consumption was observed for simulated water prepared with Suwannee River NOM, as compared to three other waters from natural sources.

The R_{ct} values, ozone exposure (Table 4.10), and Equation (4.1) can be used to interpret the results observed in the present study. At the low DOC content (0.8 mg/L) and low ozone dose (Expts. 4 & 8), $R_{ct} > 1.6\times10^{-7}$ and ozone exposure > 1.3 mg/L.min ensured > 90% oxidation of Group B compounds with reported $k_{.OH}$ values $\geq 7.4\times10^{9}$ (Table 4.2), as shown in Figure 4.9. Since ozone exposure was sufficient to significantly transform the compounds at ozone dose of 1 mg/L, increase of ozone dose to 3 mg/L was not seen to have an impact on the transformation efficiencies (Figure 4.9). At the high DOC content (4.5 mg/L) (Expts. 7 & 12) and low ozone dose, both the ozone exposure and R_{ct} values (Table 4.10) were seen to decline resulting in poor transformation efficiencies for Group B compounds (Figure 4.10). This suggests that due to the increase in DOC content, the enhanced ozone consumption by organic matter of the type that does not result in the formation of •OH radical limited its availability for •OH radical production. With

increase in the ozone dose to 3 mg/L, the ozone exposure value increased to 1.3 mg/L.min and Rct to values > 1.6×10^{-7} (Table 4.10), and the transformation of Group B compounds was restored to > 80% (Figure 4.9). These results show that ozonation or ozonation-based AOP may be effective for the transformation of compounds that are slow to or do not directly react with ozone. However for such compounds, the extent of transformation could be quite variable and strongly dependent on the water matrix, especially the nature and content of organic matter.

Based on the results of the current study, it is suggested that transformation of Group B compounds that can be expected for a given water matrix under the ozonation conditions applied at a given location may be estimated based on Rct and ozone exposure determinations. Rct and ozone exposure values can be separately computed for an initial ozonation period of 2 minutes or so and the period beyond (minute range), and the expected transformation during each period and total may then be approximately estimated using Equation (4.1). For situations where Rct and ozone decomposition rates are lower and result in poor transformation efficiencies for Group B compounds, the possibility of enhancing the transformation by using ozone-based AOP with the addition of H_2O_2 may be investigated and optimized as discussed by Acero and von Gunten (2001). Because of the low applied dosage of ozone and high content of DOC present in experiments 1, 7, 12 and 15, the much higher transformation efficiencies of ibuprofen and clofibric acid (30 - 40%) than pure water system (8 - 12%) were assumed mainly attributed to the effect of •OH. For the same operating conditions, however, the average transformation efficiencies for fast-reacting compounds (group A) are in the range of 50 - 70% (Table 4.4). It has been an interest to assess the relevance of two oxidation pathways for those fast-reacting compounds because different products will be formed depending

on the oxidation pathway and identification of by-products and their toxicity will be a potential concern for ozonation process. The fraction of oxidation by •OH, f(•OH) , can be calculated according to Equation 2.20 (Section 2.3.4). As an example, the f(•OH) of carbamazepine was calculated to be 57% in experiment 1, therefore 43% of oxidation was attributed to O_3 molecules. In the same manner, 29% and 71% of oxidation were caused by •OH and O_3 respectively in experiment 12. A calculation based on Equation 2.20 by Huber et al. (2005) has shown that •OH accounts for 20 - 50% of the parent oxidation in wastewater for 4 fast-reacting compounds including naproxen and sulfmethoxazole. They concluded that unlike the pure water system, •OH radicals in wastewater cannot be neglected despite the high reactivity of selected compounds toward O_3.

4.2.3 Effect of pH, Temperature and Contact Time

Statistical analyses showed that variables pH, temperature and contact time generally showed limited impacts on ozonation in this bench-scale study (see Appendix B). Temperature is a significant main effect factor for most of the fast-reacting compounds in group A except carbamazepine, gemfibrozil, tylosin and tetracycline at the confidence level of 90%. The effect was best illustrated in Figure 4.12 when DOC was at high level (i.e., 4.5 mg/L) and ozone at low level (i.e., 1.0 mg/L). The negative effect of temperature under these four experimental conditions is contrary to the normal notion of high temperature accelerating reaction rate, and might be explained due to the increase of ozone decomposition and/or decrease of dissolved ozone in the solution. No obviously similar trend was found for slow-reacting compounds.

Among all the 16 Group A and B target compounds, pH was observed to have a significant but small positive effect only for the transformation of tetracycline at the

confidence level of 90%. Results for the effect of pH in the literature are mixed with some studies showing a significant positive effect (Calvosa et al., 1991; Benitez et al., 1997), whereas the others do not (Venosa, 1972; Farooq et al., 1977; Rice, 1997; Chen, 2000). Change in pH can influence ozone stability and formation of hydroxyl radicals •OH through hydroxide ions (OH^-). For speciating chemicals, change in pH can also influence transformation if there is a significant shift in species composition. The protonated form typically has a higher reaction rate with ozone than the deprotonated form (Table 4.2). The lack of effect of pH observed in the current study maybe due to the relatively narrow range used, as well as the dominance of other factors such as DOC content and ozone dose. The small but significant effect of pH for tetracycline may be due to a change in its speciation as one its pK_a value (Table 4.2) is within the range of pH values used in the current study. However, the effect was not significant for other chemicals with similar pK_a values.

Contact time is considered an important parameter in many water treatment processes, including the process of ozonation. Due to the high R_{ct} and ozone exposure values observed in the current study, compounds of both Group A and B were rapidly transformed within 2 min under most experimental conditions. Increasing the contact time to 6 min was therefore not observed to be significant for either Group A nor Group B compounds.

4.3 Ozone Decay Study

To understand the kinetics of ozone decay as a function of the experimental conditions of the present study, several ozone decay experiments were performed using the simulated water matrix under conditions listed in Table 4.11.

Table 4.11 Summary of ozone decay studies

Expt.	Temp. (°C)	DOC (mg/L)	Starting ozone conc. (mg/L)	pH	IOD* (mg/L)	k (s^{-1})	Half-life* (s)
1	5	4.5	3	6.8	2.5		
2	23	4.5	3	6.8	2.8		
3	5	0.8	3	6.8	0.7	0.0444	15.5
4	23	0.8	3	6.8	1.9	0.0824	8.4
5	23	0.8	3	8.1	1.8	0.1116	6.2
6	23	0	3	6.8	0.6	0.0635	10.9
7	5	0	3	6.8	0.2	0.0153	45.1

* IOD (Initial ozone demand) = (starting ozone concentration) – (ozone concentration at 60s); Half life=0.69/k

Ozone decomposition in natural water is generally divided into an initial and a second phase. However the boundary line of two phases is not clearly defined. Buffle and co-workers (Buffle et al., 2006a and 2006b) defined t ≤20s as the initial phase and others used t≤60s (Rakness et al., 1999; Westerhoff et al., 1999; Sladic, 2001). The initial phase in the current study was assumed to be 60 s, and the data beyond was analyzed for calculating the first-order kinetic constant and half-life for the second phase of ozone decompositions as reported in Table 4.11. At the high DOC content of 4.5 mg/L (Expts. 1 & 2), ozone consumption was very rapid and the residual ozone concentration reduced to about 0.2 mg/L or lower in about 2 min. Due to these low concentrations and the reduced sensitivity of the indigo method, the first-order rate constant for the second phase was not determined for these experiments. For Experiments 4 and 5, about 60 - 63% of the ozone was consumed during the first minute in the presence of 0.8 mg/L DOC at high temperature of 23 °C, whereas the consumption was about 30% in DOC-free water (Expt. 6). These numbers are similar to those reported by Westerhoff and co-workers

(Westerhoff et al., 1999). The first-order decay rate constants obtained at the high temperature in waters with or without DOC (Expts 5 & 6) are also in agreement with those reported in literature (Ku et al., 1996; Sladic, 2001).

Regression analyses were performed to determine the influence of the pH range used in the current study on ozone decomposition rate at 23 °C and 0.8mg/L DOC (graphs a and b in Figure 4.15). The analyses obtained using the software Minitab gave a confidence limit (90%, $\alpha = 0.10$) of regression coefficient β (i.e. slope) as (-0.1116 ± 0.0114) for graph a, and (-0.0824 ± 0.0125) for graph b (for detailed calculation, see Appendix D). These two confidence limits do not overlap indicating that statistically, the first-order decay rate constant at pH 8.1 is significantly different from pH 6.8 at 90% confidence level under the given conditions. However, the initial ozone demands under both conditions are similar, i.e., 1.9 mg/L vs 1.8 mg/L (Table 4.11), which is consistent with the previous finding that pH has no effect on direct reactions between ozone and compound.

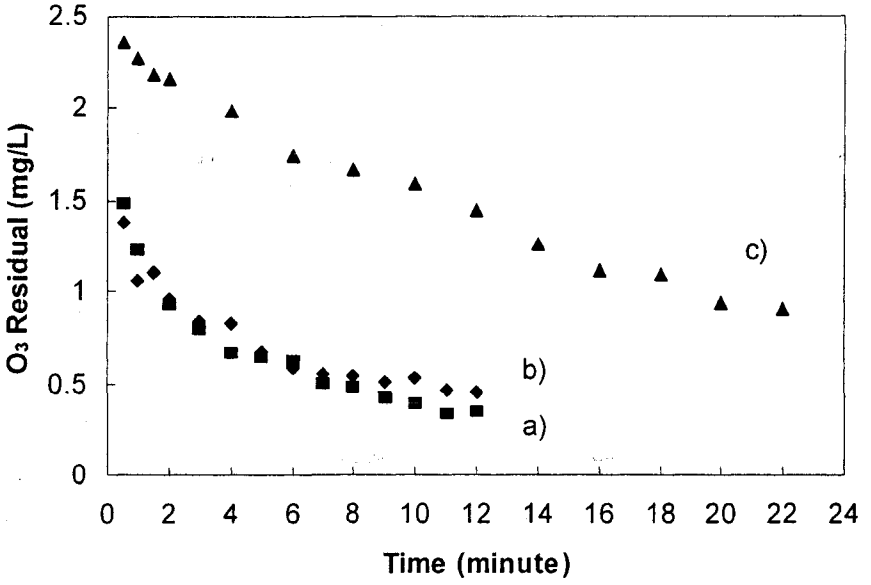


Figure 4.14 Ozone residual profile, DOC = 0.8 mg/L, starting O_3 =3.0 mg/L. a) T = 23 °C, pH = 8.1; b) T = 23 °C, pH = 6.8, and c) T = 5 °C, pH = 6.8.

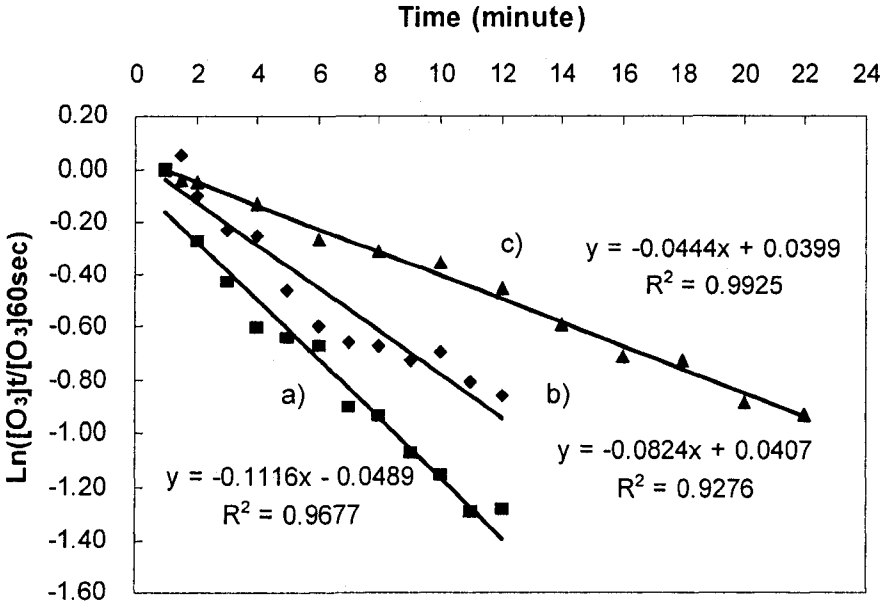


Figure 4.15 First-order decay profile, DOC = 0.8 mg/L, starting O_3 =3.0 mg/L. a) T = 23 °C, pH = 8.1; b) T = 23 °C, pH = 6.8, and c) T = 5°C, pH = 6.8.

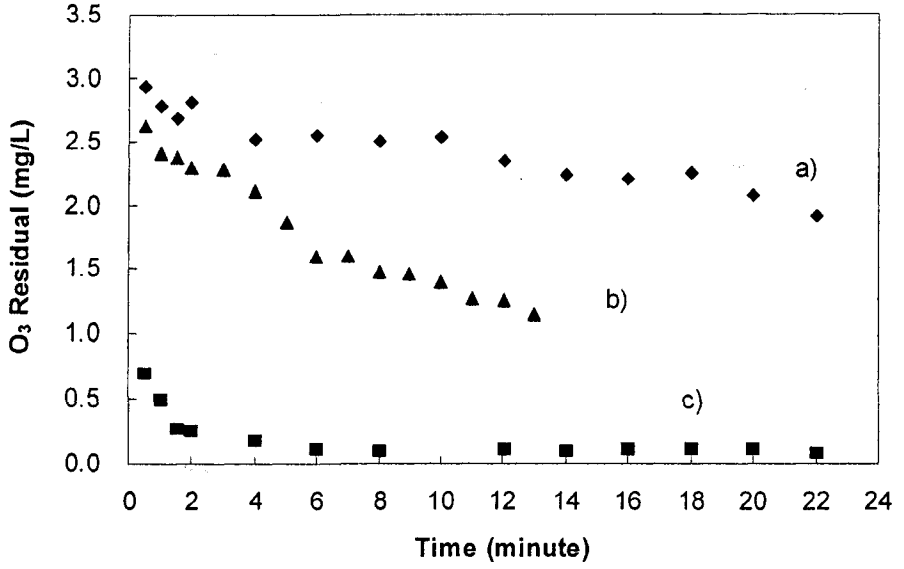


Figure 4.16 Ozone residual profile, starting O_3 = 3.0 mg/L. a) DOC = 0 mg/L, pH = 6.8, T = 5 °C; b) DOC = 0 mg/L, pH = 6.8, T = 23 °C, and c) DOC = 4.5 mg/L, pH = 6.8, T = 5 °C.

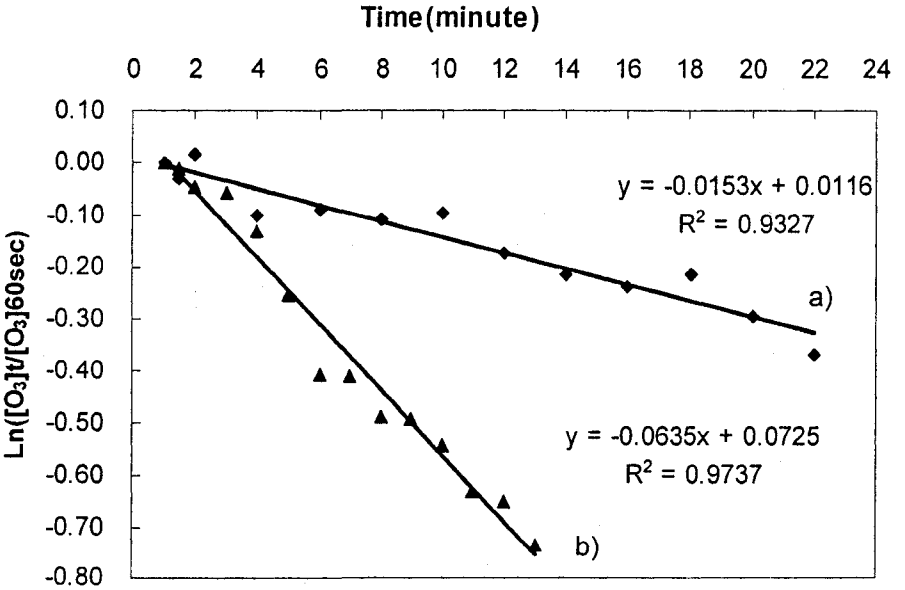


Figure 4.17 First-order decay profile, starting O_3 =3.0 mg/L. a) DOC = 0 mg/L, pH = 6.8, T =5°C; b) DOC = 0 mg/L, pH = 6.8, T = 23 °C.

Regression analyses were also performed under other operating conditions, as presented in Figures 4.15 and 4.17, and compared to assess the effect of other process variables on the decay rate constant. Significantly different decay rate constants (k value) of experiments 3 and 4 (0.0444 vs 0.0824 s^{-1}), and experiments 6 and 7 (0.0635 vs 0.0153 s^{-1}) were indicative of strong influence of temperature on O_3 decay. The k values for experiments 3 and 7 (0.0444 vs 0.0153 s^{-1}) were also significantly different at lower temperature of 5 °C, which indicated the significant effect of DOC loading. However, no significant difference was found between k values of experiments 4 and 6 (0.0824 vs 0.0635 s^{-1}), suggesting that at higher temperature of 23 °C, the DOC loading effect was overshadowed by temperature effect during the second phase of ozone decomposition. The much higher initial ozone demand of experiment 4 (1.9 mg/L) than that of 6 (0.6 mg/L) suggested that most of the reactive DOC in experiment 4 was quickly oxidized by ozone, thus limited the impact of DOC on ozone decay during second phase.

Although ozone is rapidly consumed by DOC in water matrix, it is interesting to point out that no obvious reduction of DOC was observed after each decay study experiment completed. Similarly, no significant difference of DOC was measured before and after ozone treatment for all the bench-scale experiments. It is believed that ozone reacts preferentially with molecular structures that absorb UV light as opposed to completely oxidizing organic carbon to CO_2 and water (Amy et al., 1988). Ozone provides a significant contribution to breaking down organic compounds, but ozonation alone has a negligible effect on the overall concentration of DOC in raw water (Qasim et al., 2000). Although no intermediate oxidation products for DOC are analyzed, pH values of treated samples are generally 0.2 - 0.6 units lower than that of the control samples (untreated), which indicates that some organic acid were produced during ozonation.

CHAPTER 5: CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

The research examined the effect of five process variables (DOC content, ozone dose, ozone contact time, pH and temperature) on the transformation of 16 select PPCPs/ EDCs in a laboratory-scale simulated drinking water ozonation process. Within the range of experimental conditions examined, the results revealed the following:

- Ozonation is an effective process for significant transformation (up to >90%) for all of the 16 PPCPs/EDCs examined.
- Ozone dose, DOC content and their interaction were the most significant factors, which accounted for 61–98 % of the variability in observed transformation rates for the chemicals studied.
- Temperature and its interaction with ozone dose and DOC content significantly affected the transformation for seven (bisphenol A, lincomycin, indomethacin, sulfamethazine, sulfamethoxazole, sulfachloropyridazine and naproxen) of the twelve Group A chemicals, and accounted for up to 27% of the observed variability. Temperature did not significantly affect the transformation for any of the four Group B chemicals.
- The effect of DOC content and temperature were insignificant or marginal when ozone exposure was high. At ozone exposure values > 1.3 mg/L.min, transformation efficiencies > 90 % were observed for Group A and > 70 % for Group B chemicals under all conditions. Transformation efficiency for Group B

chemicals is however expected to be strongly influenced by the nature and content of the natural organic matter present.

5.2 Engineering Significance

Ozone is becoming a popular primary disinfectant instead of chlorine in many water treatment plants. Also, much research, including the current study, also demonstrated that ozonation is an effective process to transform most of the PPCPs/EDCs of concern. Therefore disinfection using ozone may have an added benefit of transforming several emerging chemicals of concern that are routinely being detected in source drinking waters. The present study examined the effect of several variables on the transformation of select PPCPs and EDCs by treatment with ozone. The results show that ozone dose and organic matter content of the raw water are two important variables controlling the transformation of PPCPs/EDCs during the drinking water ozonation process. The extent of transformation for a given chemical is affected by its reaction directly with molecular ozone (characterized by k_{O3}) and with hydroxyl radicals (characterized by k_{OH}), a powerful secondary oxidant generated during the ozonation process.

