TREATMENT OF PHARMACEUTICAL WASTEWATER USING ADVANCED OXIDATION PROCESSES

A thesis submitted in partial fulfilment of the requirements for the award of degree of

Doctor of Philosophy
in
Environmental Engineering

By

Manisha Verma

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DEPARTMENT OF ENVIRONMENTAL ENGINEERING

DELHI TECHNOLOGICAL UNIVERSITY

DELHI

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DECLARATION

I hereby declare that the research work presented in this thesis entitled "Treatment of pharmaceutical wastewater using advanced oxidation processes" is original and carried out by me under the supervision of Dr. A.K. Haritash, Associate Professor, Department of Environmental Engineering, Delhi Technological University, Delhi, and being submitted for the award of Ph.D degree to Delhi Technological University, Delhi, India. The content of this thesis has not been submitted either in part or whole to any other university or institute for the award of any degree or diploma.

Manisha

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एक कदम स्वच्छता की ओर

Date: 16/10/2020

CERTIFICATE

This is to certify that the Ph.D thesis entitled "Treatment of pharmaceutical wastewater using advanced oxidation processes" being submitted by Ms. Manisha Verma for the award of the degree of Doctor of Philosophy in Environmental Engineering, Delhi Technological University, Delhi, India, is a bonafide record of original research work carried out by her under our guidance and supervision. The results embodied in this thesis have not been submitted to any other university or institution for the award of any degree or diploma.

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Manisha

Manisha Verma

Abstract

There has been a rapid increase in pharmaceutical industries in the past few years. These industries utilize natural water as a raw material in distinct manufacturing processes. The wastewater generated from manufacturing processes contains mainly the concentration of manifold chemicals, antibiotics, hormones, *etc*. Discharge of these chemicals in the aquatic environment has resulted in water pollution, bioaccumulation in aquatic organisms, death of microorganisms, disruption of nutrient cycling, and an effect over ecosystem functions. Recently, Advanced Oxidation Processes (AOPs) such as photocatalysis, Fenton, Sonication and their integrated processes have gained attention for degradation of recalcitrant compounds. Among pharmaceutical compounds, the major concern is towards antibiotics such as amoxicillin (AMX), and β-blocker like Atenolol (ATL). The present study dealt with degradation of pharmaceutical drugs using AOPs. The variable parameters regulating AOPs *viz*. pH, H_2O_2 concentration, $FeSO_4$, TiO_2 *etc*. were optimised during the study, and degradation of the order of 80% for AMX and 90% ATL, respectively, was recorded. The optimum conditions of Fenton treatment were further used to perform treatment integrated with UV and ultrasound. Similarly, optimized conditions from photocatalysis with H_2O_2 in case of AMX were utilized to perform photocatalysis and sono-photocatalysis experiments. It was observed that exposure to solar or UV light is necessary for effective degradation of pharmaceutical drugs, especially with respect to rate of treatment. Higher rate of degradation ensures treatment of larger volumes of pharmaceutical effluents. The optimised conditions of AOPs were found to be evenly effective for treatment of real pharmaceutical wastewater. The HPLC analysis confirmed no formation of intermediate product of degradation confirming that the AOPs lead to mineralisation of AMX and ATL with no residual toxicity. Photo-Fenton process has an ability to completely degrade AMX as well as ATL in lesser time duration as compared to other treatment processes. Response Surface Methodology (RSM) was used to optimize and validate the treatment processes and the model represented a good fit with the observed results. The study concluded that AOPs can be employed for treating pharmaceutical wastewater for complete degradation of residual antibiotics to manage the mounting problem of antibiotic-resistant bacteria and anti-biotic resistant genes in environment. Application of AOPs under solar light is recommended for overcoming the cost where energy input is a limitation, particularly in developing countries.