The results of the present study can be used to derive some general guidelines for water treatment utilities to obtain a first estimate of the expected transformation of a given PPCP/ EDC during their ozonation process designed to achieve a disinfection criterion. As with other disinfection processes, disinfection process using ozone is designed and monitored using a specified ozone exposure or CT value, a product of ozone concentration and time of exposure or contact, which is derived based on guidelines by the regulation agency. Table 5.1 shows the required CT values for Giardia and virus inactivation by ozone, under the "Guidance manual for compliance with the filtration and

disinfection requirements for public water systems using surface water sources" (AWWA, 1991). For example, to achieve 2.0-log removal of Giardia and 4-log removal of viruses from a typical natural water source during ozonation treatment, a minimum CT value of 1.3 mg/L.min is required at 5 °C (Table 5.1).

Table 5.1 CT values (mg/L. min) for Giardia and virus inactivation by ozone (AWWA, 1991)

Giardia (Log)	**Temperature (°C)**					
	≤ 1	**5**	**10**	**15**	**20**	**25**
0.5	0.48	0.32	0.23	0.16	0.12	0.08
1.0	0.97	0.63	0.48	0.32	0.24	0.16
1.5	1.50	0.95	0.72	0.48	0.36	0.24
2.0	1.90	1.30	0.95	0.63	0.48	0.32
2.5	2.40	1.60	1.20	0.79	0.60	0.40
3.0	2.90	1.90	1.04	0.95	0.72	0.48
Virus (Log)						
2.0	0.90	0.60	0.50	0.30	0.25	0.15
3.0	1.40	0.90	0.80	0.50	0.40	0.25
4.0	1.80	1.20	1.00	0.60	0.50	0.30

For compounds with reported or estimated k_{O3} $>10^4$ $M^{-1}s^{-1}$, the present study has shown that this CT value (O_3-exposure) may be sufficient to achieve >90% oxidization (Figure 4.13). Estimates of transformation at lower CT values may have to be determined through actual measurements. For compounds with lower k_{O3} ($<10^4$ $M^{-1}s^{-1}$), estimation of hydroxyl radical exposure may be needed in addition to quantify the expected transformation. Such an estimate may be obtained by the water utility through the determination of an R_{ct} value for their source water for the target ozone CT value used by the utility. A laboratory procedure for the determination of R_{ct} value using an ozone-

resistant probe compound proposed by Elovitz and von Gunten (1999) can be used. Since R_{ct} value is expected to be strongly influenced by the organic matter content, the value should be determined for several typical raw water characteristics experienced by the utility, to obtain an idea of the expected variability in hydroxyl radical exposure as a function of the raw water characteristics. Based on the R_{ct} value and ozone CT value, the expected minimum transformation of compounds with low k_{O3} (<~50 $M^{-1}s^{-1}$) and k_{OH} > 5×10^9 $M^{-1}s^{-1}$ may be estimated using Table 5.2.

Table 5.2 O_3-exposure (mg/L. min) needed to achieve specific percent transformation of an O_3- resistant compound (k_{O3} <~50 $M^{-1}s^{-1}$; $k_{OH} = 5\times10^9$ $M^{-1}s^{-1}$) as a function of R_{ct} value

R_{ct}	O_3-exposure needed (mg/L. min)				
	50*	**60**	**70**	**80**	**90**
10^{-8}	11	14	19	25	36
10^{-7}	1.1	1.4	1.9	2.5	3.6
4×10^{-7}	0.3	0.4	0.5	0.6	0.9
10^{-6}	0.11	0.14	0.19	0.25	0.36

*Estimated transformation (%)

Table 5.2 has been derived using the mathematical model derived by Elovitz and von Gunten (1999). For compounds with intermediate k_{O3} values (> 50 and <10^4 $M^{-1}s^{-1}$) the expected transformation would be greater than that estimated using Table 5.2 and less than the estimate for compounds with $k_{O3} > 10^4$ $M^{-1}s^{-1}$.

5.3 Recommendations

Future research should include better understanding the nature of the by-products and their toxicities as well as the reaction mechanism. The objectives will consist of studying

by-products of the reactions between ozone and water matrix and by-products formed from the reaction of ozone with specific PPCPs/EDCs. Currently, the major by-product of concern for ozonation processes is bromate, which is formed in bromide-containing waters. A low drinking water standard of 10 μg/L has been set for bromate by the EU and the U.S. Therefore, disinfection and oxidation processes have to be evaluated to fulfill these criteria. Generally speaking, bromate formation is not a problem with ozone doses that are necessary to oxidize fast-reacting PPCPs/EDCs (Huber et al., 2003). However, the effects of initially generated •OH on the formation of bromate cannot be ignored (Buffle et al., 2004). Lowering of pH and ammonia addition are the main control measurements to be proposed (von Gunten, 2003b). However, conflicting results of ammonia addition on bromate formation have been observed (Glaze et al., 1993; Krasner et al., 1993). Chlorine-ammonia process (Cl_2-NH_3), consisting of prechlorination followed by ammonia addition prior to ozonation was also studied and a 4-fold decrease in bromate formed was observed when compared to the ammonia-only process (Buffle et al., 2004). But this process still requires a full-scale investigation. Iodate is another by-product formed during ozoantion of iodide-containing waters, but is considered non-problematic because it transformed back to iodide endogenically (von Gunten, 2003b). Chlorate is only formed during ozonation if a preoxidation of the water with chlorine and/or chlorine dioxide is applied. The toxicological impact of chorate is unclear and more studies are required to permit regulation. Information is also lacking on higher molecular weight organic by-products.

Ozonation of PPCPs/EDCs produces by-products. Some oxidation by-products were identified and found to pose as serious a health risk as the parent compounds, such as atrazine (Beltran, et al., 1994 and 2000). Other by-products pose less risk than the parent

compounds such as 17β-estradiol (Alum et al., 2004). In the current study only the transformation of primary 16 target compounds was investigated, thus further research is essential to identify and confirm the structures of metabolites formed by ozonation and to clarify the kinetic behavior. To achieve this, by-product(s) of a selected PPCP/EDC must be synthesized and identified then screened for toxicity assessment. Prior to these, a suitable toxicity assessment method must be established because current standard ecotoxicity tests are probably inappropriate for assessing long-term subtle effects of many PPCPs/EDCs and their by-products (Boxall, 2004).

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Appendix A: Summary of Transformation Efficiencies

Table A-1. Transformation Efficiency of Carbamazepine

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (°C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	67	62	65	65
2	6.8	4.5	3	6	5	>99	>99	>99	>99
3	8.1	0.8	1	6	23	>99	>99	>99	>99
4	6.8	0.8	1	2	23	>99	>99	>99	>99
5	8.1	0.8	3	6	5	>99	>99	>99	>99
6	6.8	0.8	3	2	5	>99	>99	>99	>99
7	8.1	4.5	1	2	23	60	57	57	58
8	8.1	0.8	1	2	5	>99	>99	>99	>99
9	6.8	0.8	1	6	5	>99	>99	>99	>99
10	6.8	0.8	3	6	23	>99	>99	>99	>99
11	6.8	4.5	3	2	23	>99	>99	>99	>99
12	6.8	4.5	1	2	5	83	81	87	84
13	8.1	4.5	3	6	23	>99	>99	>99	>99
14	8.1	0.8	3	2	23	>99	>99	>99	>99
15	8.1	4.5	1	6	5	73	71	73	72
16	8.1	4.5	3	2	5	>99	>99	>99	>99

Table A-2. Transformation Efficiency of Monensin

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (°C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	41	28	34	34
2	6.8	4.5	3	6	5	87	80	88	85
3	8.1	0.8	1	6	23	95	97	96	96
4	6.8	0.8	1	2	23	97	>97	>97	>97
5	8.1	0.8	3	6	5	>97	>97	>97	>97
6	6.8	0.8	3	2	5	>97	>97	>97	>97
7	8.1	4.5	1	2	23	53	41	48	47
8	8.1	0.8	1	2	5	74	71	75	73
9	6.8	0.8	1	6	5	94	96	96	95
10	6.8	0.8	3	6	23	>97	>97	>97	>97
11	6.8	4.5	3	2	23	96	92	92	93
12	6.8	4.5	1	2	5	43	47	44	45
13	8.1	4.5	3	6	23	91	88	87	89
14	8.1	0.8	3	2	23	>97	>97	>97	>97
15	8.1	4.5	1	6	5	40	39	50	43
16	8.1	4.5	3	2	5	88	84	83	85

Table A-3. Transformation Efficiency of Tetracycline

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (^{0}C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	60	49	54	54
2	6.8	4.5	3	6	5	90	89	91	90
3	8.1	0.8	1	6	23	>98	>98	>98	>98
4	6.8	0.8	1	2	23	95	95	95	95
5	8.1	0.8	3	6	5	>98	>98	>98	>98
6	6.8	0.8	3	2	5	96	97	97	97
7	8.1	4.5	1	2	23	72	62	61	65
8	8.1	0.8	1	2	5	97	97	97	97
9	6.8	0.8	1	6	5	96	96	96	96
10	6.8	0.8	3	6	23	>98	>98	>98	>98
11	6.8	4.5	3	2	23	88	83	83	85
12	6.8	4.5	1	2	5	42	49	45	45
13	8.1	4.5	3	6	23	98	98	98	98
14	8.1	0.8	3	2	23	>98	>98	>98	>98
15	8.1	4.5	1	6	5	52	57	60	56
16	8.1	4.5	3	2	5	96	95	95	95

Table A-4. Transformation Efficiency of Lincomycin

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (^{0}C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	79	73	76	76
2	6.8	4.5	3	6	5	>99	>99	>99	>99
3	8.1	0.8	1	6	23	>99	>99	>99	>99
4	6.8	0.8	1	2	23	>99	>99	>99	>99
5	8.1	0.8	3	6	5	>99	>99	>99	>99
6	6.8	0.8	3	2	5	>99	>99	>99	>99
7	8.1	4.5	1	2	23	71	66	65	67
8	8.1	0.8	1	2	5	>99	>99	>99	>99
9	6.8	0.8	1	6	5	>99	>99	>99	>99
10	6.8	0.8	3	6	23	>99	>99	>99	>99
11	6.8	4.5	3	2	23	>99	>99	>99	>99
12	6.8	4.5	1	2	5	95	92	94	94
13	8.1	4.5	3	6	23	>99	>99	>99	>99
14	8.1	0.8	3	2	23	>99	>99	>99	>99
15	8.1	4.5	1	6	5	93	92	93	93
16	8.1	4.5	3	2	5	>99	>99	>99	>99

Table A-5. Transformation Efficiency of Erythromycin

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (°C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	16	2	25	14
2	6.8	4.5	3	6	5	56	57	30	48
3	8.1	0.8	1	6	23	91	91	92	91
4	6.8	0.8	1	2	23	93	89	93	92
5	8.1	0.8	3	6	5	93	93	93	93
6	6.8	0.8	3	2	5	90	94	88	91
7	8.1	4.5	1	2	23	-35	-14	17	
8	8.1	0.8	1	2	5	87	84	87	86
9	6.8	0.8	1	6	5	87	85	89	87
10	6.8	0.8	3	6	23	>99	>99	>99	>99
11	6.8	4.5	3	2	23	62	15	54	44
12	6.8	4.5	1	2	5	-60	-25	-78	
13	8.1	4.5	3	6	23	76	81	79	79
14	8.1	0.8	3	2	23	98	98	98	98
15	8.1	4.5	1	6	5	22	32	21	25
16	8.1	4.5	3	2	5	89	89	84	87

Table A-6. Transformation Efficiency of Sulfamethazine

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (°C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	79	65	71	72
2	6.8	4.5	3	6	5	>99	>99	>99	>99
3	8.1	0.8	1	6	23	>99	>99	>99	>99
4	6.8	0.8	1	2	23	>99	>99	>99	>99
5	8.1	0.8	3	6	5	>99	>99	>99	>99
6	6.8	0.8	3	2	5	>99	>99	>99	>99
7	8.1	4.5	1	2	23	74	68	69	70
8	8.1	0.8	1	2	5	>99	>99	>99	>99
9	6.8	0.8	1	6	5	>99	>99	>99	>99
10	6.8	0.8	3	6	23	>99	>99	>99	>99
11	6.8	4.5	3	2	23	>99	>99	>99	>99
12	6.8	4.5	1	2	5	86	81	86	84
13	8.1	4.5	3	6	23	>99	>99	>99	>99
14	8.1	0.8	3	2	23	>99	>99	>99	>99
15	8.1	4.5	1	6	5	82	85	82	83
16	8.1	4.5	3	2	5	>99	>99	>99	>99

Table A-7. Transformation Efficiency of Sulfachloropyridazine

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (°C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	68	54	59	60
2	6.8	4.5	3	6	5	>99	>99	>99	>99
3	8.1	0.8	1	6	23	>99	>99	>99	>99
4	6.8	0.8	1	2	23	99	99	99	99
5	8.1	0.8	3	6	5	99	99	99	99
6	6.8	0.8	3	2	5	>99	>99	>99	>99
7	8.1	4.5	1	2	23	55	49	58	54
8	8.1	0.8	1	2	5	98	98	98	98
9	6.8	0.8	1	6	5	>99	>99	>99	>99
10	6.8	0.8	3	6	23	>99	>99	>99	>99
11	6.8	4.5	3	2	23	>99	>99	>99	>99
12	6.8	4.5	1	2	5	82	77	81	80
13	8.1	4.5	3	6	23	>99	>99	>99	>99
14	8.1	0.8	3	2	23	>99	>99	>99	>99
15	8.1	4.5	1	6	5	71	77	73	74
16	8.1	4.5	3	2	5	>99	>99	>99	>99

Table A-8. Transformation Efficiency of Sulfamethoxazole

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (°C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	61	45	51	52
2	6.8	4.5	3	6	5	>99	>99	>99	>99
3	8.1	0.8	1	6	23	>99	>99	>99	>99
4	6.8	0.8	1	2	23	>99	>99	>99	>99
5	8.1	0.8	3	6	5	>99	>99	>99	>99
6	6.8	0.8	3	2	5	>99	>99	>99	>99
7	8.1	4.5	1	2	23	50	45	52	49
8	8.1	0.8	1	2	5	>99	>99	>99	>99
9	6.8	0.8	1	6	5	>99	>99	>99	>99
10	6.8	0.8	3	6	23	>99	>99	>99	>99
11	6.8	4.5	3	2	23	>99	>99	>99	>99
12	6.8	4.5	1	2	5	71	64	71	69
13	8.1	4.5	3	6	23	>99	>99	>99	>99
14	8.1	0.8	3	2	23	>99	>99	>99	>99
15	8.1	4.5	1	6	5	63	67	63	64
16	8.1	4.5	3	2	5	>99	>99	>99	>99

Table A-9. Transformation Efficiency of Tylosin

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (°C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	65	56	63	61
2	6.8	4.5	3	6	5	>98	>98	>98	>98
3	8.1	0.8	1	6	23	>98	>98	>98	>98
4	6.8	0.8	1	2	23	97	97	97	97
5	8.1	0.8	3	6	5	>98	>98	>98	>98
6	6.8	0.8	3	2	5	>98	>98	>98	>98
7	8.1	4.5	1	2	23	73	69	68	70
8	8.1	0.8	1	2	5	>98	>98	>98	>98
9	6.8	0.8	1	6	5	>98	>98	>98	>98
10	6.8	0.8	3	6	23	>98	>98	>98	>98
11	6.8	4.5	3	2	23	97	94	96	96
12	6.8	4.5	1	2	5	72	68	65	68
13	8.1	4.5	3	6	23	97	98	98	98
14	8.1	0.8	3	2	23	>98	>98	>98	>98
15	8.1	4.5	1	6	5	78	73	76	76
16	8.1	4.5	3	2	5	>98	97	98	98

Table A-10. Transformation Efficiency of Naproxen

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (°C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	64	58	54	59
2	6.8	4.5	3	6	5	>99	>99	>99	>99
3	8.1	0.8	1	6	23	>99	>99	>99	>99
4	6.8	0.8	1	2	23	>99	>99	>99	>99
5	8.1	0.8	3	6	5	>99	>99	>99	>99
6	6.8	0.8	3	2	5	>99	>99	>99	>99
7	8.1	4.5	1	2	23	65	53	55	58
8	8.1	0.8	1	2	5	>99	>99	>99	>99
9	6.8	0.8	1	6	5	>99	>99	>99	>99
10	6.8	0.8	3	6	23	>99	>99	>99	>99
11	6.8	4.5	3	2	23	>99	>99	>99	>99
12	6.8	4.5	1	2	5	78	74	78	77
13	8.1	4.5	3	6	23	>99	>99	>99	>99
14	8.1	0.8	3	2	23	>99	>99	>99	>99
15	8.1	4.5	1	6	5	70	69	69	69
16	8.1	4.5	3	2	5	>99	>99	>99	>99

Table A-11. Transformation Efficiency of Bezafibrate

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (°C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	8	20	35	21
2	6.8	4.5	3	6	5	90	87	89	89
3	8.1	0.8	1	6	23	97	96	96	96
4	6.8	0.8	1	2	23	98	98	98	98
5	8.1	0.8	3	6	5	>99	>99	>99	>99
6	6.8	0.8	3	2	5	>99	>99	>99	>99
7	8.1	4.5	1	2	23	41	38	36	38
8	8.1	0.8	1	2	5	87	88	87	87
9	6.8	0.8	1	6	5	96	97	97	97
10	6.8	0.8	3	6	23	>99	>99	>99	>99
11	6.8	4.5	3	2	23	96	94	92	94
12	6.8	4.5	1	2	5	43	39	42	41
13	8.1	4.5	3	6	23	90	90	90	90
14	8.1	0.8	3	2	23	>99	>99	>99	>99
15	8.1	4.5	1	6	5	41	41	37	40
16	8.1	4.5	3	2	5	87	86	87	87

Table A-12. Transformation Efficiency of Indomethacin

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (°C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	51	57	66	58
2	6.8	4.5	3	6	5	>97	>97	>97	>97
3	8.1	0.8	1	6	23	>97	>97	>97	>97
4	6.8	0.8	1	2	23	95	95	95	95
5	8.1	0.8	3	6	5	>97	>97	>97	>97
6	6.8	0.8	3	2	5	>97	>97	>97	>97
7	8.1	4.5	1	2	23	62	55	55	57
8	8.1	0.8	1	2	5	>97	>97	>97	>97
9	6.8	0.8	1	6	5	>97	>97	>97	>97
10	6.8	0.8	3	6	23	>97	>97	>97	>97
11	6.8	4.5	3	2	23	>97	>97	>97	>97
12	6.8	4.5	1	2	5	91	88	91	90
13	8.1	4.5	3	6	23	>97	>97	>97	>97
14	8.1	0.8	3	2	23	>97	>97	>97	>97
15	8.1	4.5	1	6	5	83	82	82	82
16	8.1	4.5	3	2	5	>97	>97	>97	>97

Table A-13. Transformation Efficiency of Gemfibrozil

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (°C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	51	52	51	51
2	6.8	4.5	3	6	5	>99	>99	>99	>99
3	8.1	0.8	1	6	23	>99	>99	>99	>99
4	6.8	0.8	1	2	23	>99	>99	>99	>99
5	8.1	0.8	3	6	5	>99	>99	>99	>99
6	6.8	0.8	3	2	5	>99	>99	>99	>99
7	8.1	4.5	1	2	23	50	48	49	49
8	8.1	0.8	1	2	5	>99	>99	>99	>99
9	6.8	0.8	1	6	5	>99	>99	>99	>99
10	6.8	0.8	3	6	23	>99	>99	>99	>99
11	6.8	4.5	3	2	23	>99	>99	>99	>99
12	6.8	4.5	1	2	5	61	56	60	59
13	8.1	4.5	3	6	23	99	97	99	98
14	8.1	0.8	3	2	23	>99	>99	>99	>99
15	8.1	4.5	1	6	5	54	55	54	54
16	8.1	4.5	3	2	5	>99	>99	>99	>99

Table A-14. Transformation Efficiency of Clofibric acid

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (°C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	94	94	94	94
2	6.8	4.5	3	6	5	82	80	83	82
3	8.1	0.8	1	6	23	92	91	91	91
4	6.8	0.8	1	2	23	>97	96	97	97
5	8.1	0.8	3	6	5	>97	>97	>97	>97
6	6.8	0.8	3	2	5	97	97	>97	97
7	8.1	4.5	1	2	23	38	36	35	36
8	8.1	0.8	1	2	5	77	78	77	77
9	6.8	0.8	1	6	5	93	93	93	93
10	6.8	0.8	3	6	23	>97	>97	>97	>97
11	6.8	4.5	3	2	23	87	86	84	86
12	6.8	4.5	1	2	5	41	40	40	40
13	8.1	4.5	3	6	23	83	82	83	83
14	8.1	0.8	3	2	23	>97	>97	>97	>97
15	8.1	4.5	1	6	5	42	40	39	40
16	8.1	4.5	3	2	5	79	78	79	79

Table A-15. Transformation Efficiency of Bisphenol A

Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (°C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	65	66	66	66
2	6.8	4.5	3	6	5	>97	>97	>97	>97
3	8.1	0.8	1	6	23	>97	>97	>97	>97
4	6.8	0.8	1	2	23	>97	>97	>97	>97
5	8.1	0.8	3	6	5	>97	>97	>97	>97
6	6.8	0.8	3	2	5	>97	>97	>97	>97
7	8.1	4.5	1	2	23	75	68	68	70
8	8.1	0.8	1	2	5	>97	>97	>97	>97
9	6.8	0.8	1	6	5	>97	>97	>97	>97
10	6.8	0.8	3	6	23	>97	>97	>97	>97
11	6.8	4.5	3	2	23	>97	>97	>97	>97
12	6.8	4.5	1	2	5	90	86	90	89
13	8.1	4.5	3	6	23	>97	>97	>97	>97
14	8.1	0.8	3	2	23	>97	>97	>97	>97
15	8.1	4.5	1	6	5	87	86	87	87
16	8.1	4.5	3	2	5	>97	>97	>97	>97

Table A-16a. Transformation Efficiency of Ibuprofen (ESI +)

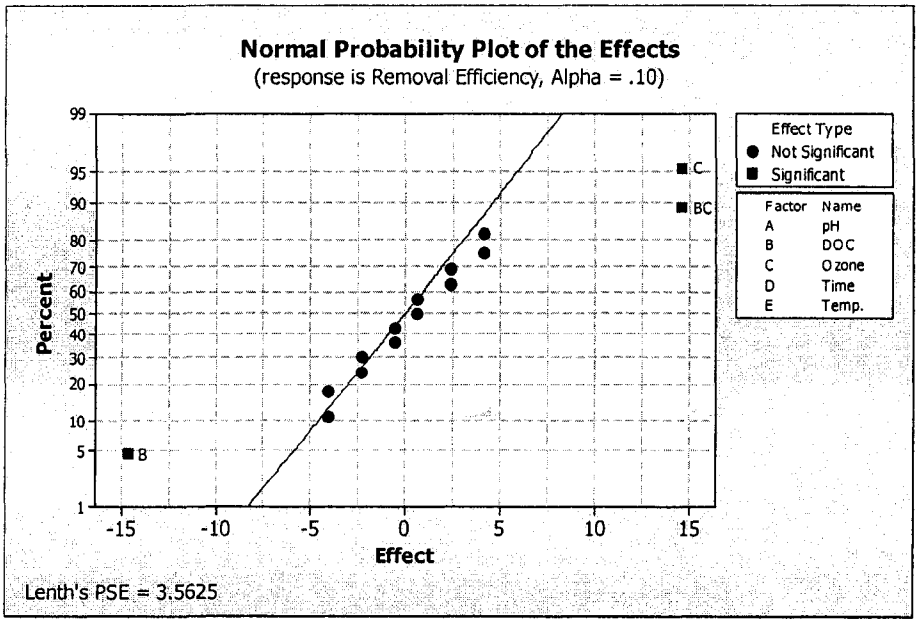
Run	Factors					Transformation efficiency (%)			
	pH	DOC (mg/L)	O_3 Dose (mg/L)	O_3 Time (min)	Temp (°C)	REP 1	REP 2	REP 3	AVG
1	6.8	4.5	1	6	23	42	40	37	40
2	6.8	4.5	3	6	5	90	85	91	89
3	8.1	0.8	1	6	23	97	96	96	96
4	6.8	0.8	1	2	23	>97	>97	>97	>97
5	8.1	0.8	3	6	5	>97	>97	>97	>97
6	6.8	0.8	3	2	5	>97	>97	>97	>97
7	8.1	4.5	1	2	23	41	45	43	43
8	8.1	0.8	1	2	5	84	86	84	85
9	6.8	0.8	1	6	5	96	96	96	96
10	6.8	0.8	3	6	23	>97	>97	>97	>97
11	6.8	4.5	3	2	23	91	90	89	90
12	6.8	4.5	1	2	5	33	37	38	36
13	8.1	4.5	3	6	23	90	88	90	89
14	8.1	0.8	3	2	23	>97	>97	>97	>97
15	8.1	4.5	1	6	5	39	39	31	36
16	8.1	4.5	3	2	5	86	85	84	85

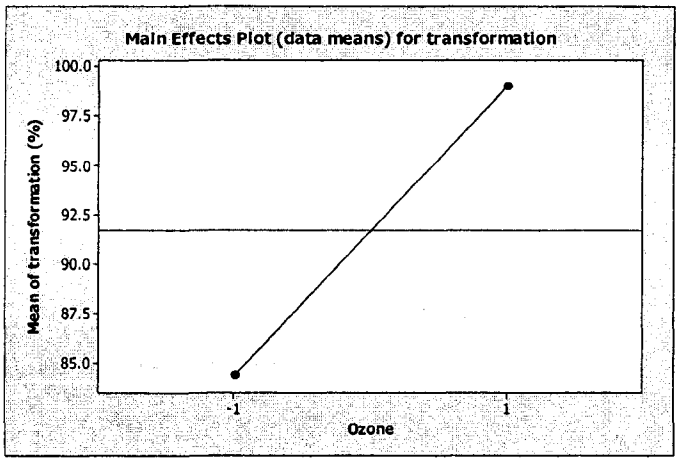
Table A-16b. Transformation Efficiency of Ibuprofen (ESI -)

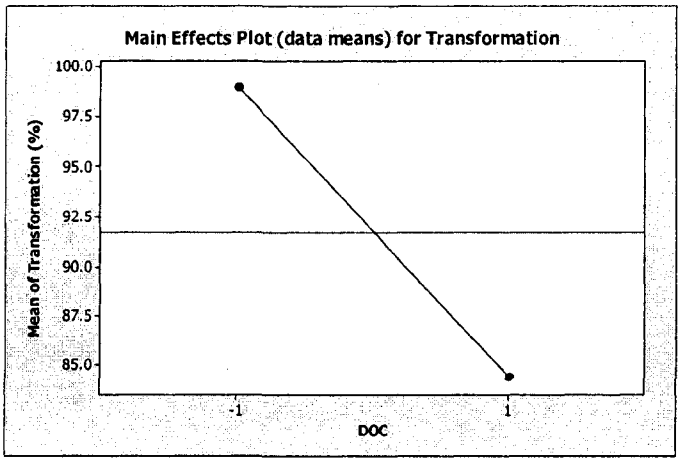
Run	Factors					Transformation efficiency (%)			
	pH	**DOC (mg/L)**	**O_3 Dose (mg/L)**	**O_3 Time (min)**	**Temp (^oC)**	**REP 1**	**REP 2**	**REP 3**	**AVG**
1	6.8	4.5	1	6	23	44	43	41	43
2	6.8	4.5	3	6	5	88	86	88	87
3	8.1	0.8	1	6	23	96	95	95	95
4	6.8	0.8	1	2	23	>97	>97	>97	>97
5	8.1	0.8	3	6	5	>97	>97	>97	>97
6	6.8	0.8	3	2	5	>97	>97	>97	>97
7	8.1	4.5	1	2	23	43	40	38	40
8	8.1	0.8	1	2	5	82	83	80	82
9	6.8	0.8	1	6	5	96	95	96	96
10	6.8	0.8	3	6	23	>97	>97	>97	>97
11	6.8	4.5	3	2	23	91	91	89	90
12	6.8	4.5	1	2	5	46	41	43	43
13	8.1	4.5	3	6	23	90	87	90	89
14	8.1	0.8	3	2	23	>97	>97	>97	>97
15	8.1	4.5	1	6	5	44	41	44	43
16	8.1	4.5	3	2	5	85	84	85	85

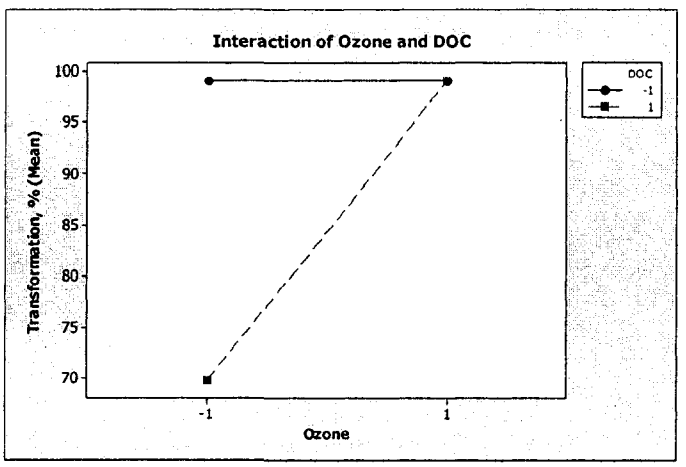
Appendix B: Statistic Analysis to Determine Main Effect Factors and Interactions

1. Carbamazepine









ANOVA Table

Source	DF [a]	Seq SS [b]	Contribution [c] (%)
B	1	855.6	29.1
C	1	855.6	29.1
B*C	1	855.6	29.1
Error	12	368.8	12.7
Total	15	2935.6	
R-Sq = 87.3 %			

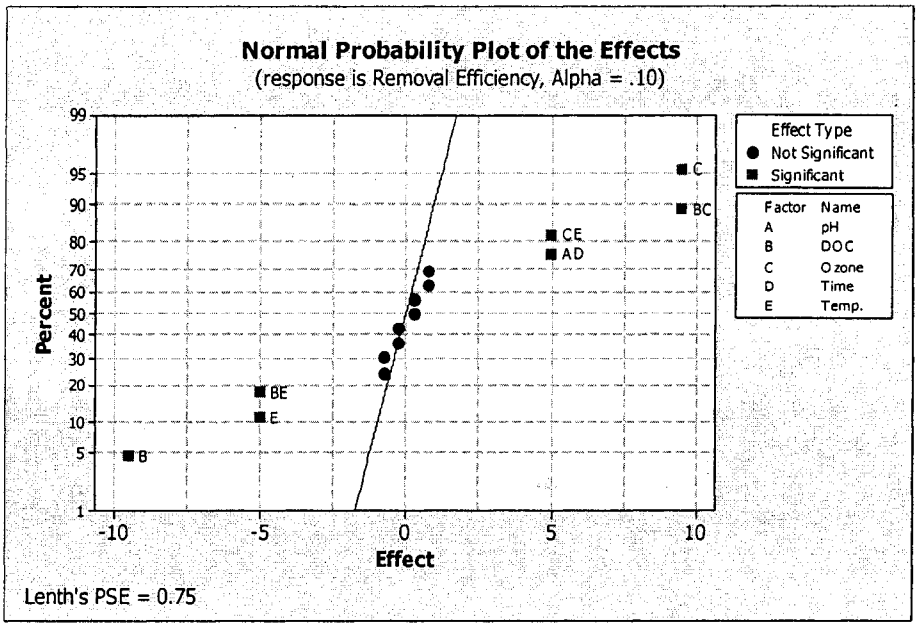
Remarks: B- DOC; C- O_3 dose; B*C- interaction between B and C

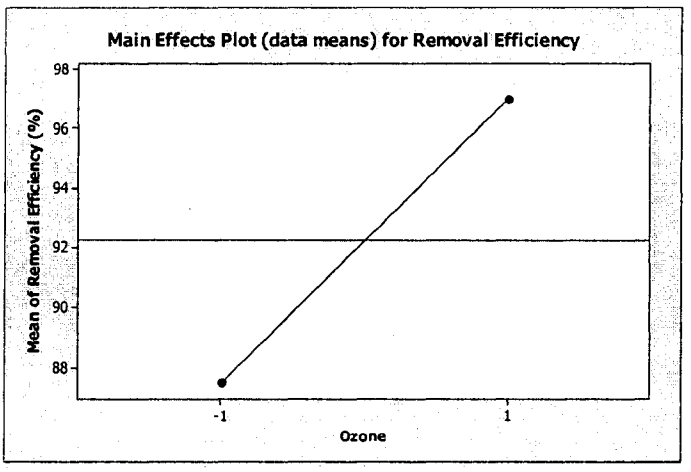
[a] DF-degree of freedom;

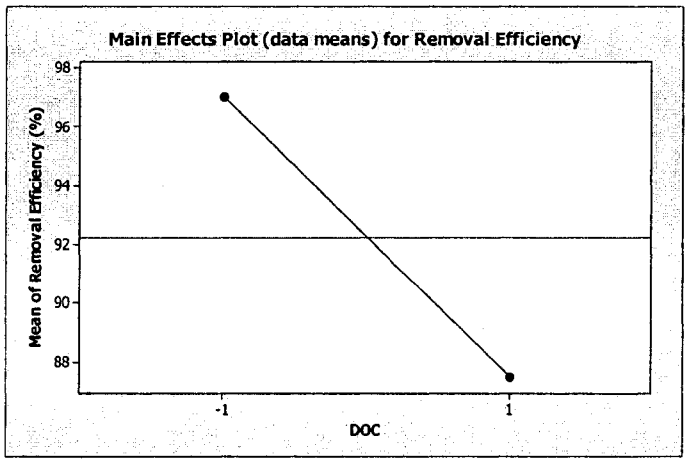
[b] Seq SS- sequential sum of squares;

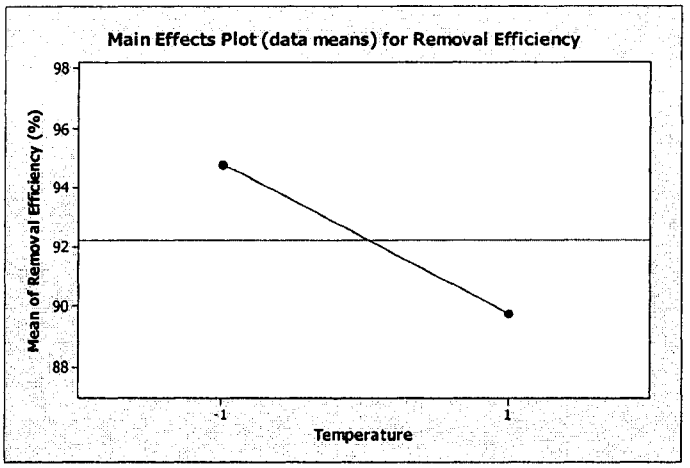
[c] Contribution 29.1%=855.6/2935.6.

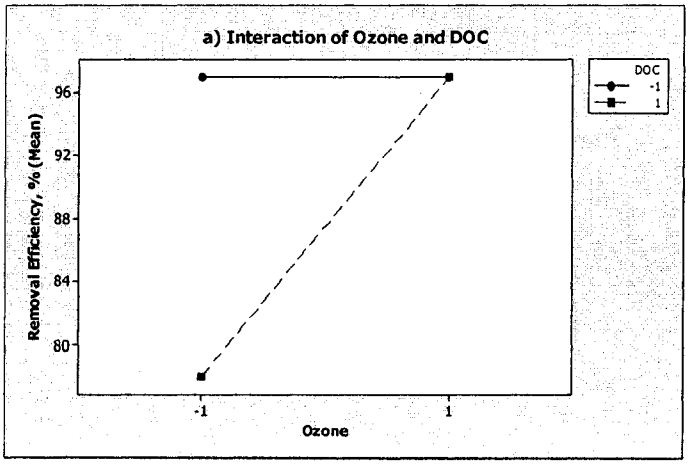
2. Bisphenol A

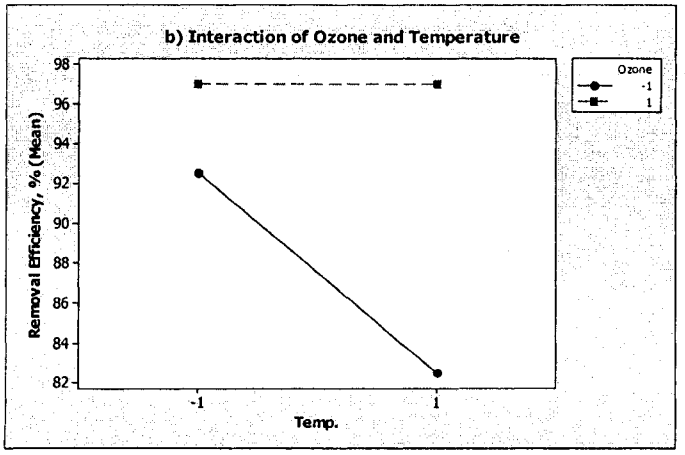


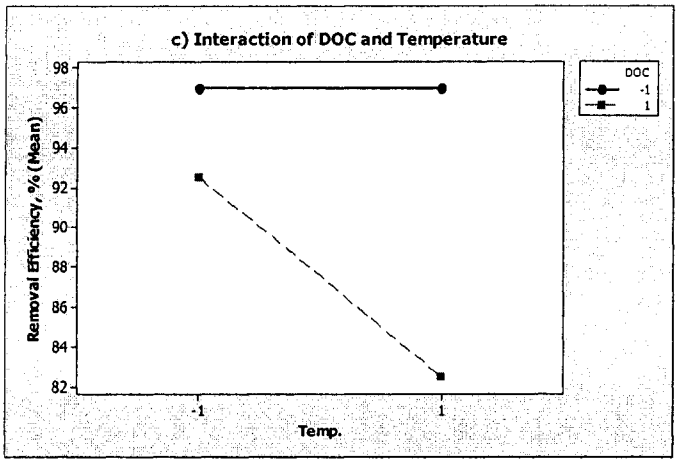





Main Effects Plot (data means) for Removal Efficiency
Mean of Removal Efficiency (%)
98
96
94
92
90
88
-1
1
Temperature


a) Interaction of Ozone and DOC
Removal Efficiency, % (Mean)
96
92
88
84
80
-1
1
Ozone
DOC
-1
1


b) Interaction of Ozone and Temperature
Removal Efficiency, % (Mean)
98
96
94
92
90
88
86
84
82
-1
1
Temp.
Ozone
-1
1