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List of Abbreviations

AMX	Amoxicillin
ANOVA	Analysis of variance
AO	Anodic oxidation
AOP	Advanced Oxidation Processes
APHA	American Public Health Association
AR	Analytical Reagent
ARB	Antibiotic Resistant Bacteria
ARGs	Antibiotic Resistant Genes
ATL	Atenolol
BBD	Box-Behnken Design
BCF	Bioconcentration Factor
BDD	Boron Doped Diamond
BOD	Biological Oxygen Demand
COD	Chemical Oxygen Demand
CPCB	Central Pollution Control Board
DDD	Defined Daily Dose
DOE	Design of Experiments
D_{ow}	Water Distribution
EAOPs	Electrochemical Advanced Oxidation Processes
EC	Electrical Conductivity
EC_{50}	Half Maximal Effective Concentration
ECs	Emerging Contaminants
EF	Electro-Fenton
ETP	Effluent Treatment Plant
GPI	Grossly Polluting Industries
HPLC	High Pressure Liquid Chromatography
K_{ow}	Water Partition
LC_{50}	Lethal Concentration 50%
LOEC	Lowest Observed Effects Concentration
NHE	Normal Hydrogen Electrode
NOEC	No Observed Effect Concentration
NSAIDs	Non-steroidal anti-inflammatory drugs
NTU	Nephelometric Turbidity Units
nZVI	Nanoscale Zero-Valent Iron
OFAT	One-Factor-At-A-Time
PCBs	Polychlorinated Biphenyls
PCs	Pharmaceutical Compounds
PPCP's	Pharmaceuticals Drugs and Personal- Care Products
RSM	Response Surface Methodology
STPs	Sewage Treatment Plants
TDS	Total Dissolved Solid
TMP	Trimethoprim
TSS	Total Suspended Solids
VOCs	Volatile Organic Compounds
VOCs	Volatile Organic Compounds
WHO	World Health Organisation
λ_{max}	Maximum wavelength

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CHAPTER 1
INTRODUCTION

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INTRODUCTION

Water is one of the essential components for supporting the life. It is dominantly required in three sectors *i.e.* domestic, agricultural and industrial. Approximately, 1.4 x 10^{18} m^3 of water is present on earth, of which 35 x10^{15} m^3 is freshwater and only 0.3% of this freshwater is present in lakes, rivers and reservoirs and the remaining 68.9% is trapped in permanent glaciers and snow. Around 11 x10^{15} m^3 (30%) of fresh water is present as ground water on earth. So only a small part of fresh water resources (<1%) is available for use of humans and other life forms (Shiklomanov 2003). The quality of freshwater resources is declining gradually. Human activities and the industries are the major contributor in adversely affecting the water quality which ultimately leads to pollution and limited use of fresh water resources (Pimentel et al., 2004).

1.1 Indian Scenario

Indian industrial sector is growing rapidly from the past few years, and it was expected that India will secure 5th largest manufacturing country in the world at the end of 2020 (IBE 2017). Indian industries produce around 0.013468 billion cubic meters of wastewater daily, out of which only 60% was treated (ASSOCHAM-2019). There has been more than 100% rise in grossly polluting industries (GPI) from 2011 to 2018, and more than 80% industries are located in Uttar Pradesh (UP), Haryana, Gujarat and Andhra Pradesh (AP) in India. Various industries that are included in GPIs are textile, distilleries, sugar, pulp and paper, dairy, fertilizer, petrochemicals and pharmaceuticals. These industries discharge the toxic effluents directly into water resources and account for inevitable degradation of ecosystem (Rajaram & Das, 2008; Manjula, 2016). Effluent discharged from industries includes various persistent pollutants such as microplastics (Li et al., 2017), polychlorinated biphenyls (PCBs) (Chevreuil et al., 1987), pesticides (Kaushik et al., 2008), and emerging contaminants (ECs) such as pharmaceuticals drugs and personal- care products (PPCPs) (Petrie et al., 2014). Over the past few years, major concern is growing towards ECs like as micropollutants because their presence is reported in various sources of water such as surface water, ground water and drinking water (Cabeza et al.,

2012). ECs like pharmaceutical compounds (PCs) are present in the environment in the range of ng/L-µg/L and its steady exposure may lead to adverse effects (Gani & Kazmi 2017).

Pharmaceutical industry is considered as one of the important industry for economic growth and health of people in the country. There is rapid growth in pharmaceutical industry in India over past few years, which leads to improvement in economic growth and public health. Among the pharma industries in whole world, India secures third largest place in terms of volume drugs produced. Every year it generates more than USD 11 billion in trade surplus. The Indian pharmaceutical industry is in the top five sectors which contributed in trade deficit reduction. It was predicted that in 2024 annual revenues of Indian pharmaceutical industry will become ~USD 65 billion and in 2030 it will hit to ~USD 120 to 130 billion approximately (https://www.ipa-india.org). The chemical and manufacturing processes in pharmaceutical industries need water as a basic material whereas various operations such as cooling, production and material processing require persistent and high-quality water supply. The manufacturing plants use distinct types of reactants, catalysts, solvents, solids, and water, handled in special equipment. The wastewater discharged from different pharmaceutical units produces different volumes of wastewater depending on the scale of production. It not only differs in volume but also in concentration of various components. It was predicted that most of the wastewater generated worldwide during pharmaceutical operations has been discarded untreated (Enick & Moore, 2007). As per recent studies, it has been shown that the higher concentration of the pharmaceuticals present in the environment is due to the untreated wastewater discharge by various pharmaceutical industries rather than caused by drugs usage (Gadipelly et al., 2014). Other sources through which PCs reach to the environment are agricultural settings, hospitals, aquaculture, and municipal wastewater treatment plants etc. (Bielen et al., 2017). There are diverse available routes and sources through which PCs enter the aquatic ecosystem. Pharmaceutical drugs may get bioaccumulated in a distinct chamber of freshwater such as sediments, invertebrates, biofilms including *Ceriodaphnia dubia, Daphnia magna, Hyalella azteoa* as well as fishes like brown trout *(salmo trutta)* etc. These drugs have a capability to affect the ecological functions, ecological processes and biogeochemical cycles of various elements by affecting bacterial *(V. fischeri, A. salmonicida) and algal (M.aeriginosa, S.acutus)* communities. Various ecological functions such as transformation of nutrients, and decomposition of organic matter moderated by fungi and bacteria are also affected by these drugs (Fatta-Kassinos et al., 2011).

1.2 Pharmaceuticals and Environmental Issues

Various classes of pharmaceuticals detected in environment are antibiotics, anti-inflammatory drugs, cancer therapeutics, analgesics, ste drugs roids, lipid regulators, and beta-blockers. These pharmaceutical drugs show numerous effects on human, animals and ecosystems. The possible pathways through which drugs invade into environment are drug discharge from manufacturing units directly into wastewater system, excretion of parent compound from treated patients, and domestic discharges of unused drugs (Corcoran et al., 2010). Amoxicillin, diclofenac, erythromycin, gemfibrozil, propranol, atenolol, ibuprofen, ofloxacin, and sulfamethoxzole are some of the most frequently detected drugs in wastewater as well as in aquatic environment (Fatta-Kassinos et al., 2011). Among PCs, major concern is towards antibiotics because these are responsible for spreading and evolving of Antibiotic resistant genes (ARGs) and Antibiotic resistant bacteria (ARB). ARB are those bacteria which can develop resistant against antibiotics (Sivagami et al., 2018). Antibiotics are immensely used for human and veterinary medicine contrary to infections from microbes, and these are defecated from the body of the organism within a short period of time after the consumption. It was reported that at present, there are approximately 20 non-identical classes of antibiotic containing more than 250 distinct antibiotics (García et al., 2020). India is one of the leading consumers of antibiotics among the low middle-income countries during 2000–2015, the consumption increased by over 100% with the base consumption being 3.2 billion defined daily dose (DDD) (Klein et al., 2018). Rate of morbidity and mortality in case of ARB infection is high, and it is expected to increase to approximately 10 million at the end of year 2050 (Amarasiri et al., 2019). It has also been reported that higher levels of antibiotics were released from manufacturing plant in Asian countries compared to discharge in other countries of the world (Bielen et al., 2017). Pollution from antibiotics may harm the ecosystem through the changes in species distribution and by inducing biotoxic effects in organisms (Grenni et al., 2018). In tropical countries, the presence of ARB's causes disturbances to the ecological system and affect human health. Antibiotics present in the soil get absorbed by the plants and can get relocated to groundwater and surface water (Verma & Haritash, 2019). Several researchers have reported the presence of antibiotics in the range of μg/L in surface water, ground water (Ma et al., 2015), drinking water (Sanganyado& Gwenzi 2019), effluents of sewage treatment plants (Birosova et al., 2014), municipal sewage (Watkinson et al., 2009), hospital effluents (Brown et al., 2006) and marine water (Kümmerer, 2009).

Similarly, contamination of water resources due to other pharmaceuticals were reported causing detrimental effects on aquatic organisms. The pharmaceuticals in the environment gets bioaccumulate and bioconcentrate in an organism of trophic level and transfer to higher trophic level i.e. top carnivore through the food chains (Brown et al,. 2007; Paterson & Metcalfe, 2008; Arnold et al., 2015). A study carried out on an antidepressant drug, fluoxetine reported the bioconcentration factor (BCF) of above 1000 in *Elliptio complanate* (mussels) found in fresh water ecosystem. This species of mussel is swallowed by the different species of vertebrae predators which ultimately transferring the drug from one trophic level to other trophic level (Bringolf et al., 2010). PCs not only affect the organisms transferring through food chains but also affects at population level. One of the study reported in India on population of three species of vulture *Gyps bengalensis*, Gyps *tenuirostris* and *Gyps indicus* revealed that population of the vultures got reduced upto 95% due to diclofenac (Prakash et al., 2003; Green et al., 2004; Swan et al., 2006; Gadipelly et al., 2014). The wastes generated from pharmaceutical industries are extensive in volume, complex and hazardous in nature, which makes it difficult to treat the effluents efficiently. The residual drug present in pharmaceutical waste has high chemical oxygen demand (COD), biological oxygen demand (BOD) and also PCs such as antibiotics, hormones, toxic substances and volatile organic compounds (VOCs) which are responsible for contaminating the environment in one way or another (Pal, 2017).