ANOVA Table

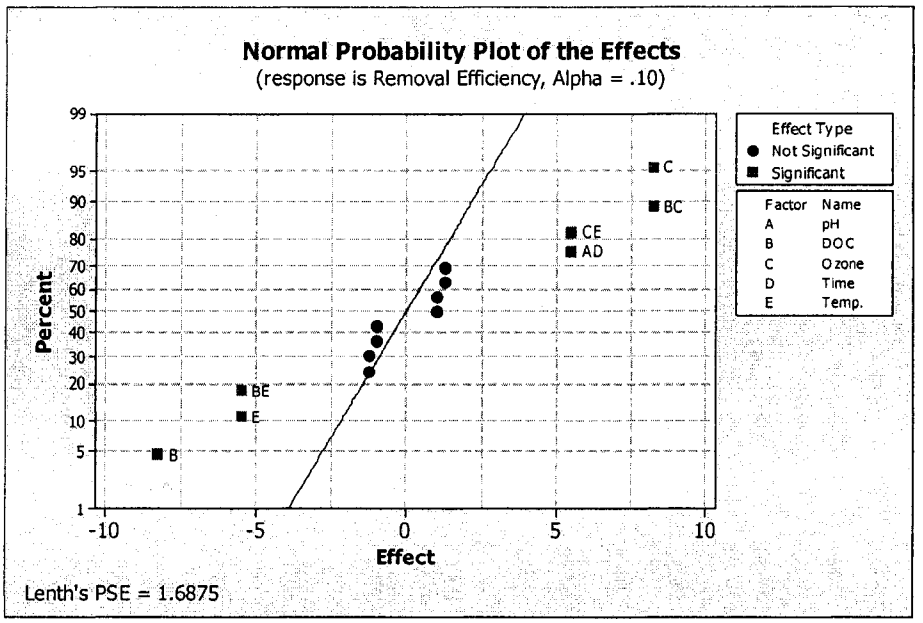
Source	DF [a]	Seq SS [b]	Contribution [c] (%)
B	1	361.0	24.2
C	1	361.0	24.2
E	1	100.0	6.7
A*D	1	100.0	6.7
B*C	1	361.0	24.2
B*E	1	100.0	6.7
C*E	1	100.0	6.7
Error	8	10.0	0.6
Total	15	1493.0	
R-Sq =99.4 %			

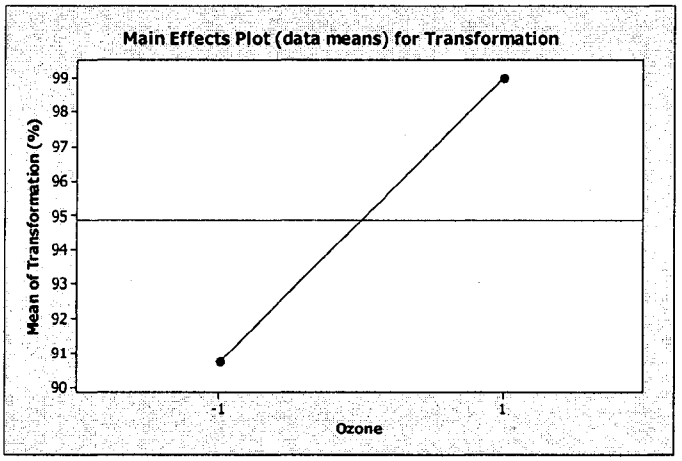
A- pH; B- DOC; C- O_3 dose; D- contact time; E- temperature;
B*C- interaction between B and C

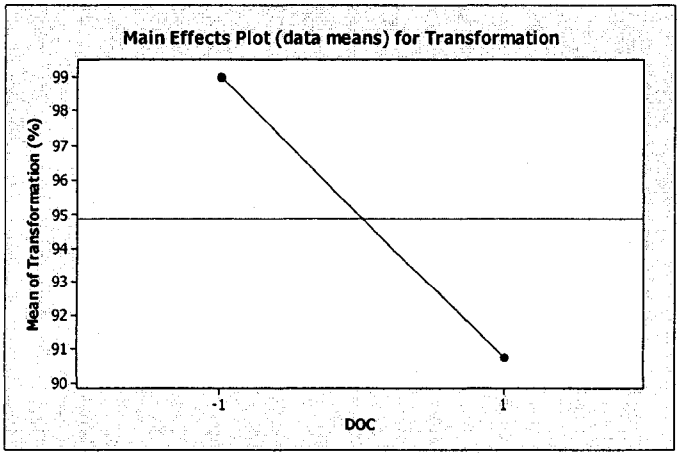
[a] DF-degree of freedom; [b] Seq SS- sequential sum of squares

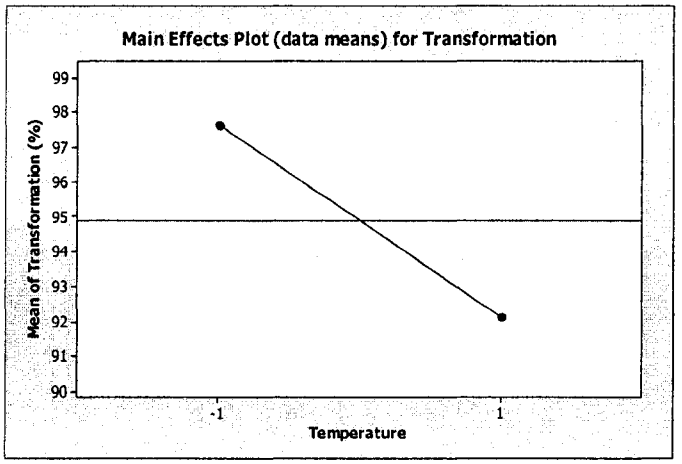
[c] Contribution 24.2%=361.0/1493.0

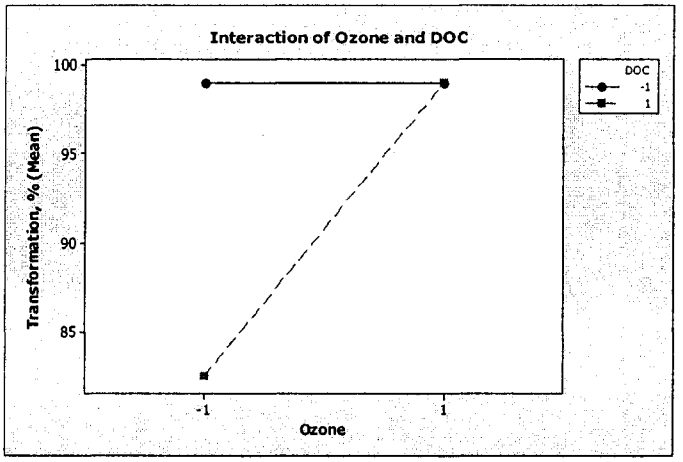
3. Lincomythcin

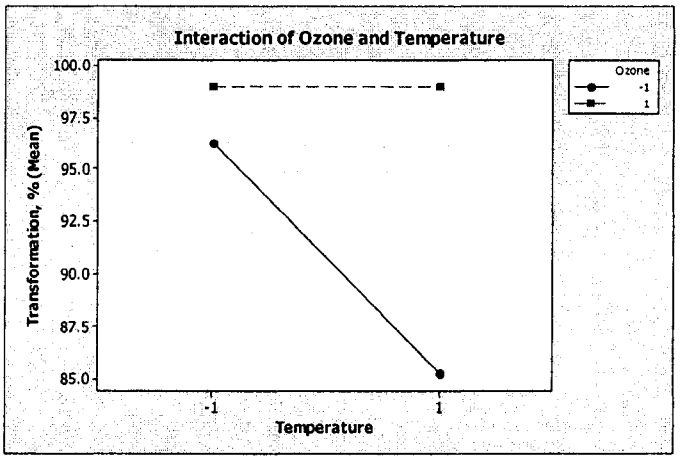


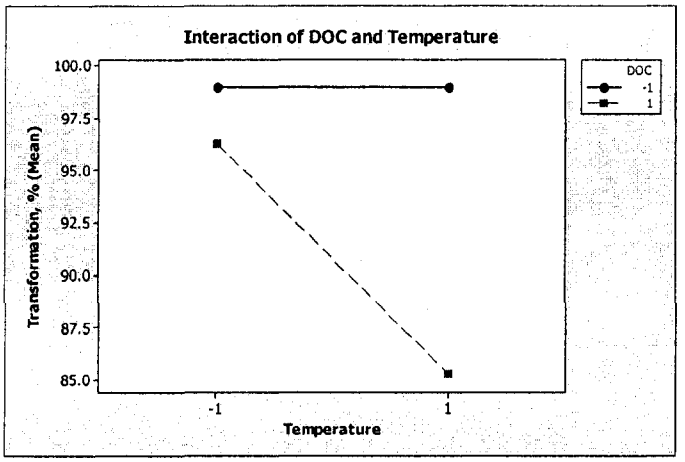





Main Effects Plot (data means) for Transformation
Mean of Transformation (%)
99
98
97
96
95
94
93
92
91
90
-1
1
Temperature


Interaction of Ozone and DOC
Transformation, % (Mean)
100
95
90
85
-1
1
Ozone
DOC
-1
1

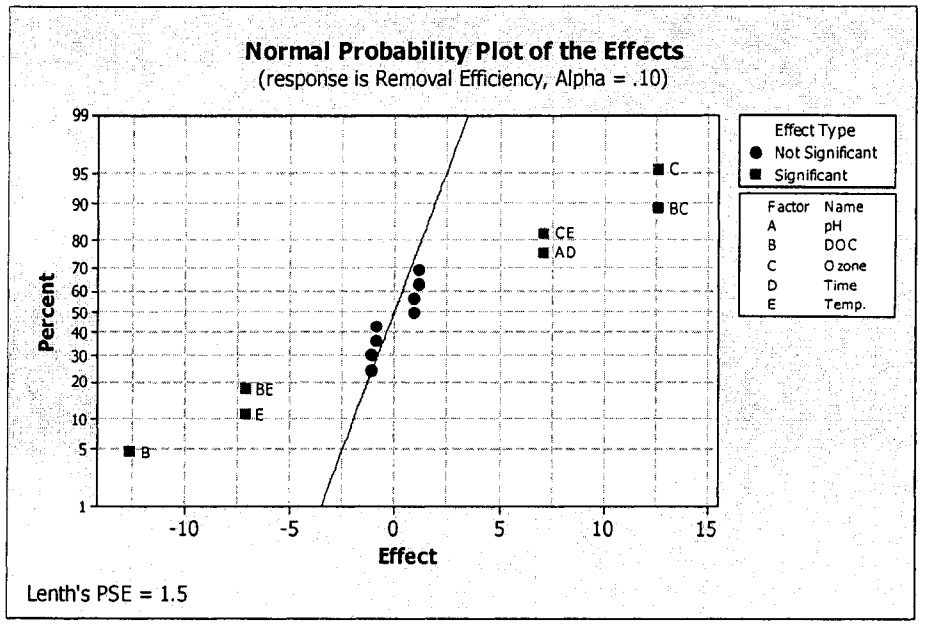

Interaction of Ozone and Temperature
Transformation, % (Mean)
100.0
97.5
95.0
92.5
90.0
87.5
85.0
-1
1
Temperature
Ozone
-1
1

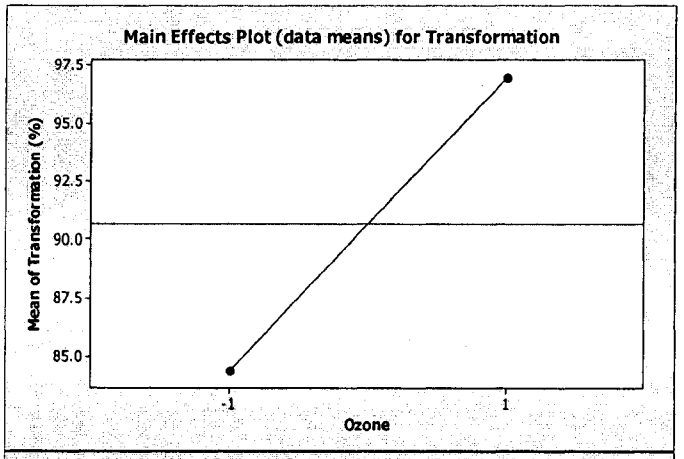


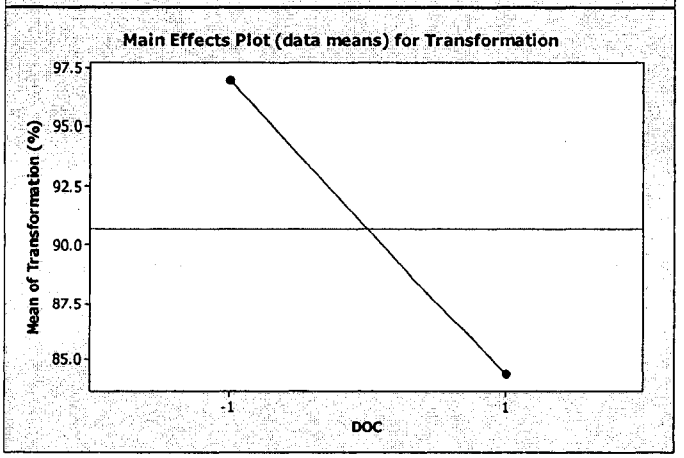
ANOVA Table

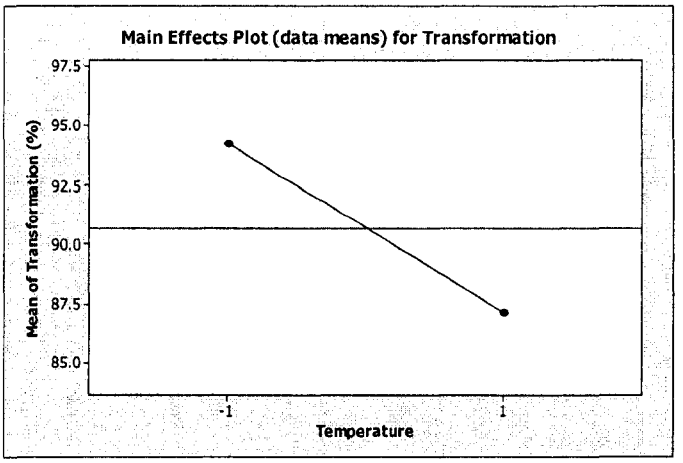
Source	DF	Seq SS	Contribution (%)
B	1	272.3	20.3
C	1	272.3	20.3
E	1	121.0	9.0
A*D	1	121.0	9.0
B*C	1	272.3	20.3
B*E	1	121.0	9.0
C*E	1	121.0	9.0
Error	8	41.0	3.1
Total	15	1341.9	
R-Sq =96.9 %			

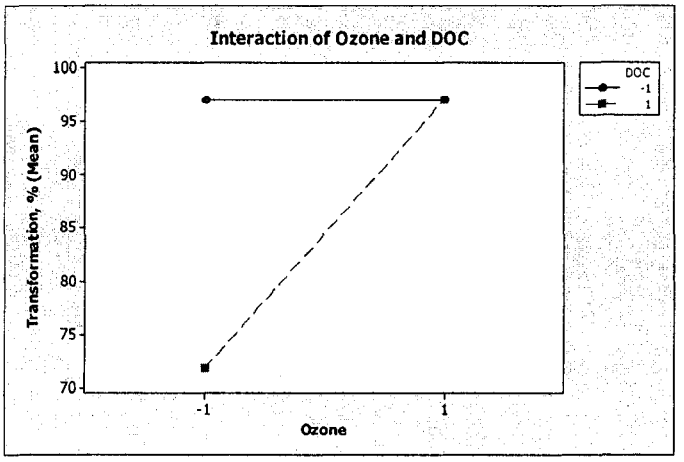
4. Indomethacin

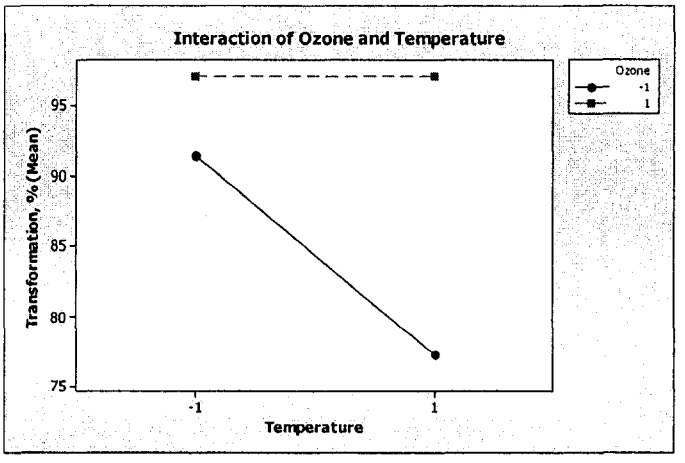


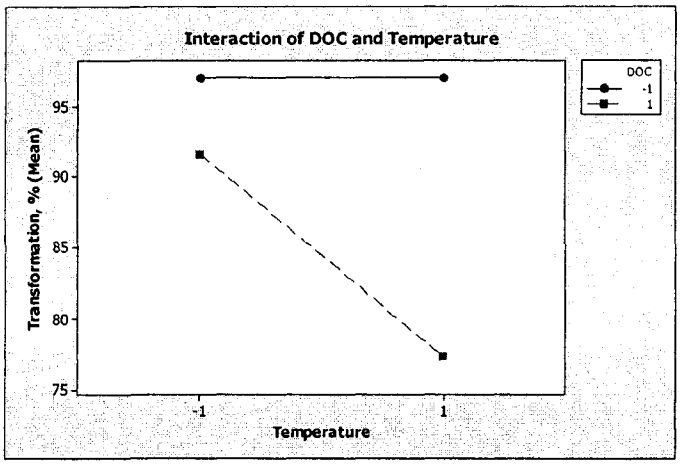





Main Effects Plot (data means) for Transformation
Mean of Transformation (%)
97.5
95.0
92.5
90.0
87.5
85.0
-1
1
Temperature


Interaction of Ozone and DOC
Transformation, % (Mean)
100
95
90
85
80
75
70
-1
1
Ozone
DOC
-1
1

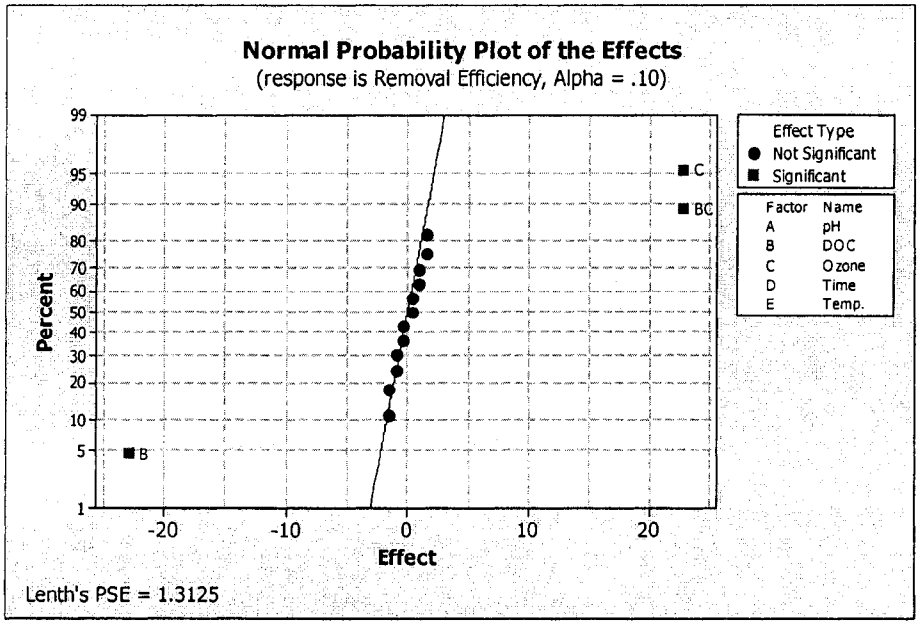

Interaction of Ozone and Temperature
Transformation, % (Mean)
95
90
85
80
75
-1
1
Temperature
Ozone
-1
1