1.3 Treatment of Pharmaceutical Waste

Conventional treatment methods such as physicochemical and biological methods can be used for the treatment of pharmaceutical wastewater. Physicochemical methods include adsorption, frothing, precipitation, electrochemical processes, coagulation-flocculation and combination of these technologies can also be used to treat wastewater. The efficiencies of these processes are poor in eliminating the COD from wastewater, and they are responsible for introducing complex chemicals in wastewater (Pal, 2017). Biological degradation methods such as composting, vermicompositing, aerobic and anaerobic can be used to degrade the pharmaceutical wastewater. Among these methods, anaerobic process is observed to be the most suitable method for degradation due to high COD of pharmaceutical wastewater. It was demonstrated that up-flow anaerobic reactor removes around 75% of COD from the waste having antibiotics. The substances present in pharmaceutical wastewater are complex, which makes them resistant to biological degradation. The residence time required to degrade the pollutants in biological degradation is more, which leads to biomass poisoning and making it

unfit for treating toxic waste. Due to these reasons, conventional treatment is not effective to treat pharmaceutical wastewater (Vlyssides et al., 2008). Therefore, there is a need of more efficient advanced treatment technologies to overcome the existing challenges. Advanced oxidation processes (AOPs) are more efficient in comparison with other techniques because other techniques only transfer the pollutants from one phase to another instead of mineralizing those (Elmolla & Chaudhuri, 2010). Several technologies like Fenton, photo-Fenton, cavitation, photocatalysis, etc. are included in the AOPs and their main difference is the mechanism of radical generation (Kim & Ihm, 2011). AOPs are defined as aqueous phase oxidation processes, which are based on intermediacy of hydroxyl radical resulting in destruction of target pollutant (Chelliapan & Sallis, 2013). Hydroxyl radicals have oxidation potential of 2.80 V vs NHE, second only to Fluorine. They react rapidly and non – selectively with nearly all electron – rich organic compounds.

Advanced treatment methods such as membrane process, ozonation, and advance oxidation process are considered to be efficient to remove pharmaceuticals. Membrane techniques are not advisable because of investment costs, required pretreatment of effluent, and generation of concentrated side streams. Ozonation is able to eliminate some pharmaceuticals but by-products in ozonation effluent are poorly characterized (Dehgani et al., 2013). Fenton process involves reaction of Fe^{2+} and H_2O_2 for the production of hydroxyl radicals and is one of the effective technology in degradation of recalcitrant compounds (Ay & Kargi , 2010). When the optimum pH of the aqueous solution is 2.8-3.0, the Fenton process is more effective (Oturan & Aaron, 2014). Effectiveness of the Fenton process can be increased under UV irradiation as this will lead to generation of more hydroxyl radicals, and this process is known as photo-Fenton process (Klavarioti et al., 2009). Another AOP which makes use of a chemical catalyst to degrade the complex organic pollutants is photocatalysis. It is the process which can be employed for the degradation of organic inorganic in the presence of a chemical and light. All the photocatalysts used in process are semiconductors. There are two kinds of photocatalysis: Homogenous photocatalysis and Heterogenous photocatalysis. In homogenous photocatalysis, both photocatalyst as well as reactant remain in same state. Heterogenous photocatalysis using TiO_2 is the customary used photocatalysis process in which at higher energy (3.2eV) adsorption of photons takes place leading to excitation of particles (Gadipelly et al., 2014).

Ultrasonic waves are also one of the agents which can produce ·OH radicals in aqueous medium thereby facilitating removal of toxic pollutants from it. It removes pollutants without

the generation of toxic secondary metabolites and can be regarded as a 'green' technology. Under the periodic pressure variations, acoustic cavitation implies the formation and subsequent expansion of micro-bubbles which leads to production of ·OH radicals. The AOPs have different modes/mechanisms for removal/degradation of organic impurities from the aqueous medium. Based on the effectiveness of treatment, the efficiency towards removal may vary. Sometimes, the AOPs are responsible for chemical transformation of pharmaceutical compounds to a relatively less/more toxic secondary metabolite without complete mineralization. Therefore, selection of a particular method of AOP, optimization of its regulating parameter; or combination of two or more AOPs may be investigated for enhanced removal efficiency. Keeping in view, the facts mentioned above, the present study was designed with the following objectives.

1.4 Objectives of the Present Study

I. Characterization of pharmaceutical industry wastewater, and determination of drug specific toxicity.
II. To study and compare the efficiencies of different Advanced oxidation processes (photo – Fenton, photo – catalysis, Ultrasonication etc.) towards treatment of pharmaceutical wastewater.
III. To establish the feasibility of different AOPs; and their optimization and validation by Response surface methodology.

CHAPTER 2
REVIEW OF LITERATURE

CHAPTER 2
REVIEW OF LITERATURE

2.1 Status of Pharmaceuticals

Pharmaceuticals can be defined as the chemicals which are utilized to treat, prevent, cure and diagnose the human and animal diseases. These are contemplated as emerging contaminants due to their existence in the environment at trace concentration and may affect health of humans and ecosphere (Quesada et al., 2019; Daughton, 2003). In Asian countries like India, Bangladesh, and China, pharmaceutical industries as well as consumption of pharmaceutical drugs has been rising rapidly (Rehman et al., 2013). Effluents generated from pharmaceutical manufacturing industries find their way to domestic wastewater sewers, natural water streams (rivers, lakes, and ponds), soils, sediments, and plants (Lester et al., 2013; Tran et al., 2018). The concern towards pharmaceutical wastewater was increased when around 100 pharmaceuticals and their metabolites were observed in effluent and surface water in various countries (Ashton et al., 2004; Ankley et al., 2005) The basic crude material needed for the manufacturing of pharmaceuticals is high quality water and most of the wastewater generated from manufacturing processes are discharged without any particular treatment (Enick & Moore, 2007). The processes involved in manufacturing of pharmaceuticals can be categorized as: Synthesis of chemicals, Fermentation, Extraction (Biological/Natural), and Formulation. The detail of each process with their wastewater characteristics is discussed below and **Table 2.1**.

2.1.1 Synthesis of chemicals

In this process, various organic and inorganic chemicals are used to carry out multiple reactions in various stages of the process. This process includes numerous reactors, vessels, and heat exchangers to run the process operations continuously. Generation of mother liquor at various stages of the process undergo production of surplus products in solvents, byproducts and reactants, which have not reacted. This may also give rise to halides, sulfates, nitrates, cyanides, bases, metals, and acids (Kroschwitz, 1992). During purification process, wastewater is produced that contains spills, different cleaning and finished products, and solvents (EPA 1993). Toxicity level

of this wastewater is very high, which needs treatment immediately. Overall, wastewater produced from the chemical synthesis process possesses pH within the range of 1-11, high COD, total suspended solids, and high BOD (EPA 1983; Browner et al., 1998).

2.1.2 Fermentation

This is a biochemical process which has three stages: inoculum of seeds and their preparation, fermentation and recovery of products. For the inoculum, suitable microbes are required and basic conditions of the process are to be maintained. Further, the concentrated mixture is shifted to fermenter in which inorganic salts and nutrients are added (Theodore & McGuinn, 1992). Coolers and heat exchangers are used to control the temperature. The broth produced during process go through the array of various steps like metal salts precipitation, extraction of solvents, addition of phenolics as disinfectants and filtration. Wastewater generated from the fermentation process consists of dead cells, a large amount of unused crude nutrient broth, nitrates, salts and starch. The pH of the wastewater range from 4-8 with high BOD, COD and total suspended solid (TSS) values (EPA 1983; Gadipelly et al., 2014). Production of antibiotic penicillin is mainly executed from the fermentation process (Najafpour, 2007). This may also involve in production of vitamins and steroids.

2.1.3 Extraction

This process involves the processing of huge quantity of natural (plant/animal) substances to extract pharmaceutical compounds from the raw products. To eliminate the lipophilic material and extraction of ultimate product needs large amount of water and solvent like hexane. Metals and phenolic compounds are added for precipitation and disinfection in the process respectively which added numerous components and cause problem in treatment (Gennaro, 1990; Swarbick & Boylan, 1996). Apart from this, acid and bases are also used for adjustment of pH of the solution. Ultimately, the final product from the extraction process is small. Wastewater from extraction mainly constitutes spills, solvents, spent from crude material, wash water and inorganic and organic chemicals in the form of residues. The wastewater has low TSS, BOD, COD and pH from 6-8 (EPA 1983; Gadipelly et al., 2014).