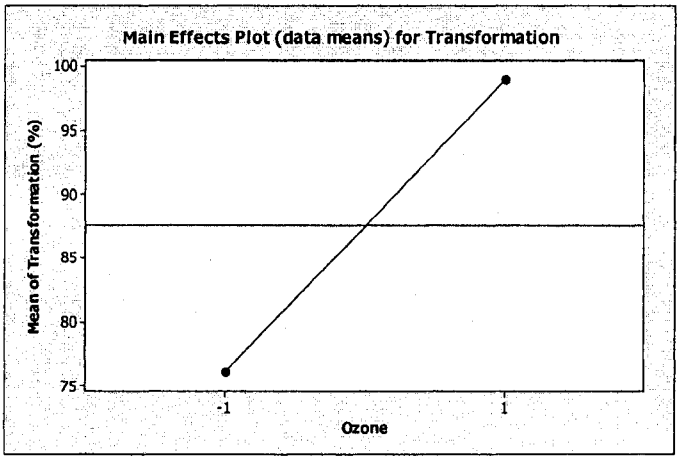


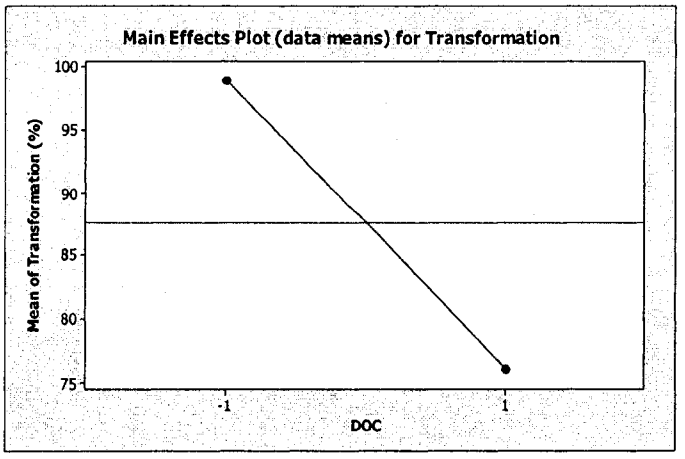
ANOVA Table

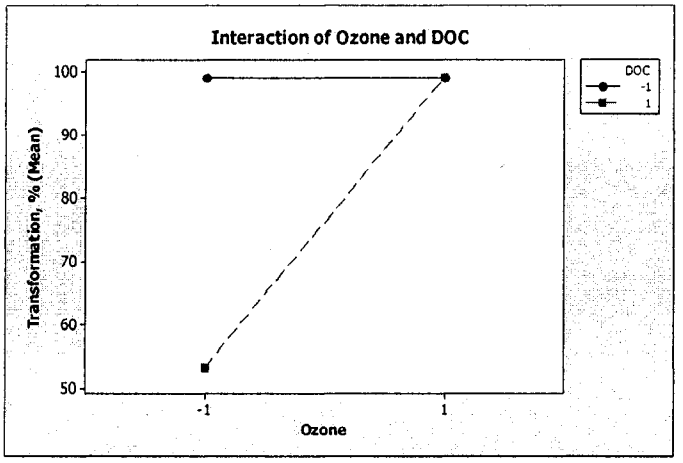
Source	DF	Seq SS	Contribution (%)
B	1	637.6	23.1
C	1	637.6	23.1
E	1	203.1	7.4
A*D	1	203.1	7.4
B*C	1	637.6	23.1
B*E	1	203.6	7.4
C*E	1	203.6	7.4
Error	8	32.5	1.1
Total	15	2757.7	
R-Sq =98.9 %			

5. Gemfibrozil





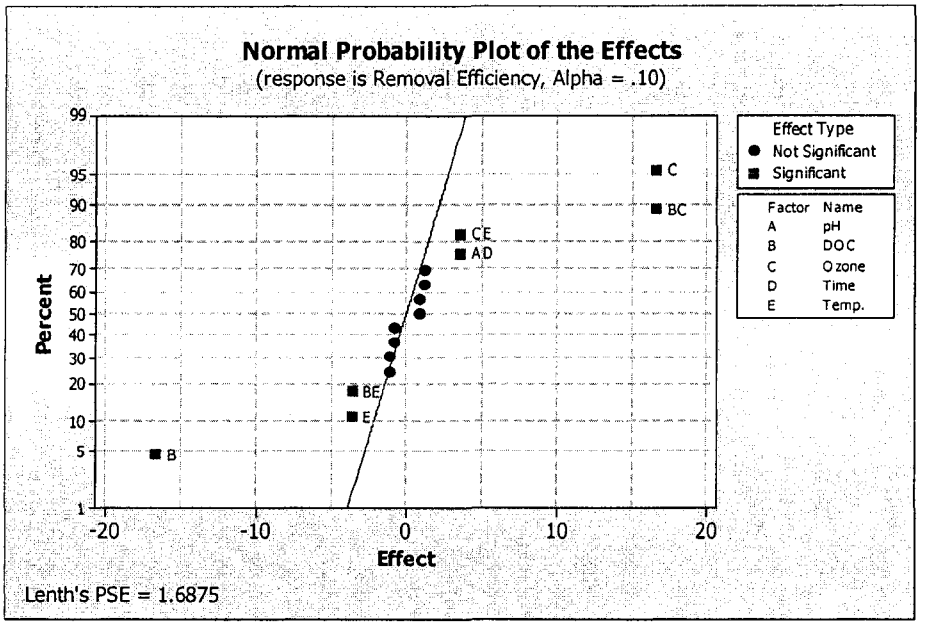


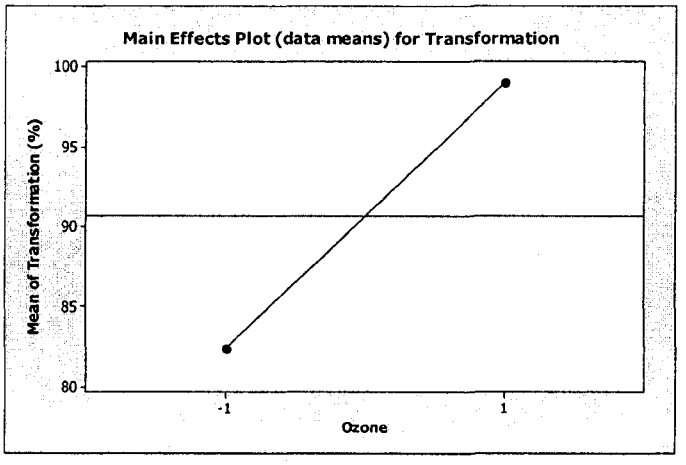


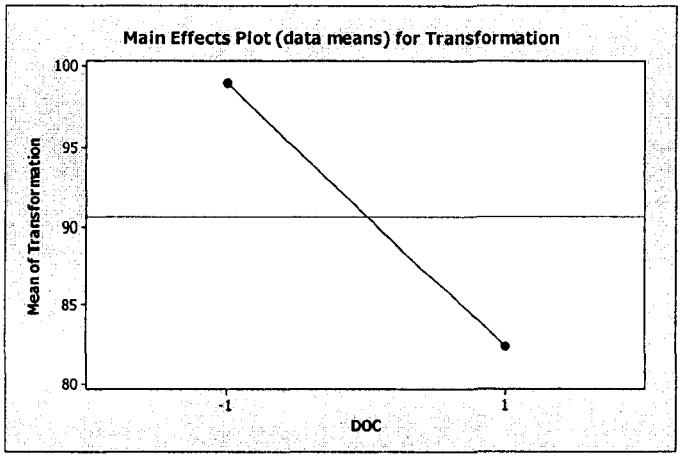
ANOVA Table

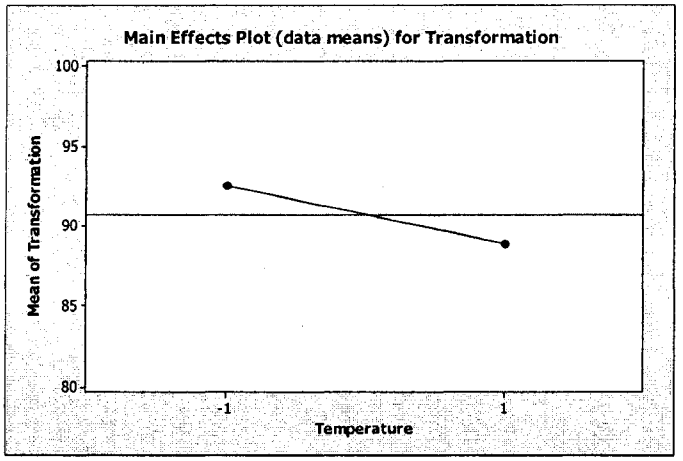
Source	DF	Seq SS	Contribution (%)
B	1	2093.1	33.0
C	1	2093.1	33.0
B*C	1	2093.1	33.0
Error	12	56.8	1.0
Total	15	6335.9	
R-Sq = 99.0 %			

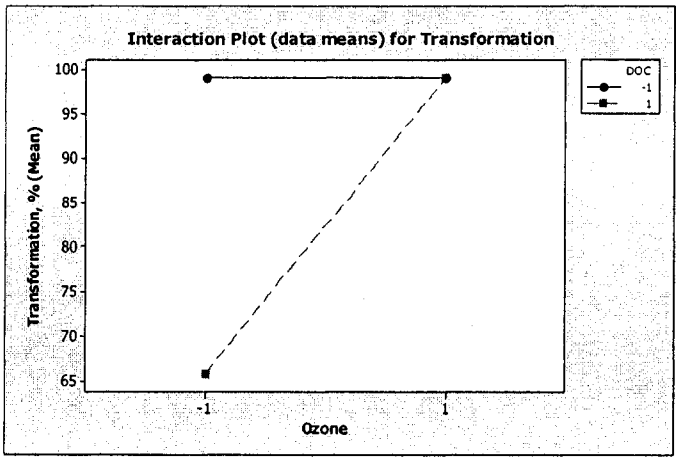
6. Naproxen

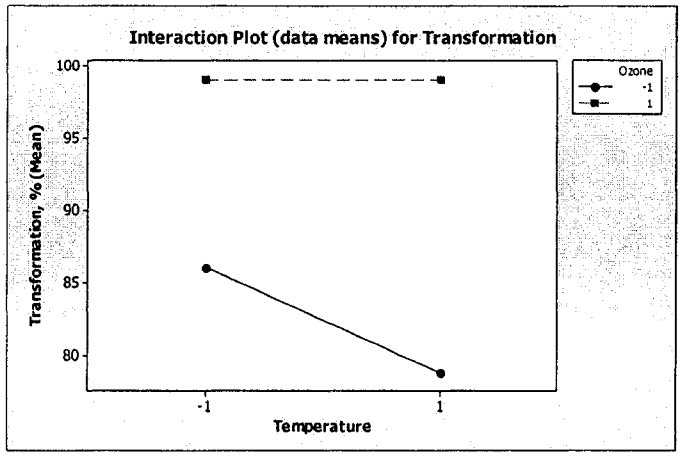

Normal Probability Plot of the Effects
(response is Removal Efficiency, Alpha = .10)
Effect Type
Not Significant
Significant
Factor Name
A pH
B DOC
C Ozone
D Time
E Temp.
Percent
Effect
C
BC
CE
AD
BE
E
B
Lenth's PSE = 1.6875

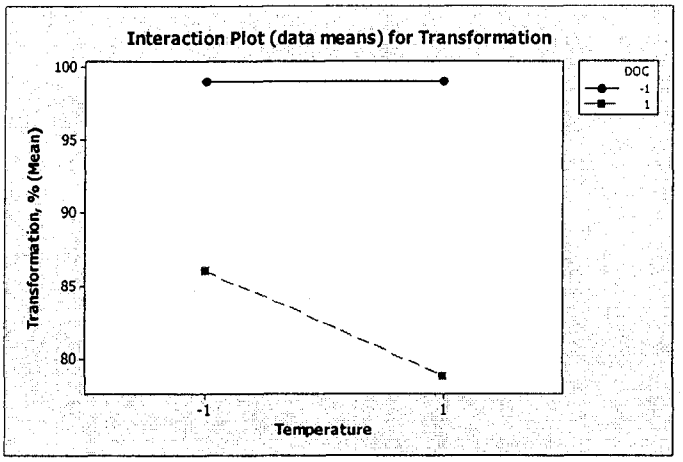

Main Effects Plot (data means) for Transformation
Mean of Transformation (%)
Ozone


Main Effects Plot (data means) for Transformation
Mean of Transformation
DOC


Main Effects Plot (data means) for Transformation
Mean of Transformation
100
95
90
85
80
-1
1
Temperature


Interaction Plot (data means) for Transformation
Transformation, % (Mean)
100
95
90
85
80
75
70
65
-1
1
Ozone
DOC
-1
1

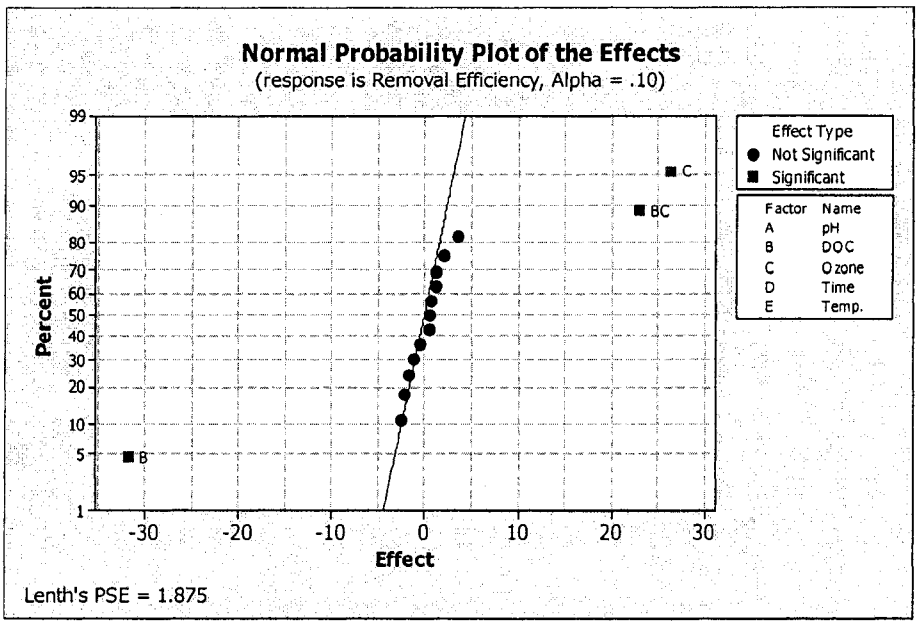

Interaction Plot (data means) for Transformation
Transformation, % (Mean)
100
95
90
85
80
-1
1
Temperature
Ozone
-1
1

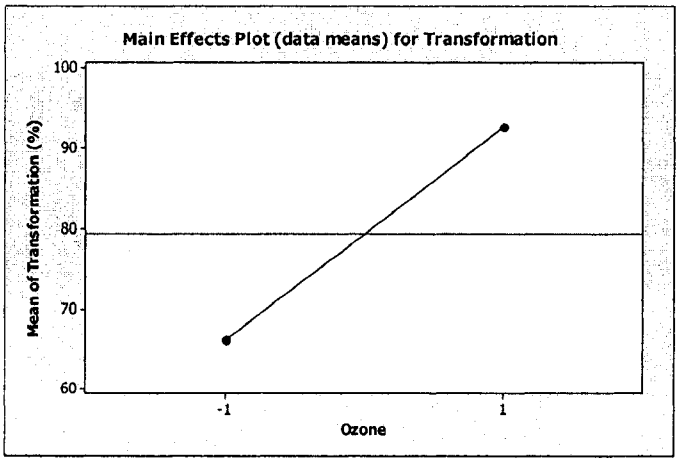


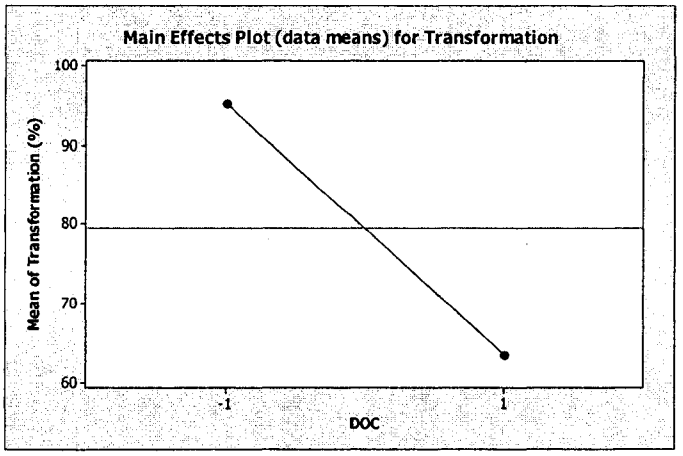
ANOVA Table

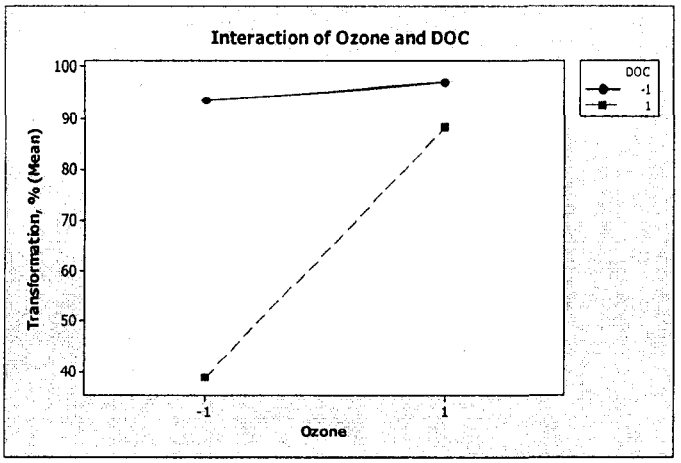
Source	DF	Seq SS	Contribution (%)
B	1	1105.6	31.1
C	1	1105.6	31.1
E	1	52.56	1.5
A*D	1	52.56	1.5
B*C	1	1105.6	31.1
B*E	1	52.56	1.5
C*E	1	52.56	1.5
Error	8	32.49	0.7
Total	15	3559.4	
R-Sq = 99.3 %			