Table 2.1. Characteristics of pharmaceutical waste water based on manufacturing process

Process	Inputs	Characteristics
Chemical synthesis	catalysts, benzene, solvents, chloroform, halides, sulfates, nitrates, cyanides, bases, metals, and acids	Process wastewaters with spent solvents, catalyst, reactants. High in BOD, COD, TSS with pH of 1–11
Separation	Solvents such as hexane, methanol, acetone and toluene	Spills, leaks, spent separation solvents
Purification	Purification of solvents, e.g. Methanol, Toluene, Acetone and Hexane	Spills, leaks, spent separation solvents
Natural product extraction	Plant roots, animal tissues, extraction solvents, e.g. ammonia, chloroform and phenol	Equipment cleaning, Spills, leaks, spent solvents. Low BOD, COD, TSS and pH of 6–8
Fermentation	Dead cells, a large amount of unused crude nutrient broth, nitrates, salts and starch	Spent fermentation broth, wastewater containing sugar, nutrients, etc. High BOD, COD and pH 4–8
Formulations/compounding	Active drug, binders, preservatives fillers, etc.	Equipment cleaning, Spills, leaks, spent solvents. Low BOD, COD, TSS and pH of 6–8.

2.1.4 Formulation/Compounding

The products of the drugs retrieved from the above discussed processes are further used to obtain syrups, ointments, tablets and other form of drugs. This process includes compression, packaging, grinding, mixing and milling. During compounding process different kinds of binders,

preservatives, antioxidants, flavoring agents and fillers are computed. Throughout the process, maintenance of hygienic conditions is needed, which ultimately increases the usage of phenols and steam fumigation. The various stages of the process such as mixing, dilution, addition, filtration, sieving, washing, drying, grinding, encapsulation and eventually packing of drugs may lead to generation of wastewater (Hindiyeh et al., 2018). Manufacturing of drugs may be result of batch, continuous or combination of both depending upon volume to be produced and product value.

2.2 Characteristics of pharmaceutical wastewater

Characteristics of wastewater play a significant role in selection of the treatment process for the wastewater. The pharmaceutical wastewater originates from variety of processes and raw materials used in manufacturing of drugs differing in their volume and composition not only from plant to plant but also from section to section within a plant (Davis & Cornwell, 1998; Davis et al., 1998). The waste water is characterized by high BOD, chemical oxygen demand (COD) and a low BOD/COD ratio because of which biological treatment is ineffective (Ferrari et al., 2003) (Table 2.2). Apart from it, there is significant concentration of antibiotics and other drugs, which can kill microorganisms involved in wastewater treatment. Pharmaceuticals exhibit properties such as polymorphism, metabolism, their complex molecular structure, their ionization, dissociation constant and sorption/desorption to soils, which are attributed to their physico-chemical and biological nature in the environment. Polymorphism appears in the compounds when molecules acquire the capacity to crystallize in different forms. These forms occupy distinct thermal, chemical, electrical and physical properties. They may also vary in color, solubility, density, melting point and rate of dissolution. The pharmaceuticals may get introduced into the environment after human metabolism and get metabolized into more water soluble or polar forms, which ultimately diminishes the activity of a parent pharmaceutical compound. The molecular structure of pharmaceuticals is complex in nature. Their variation also depends on weight, forms of salt, functions of molecules, etc.

Table 2.2. General Characteristics of pharmaceutical wastewater

Parameters	**India**				**Pakistan** (Saleem et al., 2007)	**Egypt** (Badawy et al., 2009)	**Korea** (Behera et al 2011)	**UK** (Chelliapan et al., 2006)	**China**	
	Hussain et al., 2011	Rana et al., 2014	Raj et al., 2003	Saravanane et al., 2001					Chen et al., 2008	Madukasi et al., 2010
pH	Alkaline	6.9	7.9	4	6.2-7.0	8.4	-	5.2-6.8	6.0-7.0	
TSS (mg/l)	-	370	7131.8	6000	690-930	133.3	109.3		-	8480
TDS (mg/l)	20,000-35,000	1,550	28814.2	11,000-18,500	600-1300	17,251	-		-	425
Total solids (mg/l)	-	1,920	35886	-	-	-	-		-	
BOD (mg/l)	-	120	5992	2000	1,300-1,800	2,650	83.9	3500	750-10,800	533.7
COD (mg/l)	30,000-42,000	490	12378.4	12,000-15,000	2,500-3,200	9,703	121.8	7000-8000	5000-60,000	
Biodegradability (BOD/COD)	-	0.259			-	0.27	-	-	-	-
Alkalinity (mg/l)	-	130-564			90-180	518.3	-	-	-	-
Total nitrogen (mg/l)	-	-			-	763.5	29.2	364	560-980	1600
Ammonium nitrogen (mg/l)	-	-		15-40	-	295.8	-	-	36.31-260.6	-
Total phosphate (mg/l)	-	-			-	-	3.0	-	51.41-120.4	-
Turbidity (NTU)	-	-	-	-	2.2-3.0	-	-	-	-	-
Phenol (mg/l)	-	-	-	-	95-125	43.4	-	-	-	-