7. Ibuprofen (ESI +)





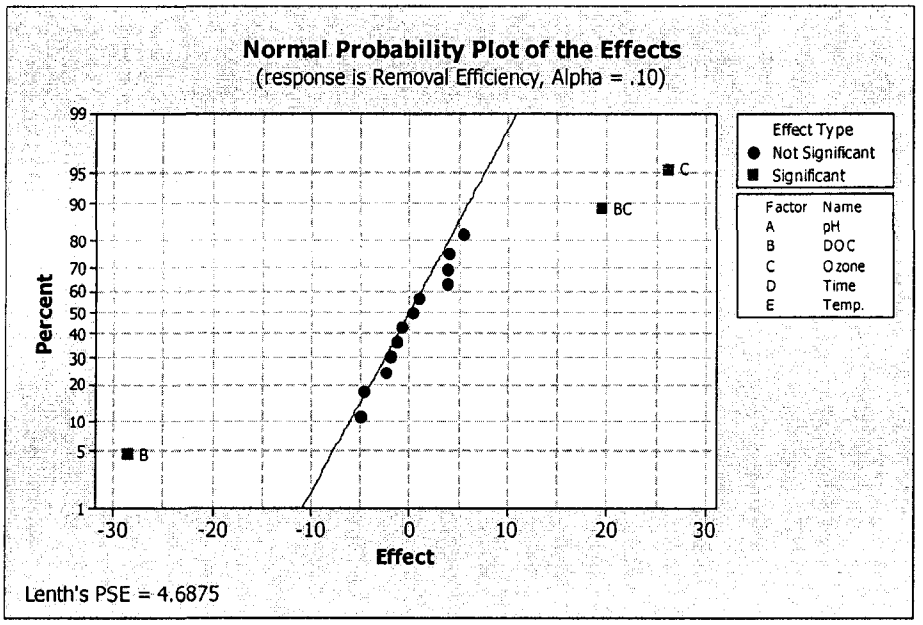


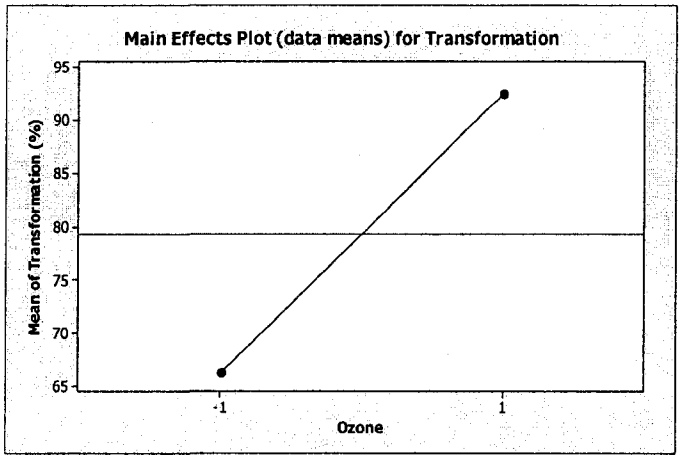


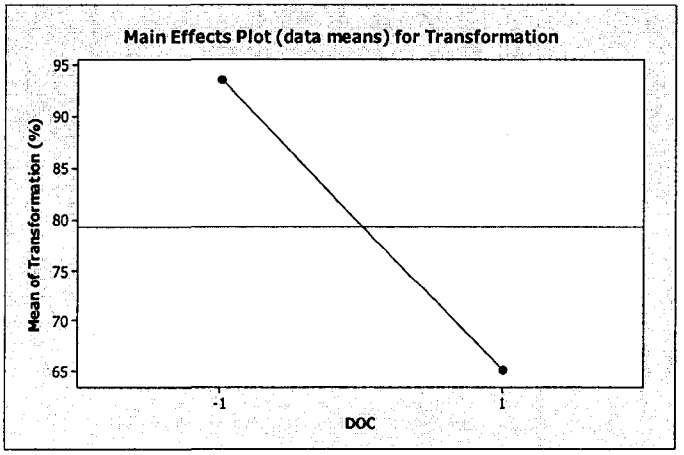
ANOVA Table

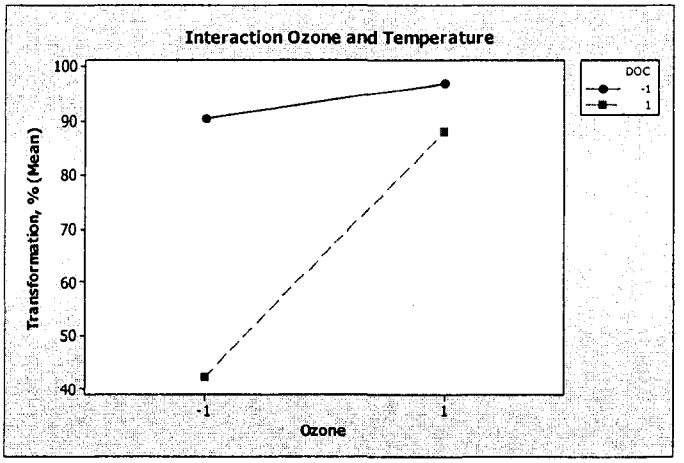
Source	DF	Seq SS	Contribution (%)
B	1	4032.3	44.3
C	1	2809.0	30.9
B*C	1	2116.0	23.2
Error	12	146.5	1.6
Total	15	9103.7	
R-Sq = 98.4 %			

8. Monensin


Normal Probability Plot of the Effects
(response is Removal Efficiency, Alpha = .10)
Percent
Effect
Lenth's PSE = 4.6875
B
BC
C
Effect Type
Not Significant
Significant
Factor Name
A pH
B DOC
C Ozone
D Time
E Temp.


Main Effects Plot (data means) for Transformation
Mean of Transformation (%)
Ozone

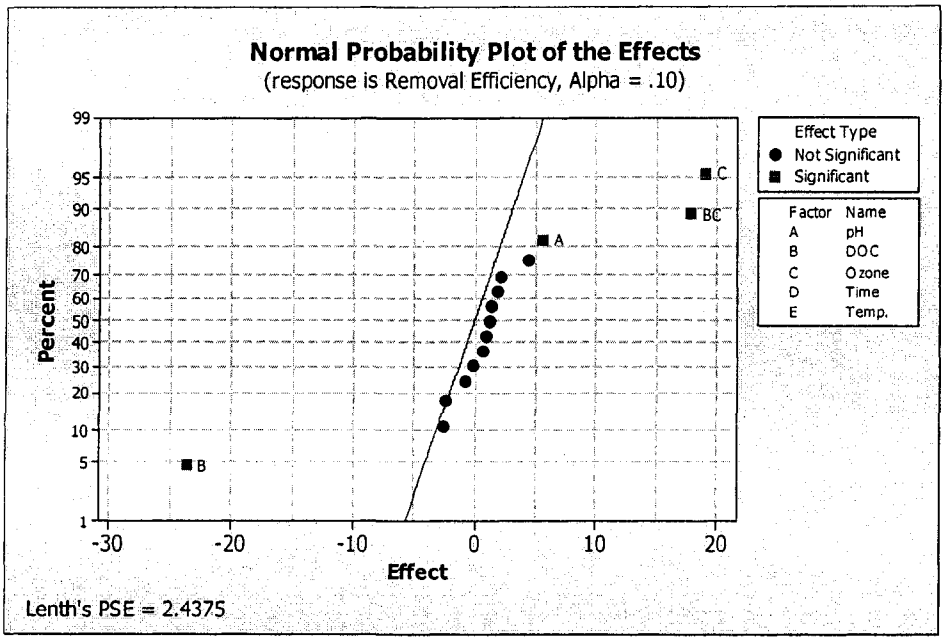

Main Effects Plot (data means) for Transformation
Mean of Transformation (%)
DOC

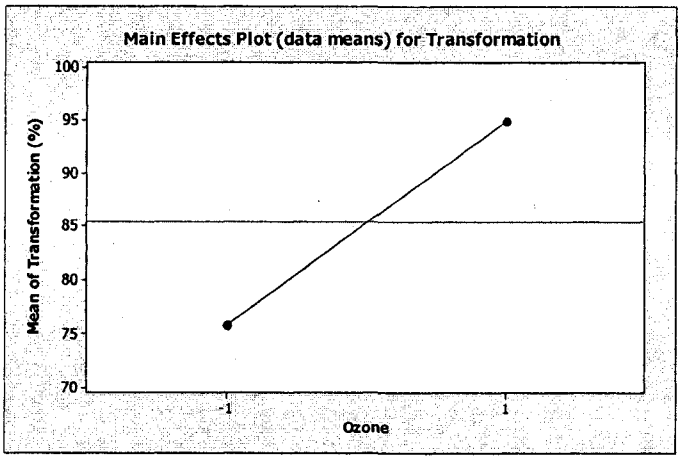


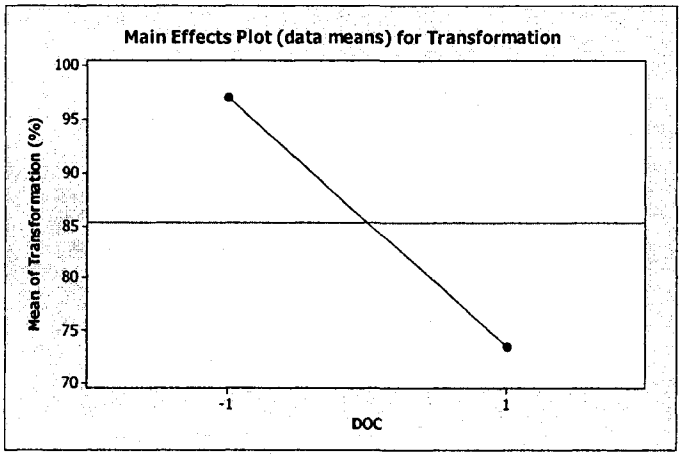
ANOVA Table

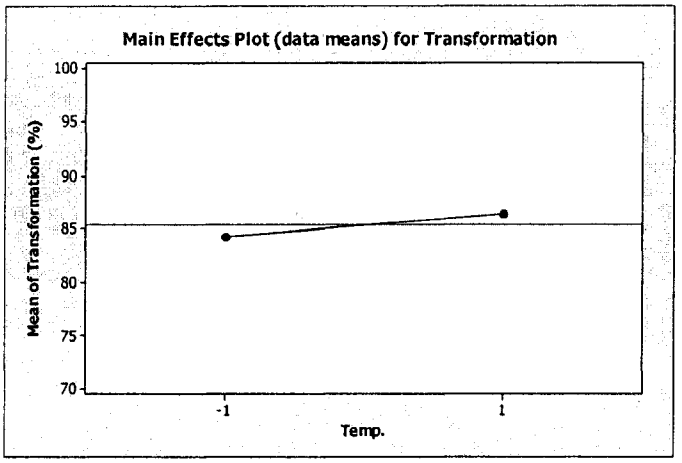
Source	DF	Seq SS	Contribution (%)
B	1	3249.0	40.3
C	1	2756.2	34.2
B*C	1	1521.0	18.8
Error	12	541.5	6.6
Total	15	8067.7	
R-Sq = 93.3 %			

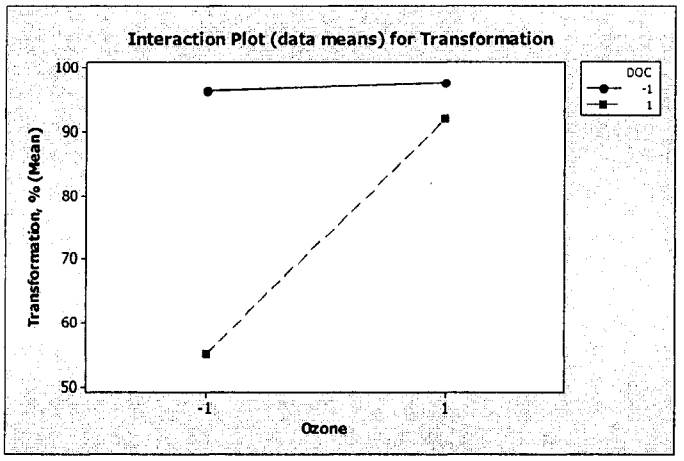
9. Tetracyline







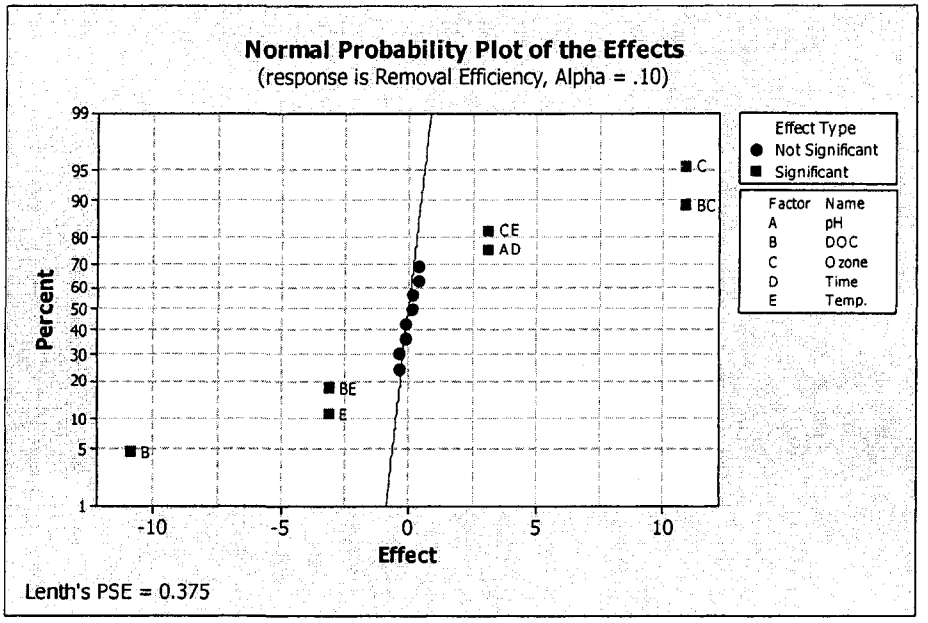


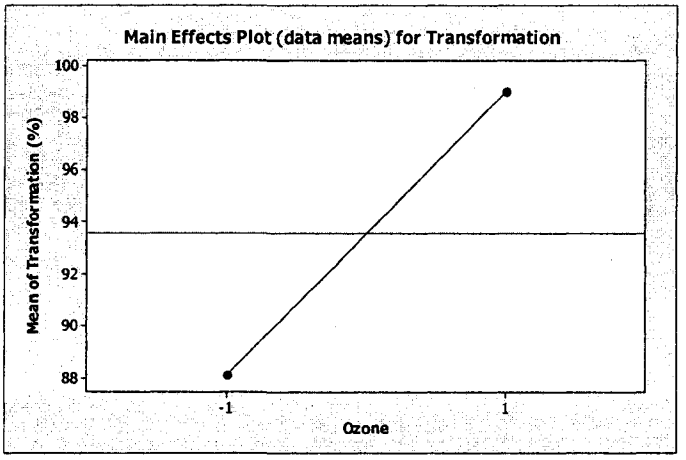


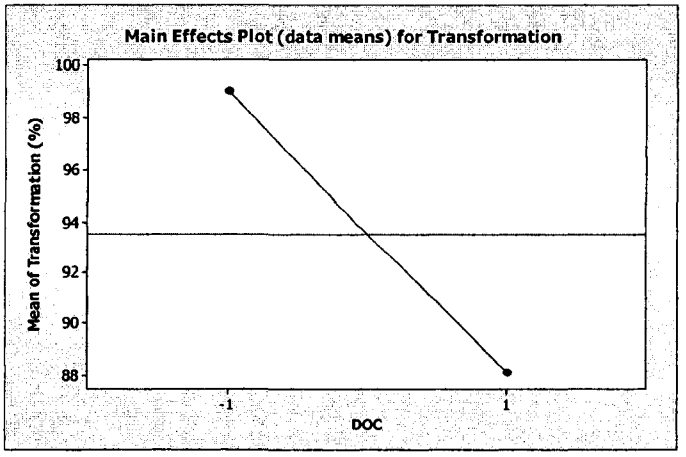
ANOVA Table

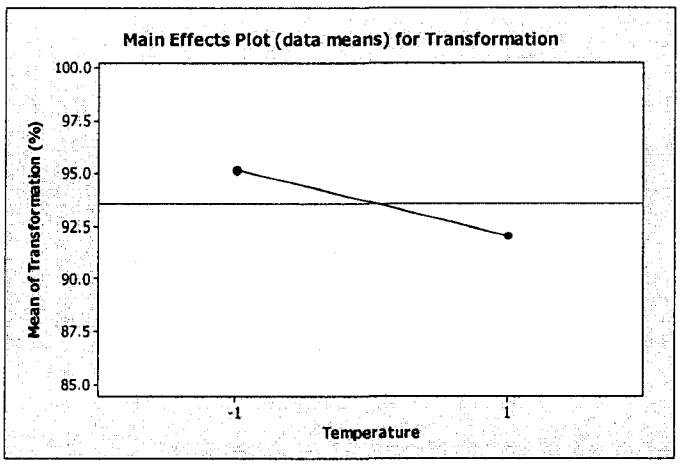
Source	DF	Seq SS	Contribution (%)
A	1	126.6	2.4
B	1	2232.6	42.3
C	1	1463.1	27.7
B*C	1	1278.1	24.2
Error	11	179.2	5.8
Total	15	5279.4	3.4
R-Sq = 94.2 %			

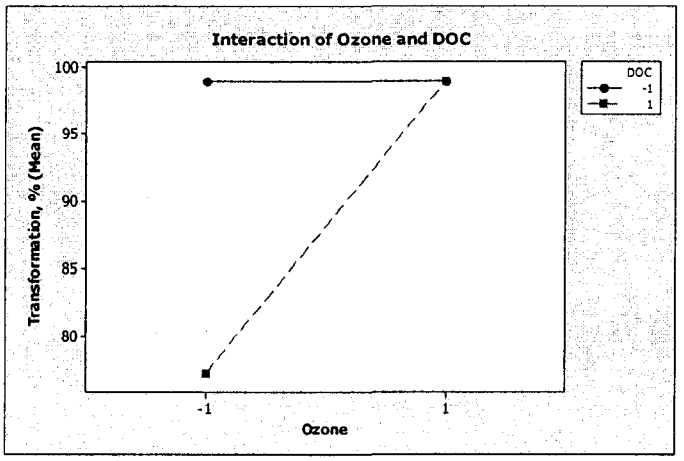
10. Sulfamethazine

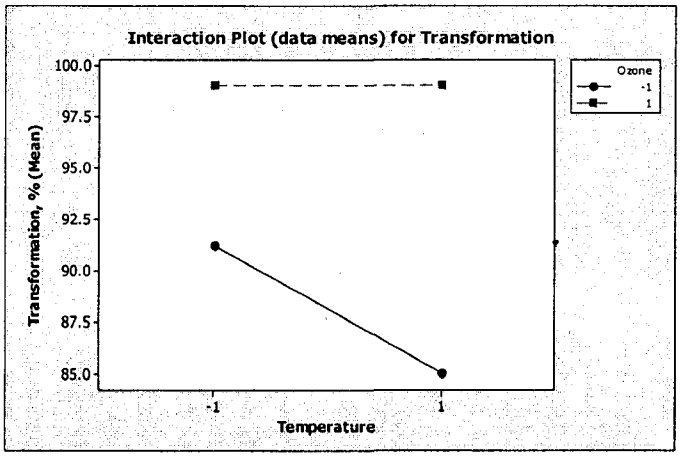


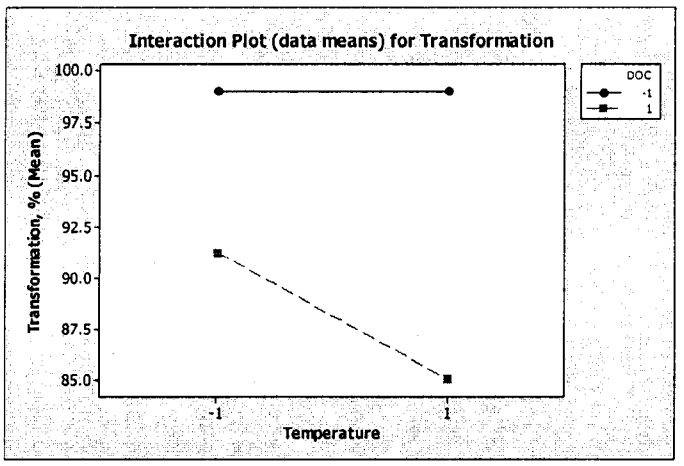





Main Effects Plot (data means) for Transformation
Mean of Transformation (%)
100.0
97.5
95.0
92.5
90.0
87.5
85.0
-1
1
Temperature


Interaction of Ozone and DOC
Transformation, % (Mean)
100
95
90
85
80
-1
1
Ozone
DOC
-1
1

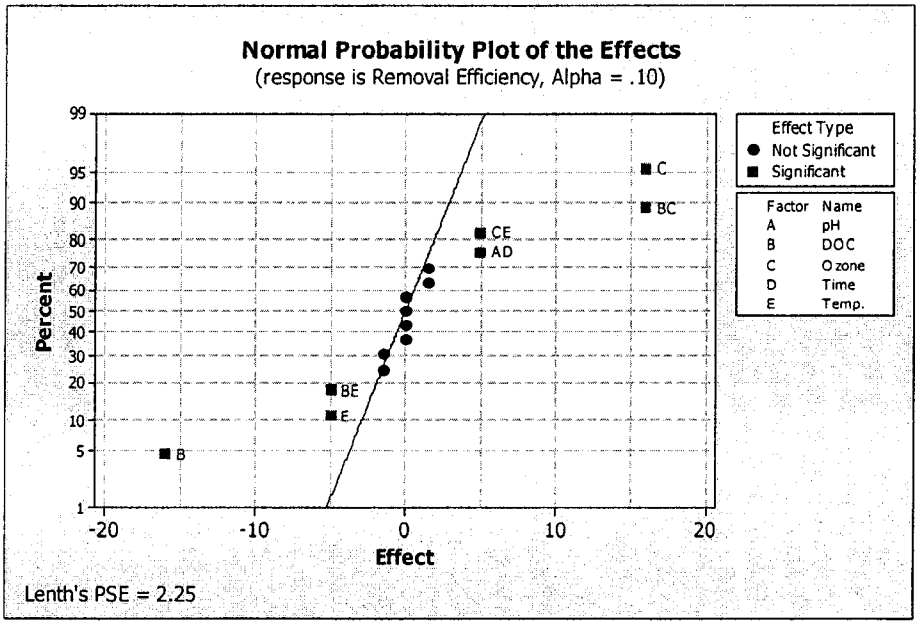

Interaction Plot (data means) for Transformation
Transformation, % (Mean)
100.0
97.5
95.0
92.5
90.0
87.5
85.0
-1
1
Temperature
Ozone
-1
1

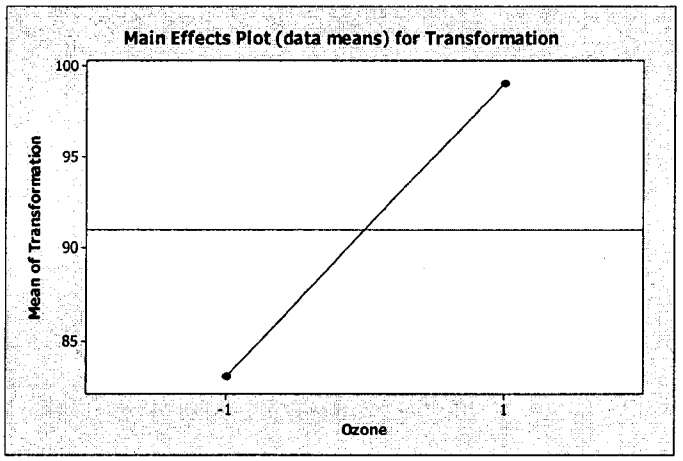


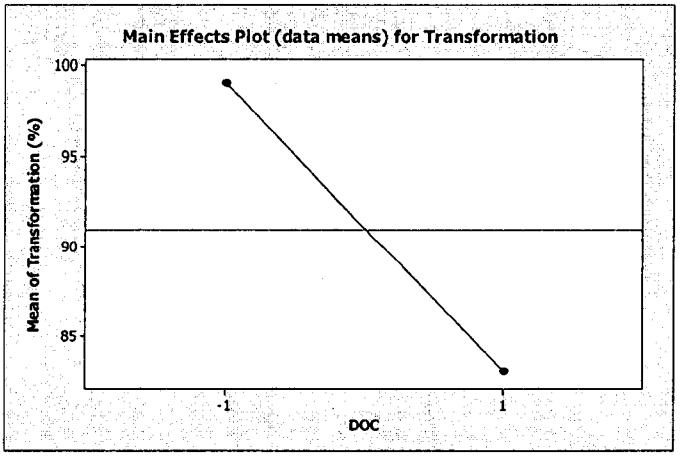
ANOVA Table

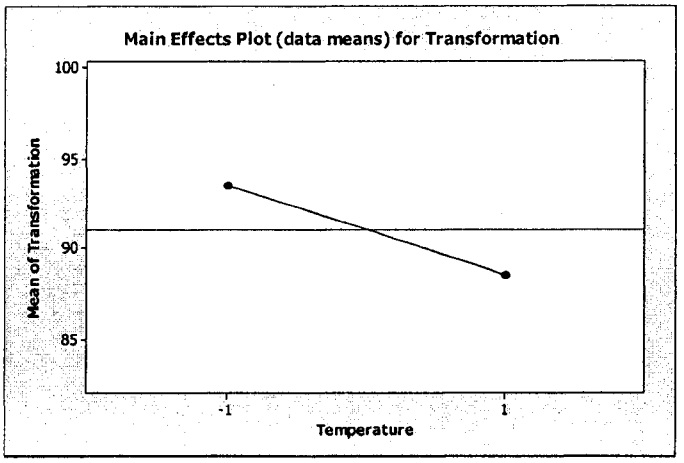
Source	DF	Seq SS	Contribution (%)
B	1	473.1	29.9
C	1	473.1	29.9
E	1	39.1	2.5
A*D	1	39.1	2.5
B*C	1	473.1	29.9
B*E	1	39.1	2.5
C*E	1	39.1	2.5
Error	8	2.6	0.3
Total	15	1578.3	
R-Sq =99.7 %			

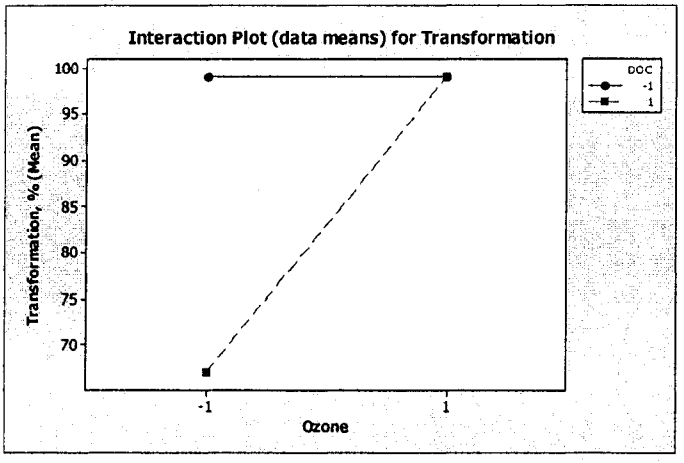
11. Sulfachloropyridazine

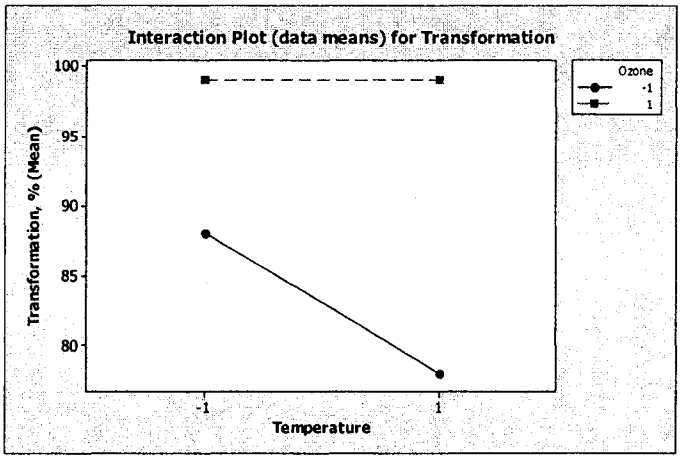


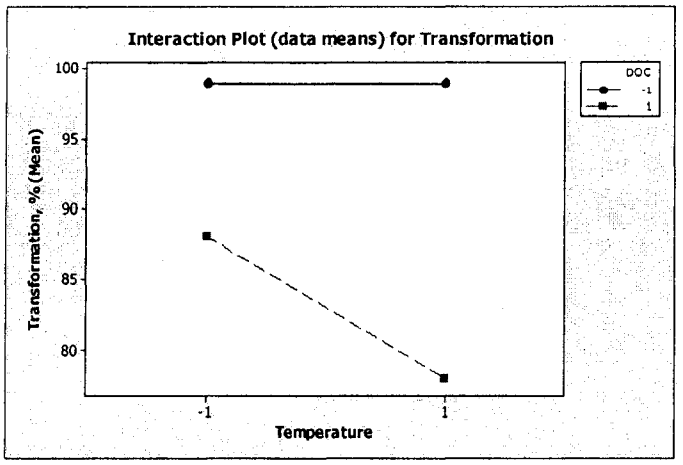





Main Effects Plot (data means) for Transformation
Mean of Transformation
100
95
90
85
-1
1
Temperature


Interaction Plot (data means) for Transformation
Transformation, % (Mean)
100
95
90
85
80
75
70
-1
1
Ozone
DOC
-1
1

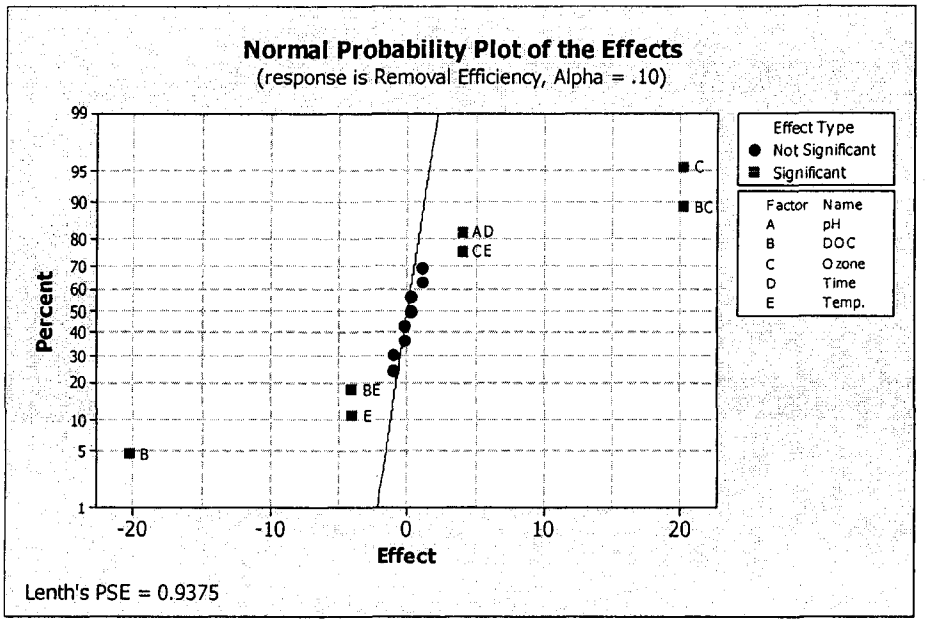

Interaction Plot (data means) for Transformation
Transformation, % (Mean)
100
95
90
85
80
-1
1
Temperature
Ozone
-1
1

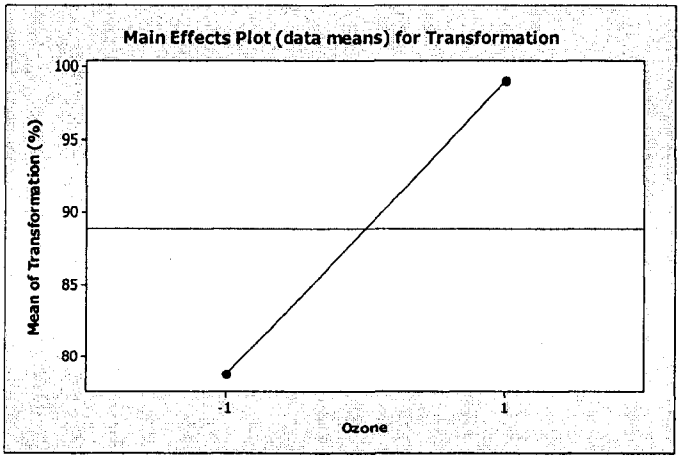


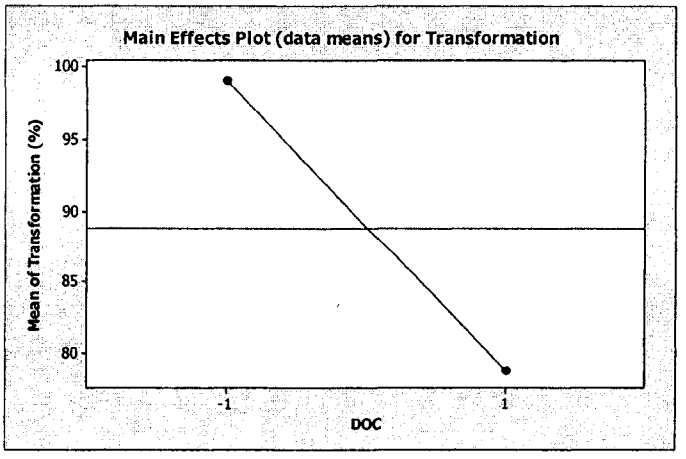
ANOVA Table

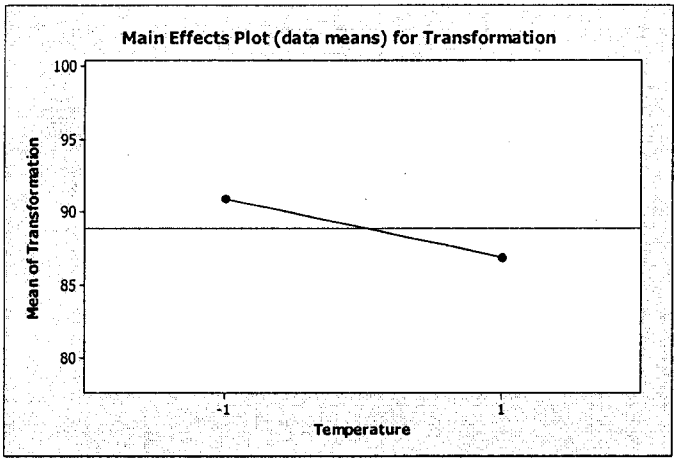
Source	DF	Seq SS	Contribution (%)
B	1	1024.0	29.2
C	1	1024.0	29.2
E	1	100	2.9
A*D	1	100	2.9
B*C	1	1024.0	29.2
B*E	1	100	2.9
C*E	1	100	2.9
Error	8	36	1.0
Total	15	3508.0	
R-Sq =99.0 %			

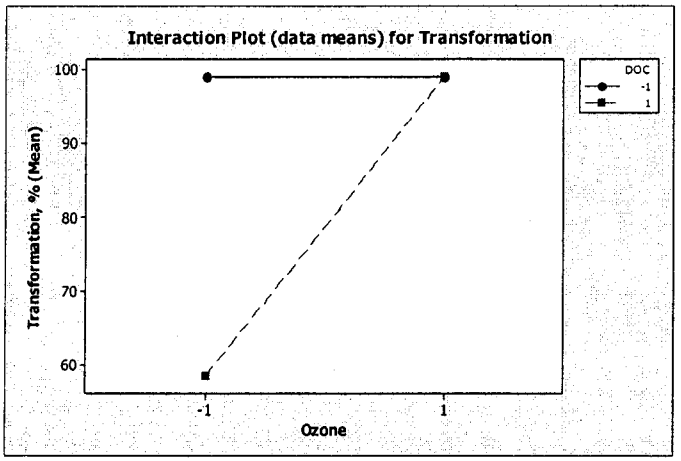
12. Sulfamethoxazole

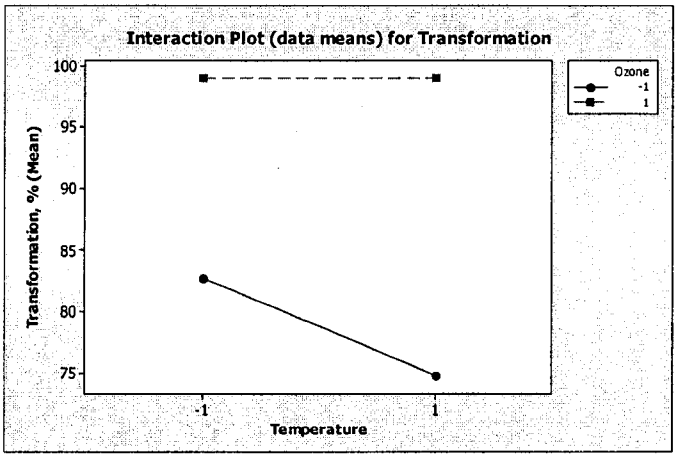


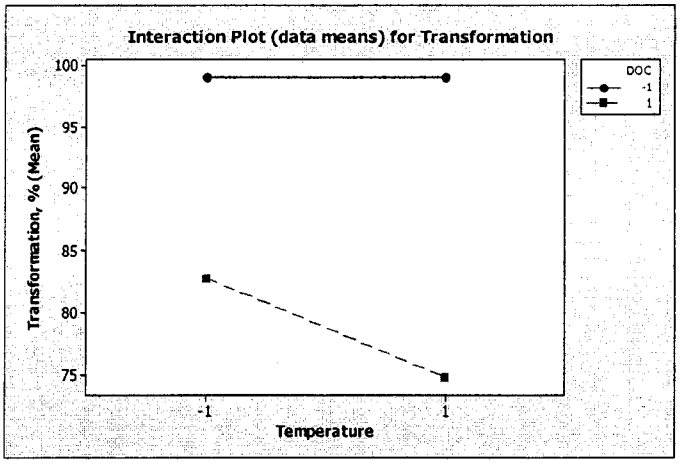





Main Effects Plot (data means) for Transformation
Mean of Transformation
100
95
90
85
80
-1
1
Temperature


Interaction Plot (data means) for Transformation
Transformation, % (Mean)
100
90
80
70
60
-1
1
Ozone
DOC
-1
1

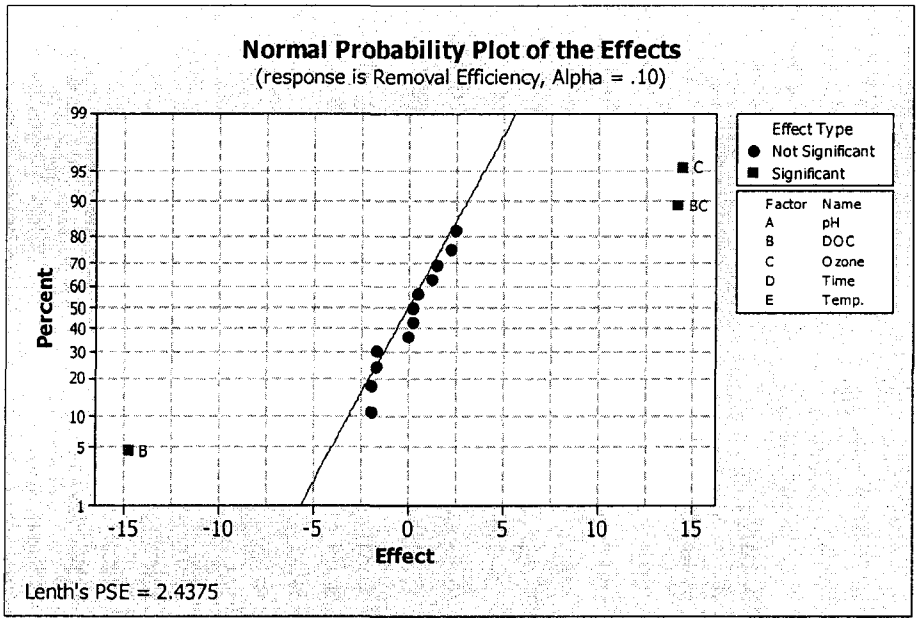

Interaction Plot (data means) for Transformation
Transformation, % (Mean)
100
95
90
85
80
75
-1
1
Temperature
Ozone
-1
1