The multifunctional configuration of pharmaceutical compounds is responsible to generate the molecules as polar as well as ionized and these may also be overwhelmed by the pH of the solution. When the sites for ionization are manifold, the estimation of a coefficient of water distribution (D_{ow}) and water partition (K_{ow}) should be done rigorously. The evaluation of sorption of pharmaceutical compounds is difficult to understand as several mechanisms such as hydrogen bonding, minerals adsorption on surface, ionic exchange, complex formations with metals etc. are engaged in sorption. pH is one of the important factors in sorption as most of the compounds are ionizable. Owing to these characteristics, pharmaceuticals are designated as unique pollutants (Cunningham VI, 2008; Fatta-Kassinos et al., 2011).

2.3. Environmental effects of pharmaceutical wastewater

There are various possible pathways through which pharmaceutical drugs, and their metabolites invaded into the environment and leads to its contamination as shown in **Fig.2.1**. These may enter the environment through effluents from pharmaceutical manufacturing industries, Sewage treatment plants (STPs), excretion, unused drugs, as parent compound and consequently, contaminate the surface water, drinking water and ground water. The sludge generated from STPs is further used as a soil fertilizer in agricultural land, which results in contamination of soil as well as ground water and surface water through run-off and leaching (Diaz-Cruz et al., 2003; Topp, et al., 2008; Mompelat et al., 2009). Although the contaminants reach to surface water can be diminished through various processes like photolysis and the process efficiency is mainly confined to solar intensity, photosensitizers like humic acid, season and latitude (Boreen et al., 2003). Several studies reported the contamination of surface **(Table 2.3)**, ground **(Table 2.4)** and drinking water due to presence of pharmaceutical compounds. Pharmaceutical drugs also enter in the environment through fish farming. In aquaculture, drugs which are used as feed are additives directly discharged into the water. It was estimated that around 70% of drugs administrated were released into the environment through over feeding, loss of appetite by diseased fish, and poor adsorption of the drugs (Jacobsen & Berglind, 1988). The veterinary drugs and active metabolites in huge amounts end up in sediments surrounded by aquaculture areas. A significant amount of these substances, available in sediments, is present in stable form and may lead to the development