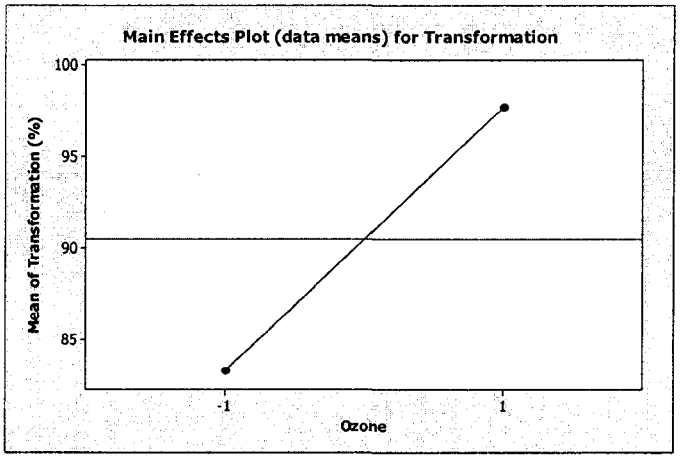


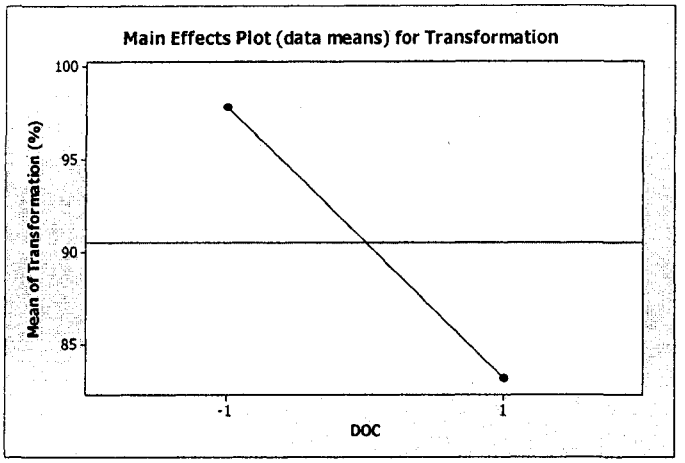
ANOVA Table

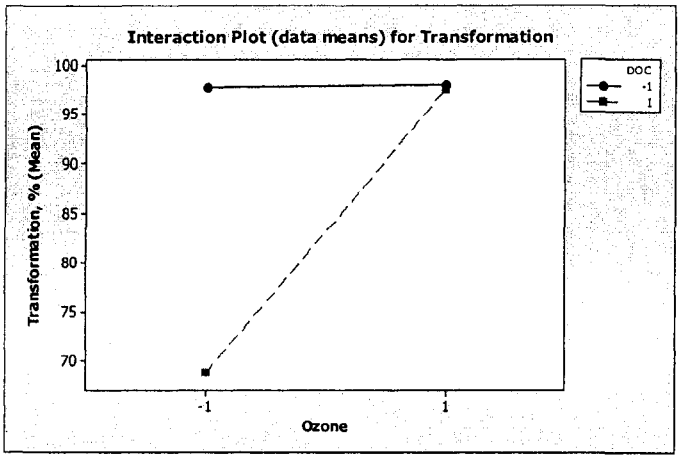
Source	DF	Seq SS	Contribution (%)
B	1	1640.3	31.6
C	1	1640.5	31.6
E	1	64.0	1.2
A*D	1	64.0	1.2
B*C	1	1640.3	31.6
B*E	1	64.0	1.2
C*E	1	64.0	1.2
Error	8	17.0	0.4
Total	15	5194.1	
R-Sq =99.6 %			

13. Tylosin


Normal Probability Plot of the Effects
(response is Removal Efficiency, Alpha = .10)
Percent
99
95
90
80
70
60
50
40
30
20
10
5
1
B
C
BC
-15
-10
-5
0
5
10
15
Effect
Effect Type
Not Significant
Significant
Factor Name
A pH
B DOC
C Ozone
D Time
E Temp.
Lenth's PSE = 2.4375


Main Effects Plot (data means) for Transformation
Mean of Transformation (%)
100
95
90
85
-1
1
Ozone

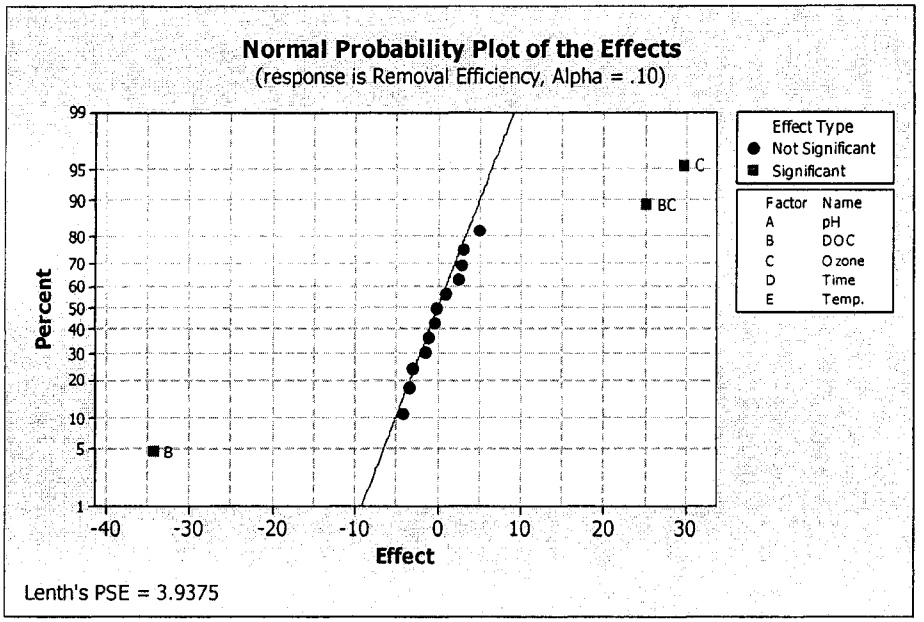


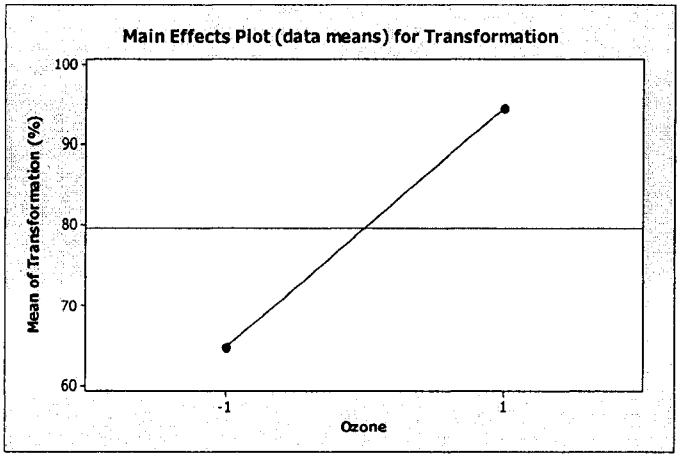


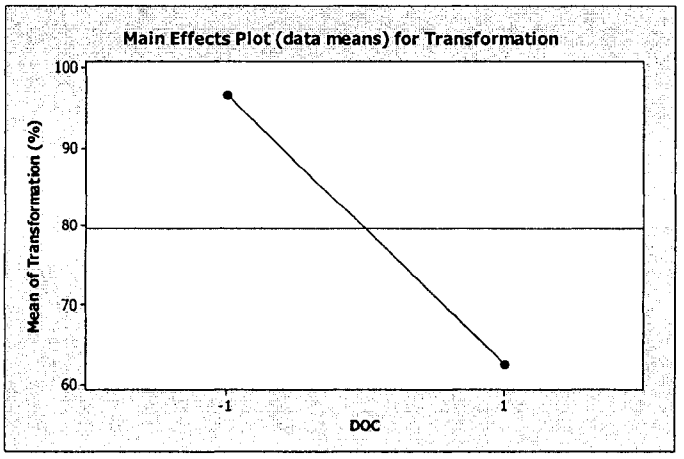
ANOVA Table

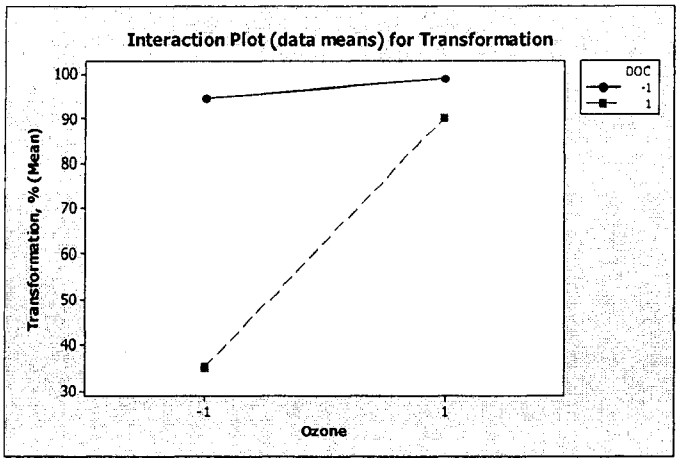
Source	DF	Seq SS	Contribution (%)
B	1	870.3	32.9
C	1	841.0	31.8
B*C	1	812.3	30.7
Error	12	118.5	4.6
Total	15	2643.1	
R-Sq = 95.4 %			

14. Bezafibrate







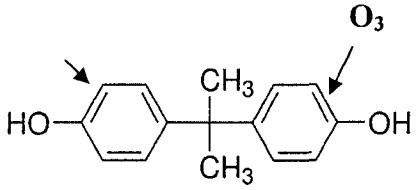


ANOVA Table

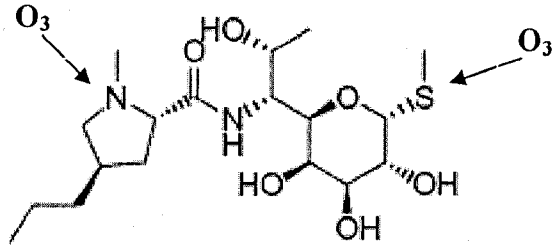
Source	DF	Seq SS	Contribution (%)
B	1	4692.2	42.1
C	1	3540.2	31.7
B*C	1	2550.2	22.9
Error	12	369.0	3.3
Total	15	11151.7	
R-Sq = 96.7 %			

Appendix C: Chemical Structure and Proposed Attack Sites by Ozone (adapted from Ikehata et al., 2006)

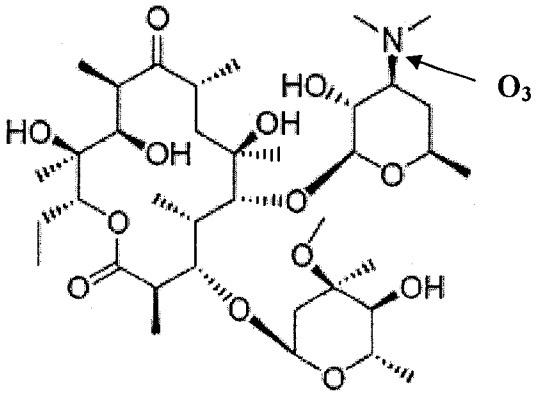
Bisphenol A



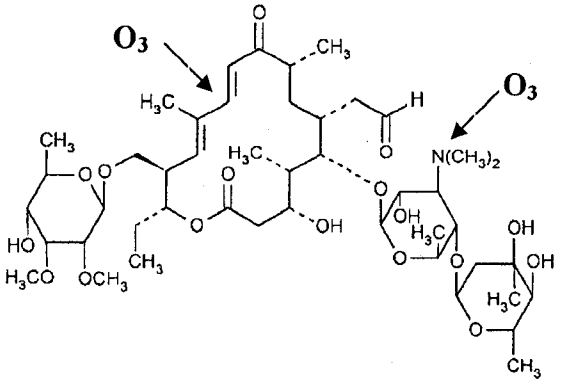
Lincomycin



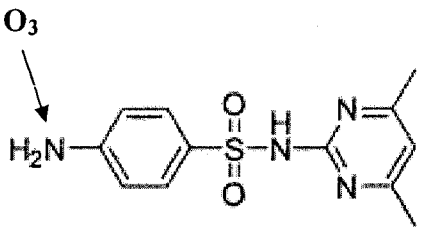
Erythromycin



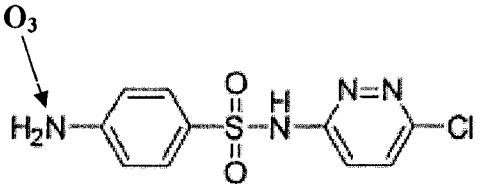
Tylosin



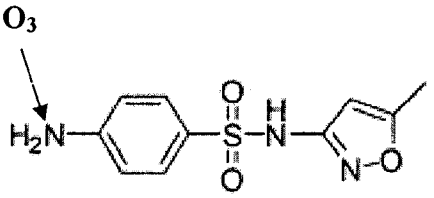
Sulfamethazine



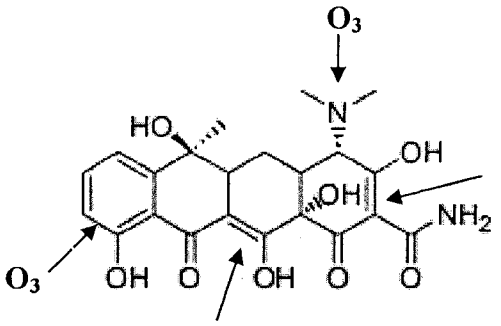
Sulfachorpyridazine



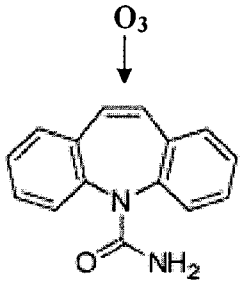
Sulfmethoxazole



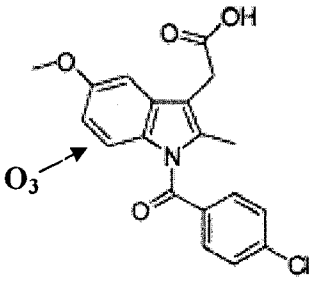
Tetracycline



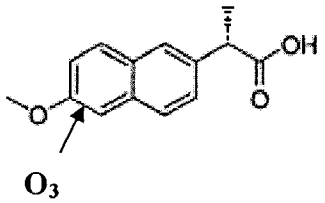
Carbamazepine



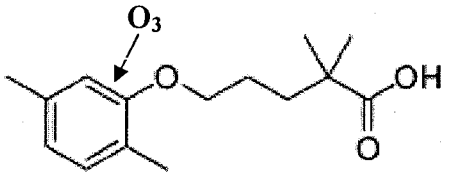
Indomethacin



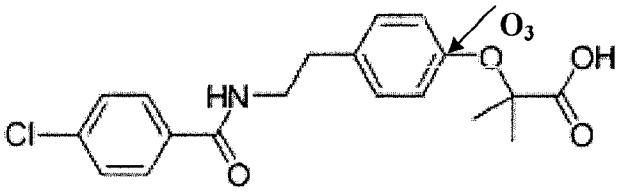
Naproxen



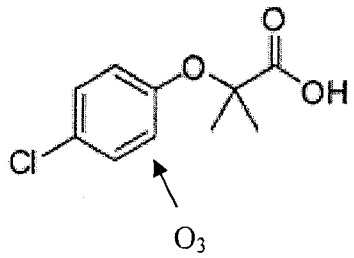
Gemfibrozil



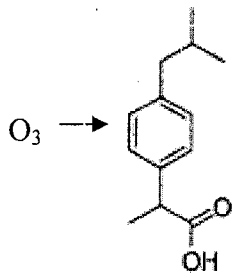
Bezafibrate



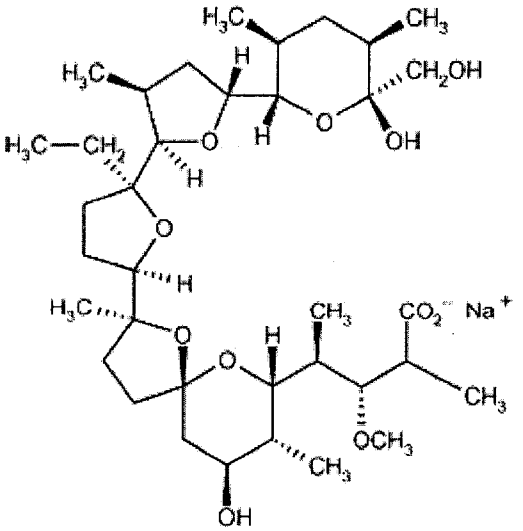
Clofibric acid



Ibuprofen



Monensin



Appendix D: Calculation of Confidence Limit for Linear Regression Coefficient β (slope) (reference: Johnson, R. Miller & Freund's probability and statistics for engineers, 7th Edition, Pearson Prentice Hall, 2005.)

For graph a in Figure 4.15, T=23°C, pH=8.1

Regression Analysis

```
The regression equation is
lnR = - 0.04894 - 0.1116 t (R=ln[O3]t/[O3]60s)


S = 0.0754570   R-Sq = 96.9%   R-Sq(adj) = 96.6%


Analysis of Variance

Source       DF       SS        MS        F       P
Regression    1  1.78015  1.78015  312.65  0.000
Error        10  0.05694  0.00569
Total        11  1.83709
```

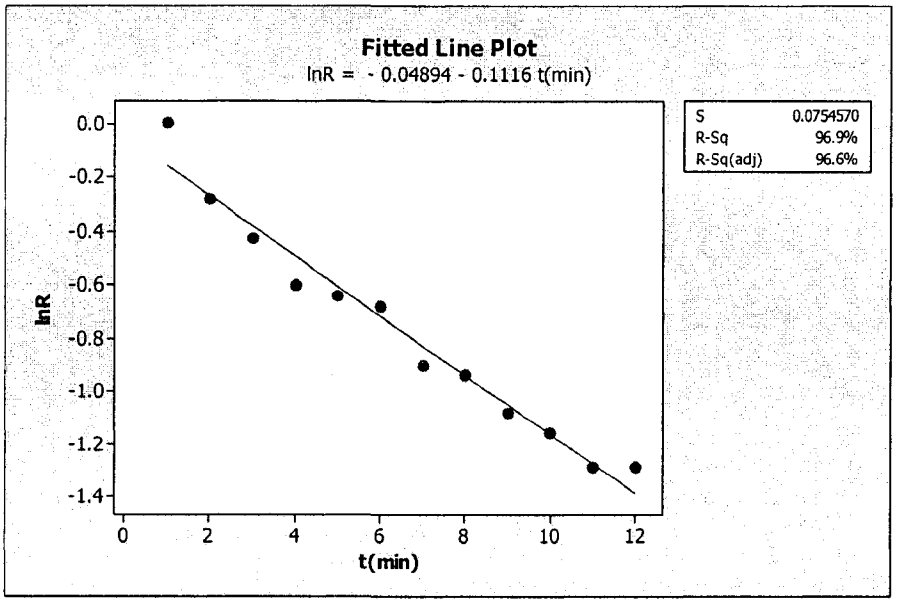


Figure 13. Linear regression

Confidence (90%, α=0.10) limits for regression coefficients

$\beta = b \pm t_{\alpha/2} Se \cdot Sxx^{(-1/2)}$

since b= -0.1116

$t_{\alpha/2, df} = t_{0.05, 10} = 1.812$

Se = 0.0754570

$(Sxy)^2/Sxx = 1.78015$

Sxy/Sxx = b= -0.1116

Therefore,

Sxy= -15.9512, Sxx = 142.93

The confidence limits for β is

$-0.1116 \pm 1.812 \times 0.0754570 \times 142.93^{(-1/2)} = -0.1116 \pm 0.0114$, i.e., **(-0.1230, -0.1002)**

For graph b in Figure 4.15, T=23°C, pH=6.8

Regression Analysis

```
The regression equation is
lnR = 0.04067 - 0.08237 t


S = 0.0894284   R-Sq = 92.8%   R-Sq(adj) = 92.1%


Analysis of Variance

Source       DF       SS       MS       F      P
Regression    1  1.12691  1.12691  140.91  0.000
Error        11  0.08797  0.00800
Total        12  1.21488
```

In a same manner, the confidence limits for β is calculated as

$-0.08237 \pm 1.796 \times 0.0894284 \times 166.0929^{(-1/2)} = -0.0824 \pm 0.0125$, i.e. **(-0.0949, -0.0699)**

Vita Auctoris

Name: Chaoyang Yue

Year of Birth: 1968

Place of Birth: Jiangxi, China

Education: Wuhan University of Technology, China

1985-1989 B. Eng.

University of Windsor, ON, Canada

2002-2005 M.Sc. (Chemistry)

2006-2008 M.A.Sc

Publications:

(1) Yue, C.; Antonelli, D. M. *Inorg. Chem.* **2007,** 46, 5084.

(2) Yue, C.; Trudeau, M.; Antonelli, D. M. *Chem. Commun.* **2006**, 18, 1918.

(3) Yue, C.; Trudeau, M.; Antonelli, D. M. *Can. J. Chem.* **2005,** 83, 308.