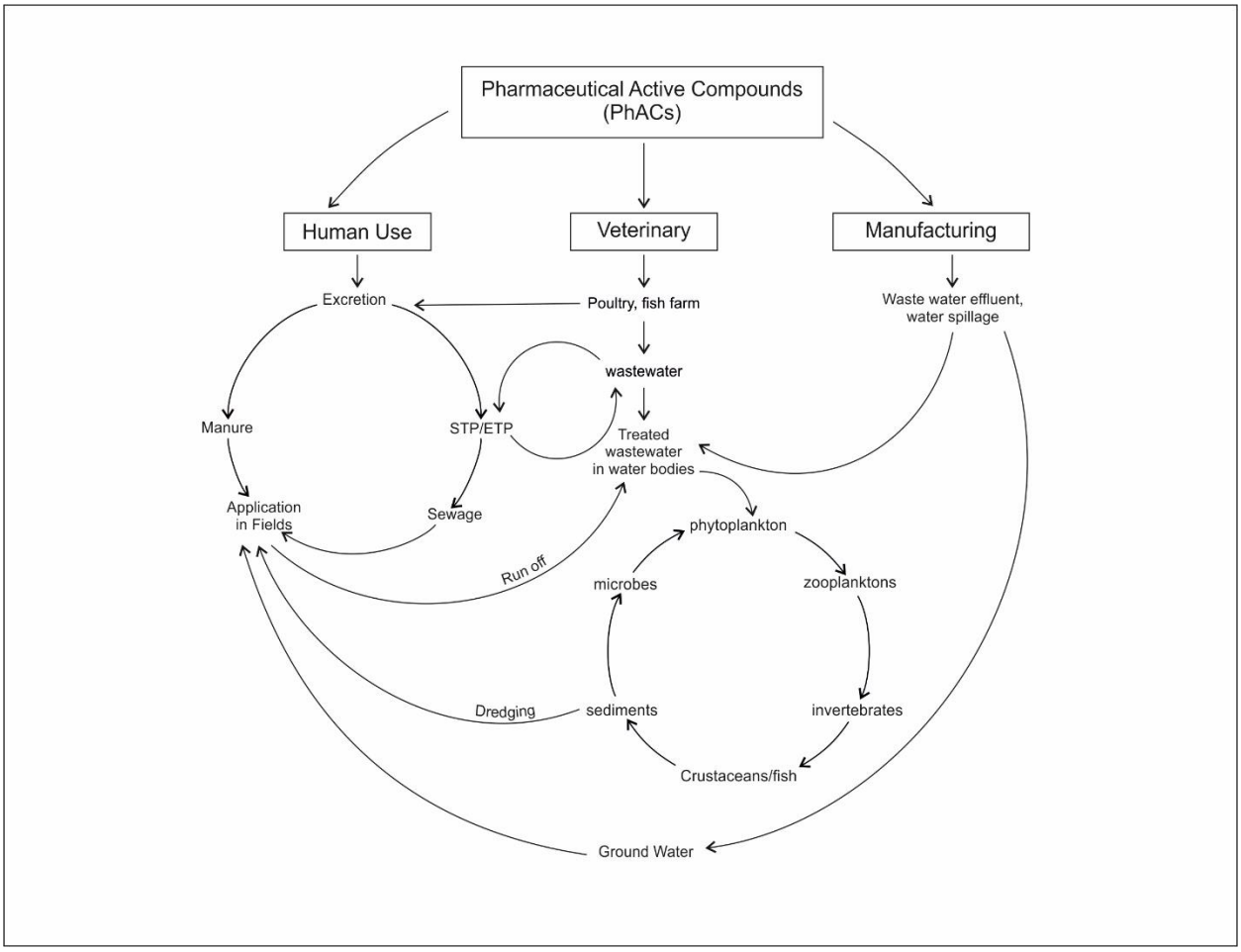

Figure 2.1. Occurrence and pathway of pharmaceutical compounds (PCs) in environment

of antibiotic resistance, which ultimately leads to infections that are difficult to treat; simultaneously, the sediments behave as a reservoir for both, the compounds and the resistant bacteria. Antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), antiepileptics, β-blockers, antidepressants, analgesics are the commonly detected drugs in terrestrial and aquatic ecosystem. Aquatic organisms, now-a-days, have gained more attention to antibiotics as these are responsible for evolution of ARB and ARGs. The presence of ARB and ARGs in water bodies affects the aquatic ecosystem, and it also poses a threat to human health (Meng, et al., 2017; Chen et al., 2018). Rate of morbidity and mortality due to infection caused by ARB is higher and it was predicted that at the end of 2050, it can leads to higher death rate of around 10 million all over the world (Amarasiri et al. 2019).

Fig. 2.3. Concentration of pharmaceutical drugs in surface water

Name of the drug	Type of drug	Country	Concentration	Reference
Acetylsalicylic acid	NSAID	Sweden	37.2 ng/l	Bendz et al., 2005
Diclofenac	NSAID	Mexico	313 ng/l	Rivera-Jaime et al., 2018
Ibuprofen	NSAID	Spain	830 ng/l	Carmona et al., 2014
Ketoprofen	NSAID	Portugal	29.51 ng/l	Pereira et al., 2017
Naproxen	NSAID	Mexico	911 ng/l	Rivera-Jaime et al., 2018
Paracetamol	NSAID	Korea	<5-127 ng/l	Choi et al., 2008
Gemfibrozil	Lipid regulator	U.S.A.	55 ng/l	Ferrer & Thurman, 2012
Benzafibrate	Lipid regulator	Italy	0.79-2.75 ng/l	Calamari et al., 2003
Clofibric acid	Lipid regulator	Germany	3.2-7.6 ng/l	Weigel et al. 2004
Carbamazepine	Antiepileptic	India	412.50 ng/l	Mutiyar et al., 2018
Gabapentin	Antiepileptic	U.S.A.	54 ng/l	Ferrer & Thurman, 2012
Atenolol	β-Blocker	Spain	470 ng/l	Huerta-Fontela et al., 2011
Metoprolol	β-Blocker	Finland	<0.8-8ng/l	Vieno et al., 2006
Sotalol	β-Blocker	Finland	<3.9-52ng/l	Vieno et al., 2006

Fluoxetine	Antidepressant	U.S.A.	12 ng/l	Kolpin et al., 2002
Sertraline	Antidepressant	Canada	0.84-2.4 ng/l	Lajeunesse et al., 2008
Propanolol	β-Blocker	United Kingdom	11.66 ng/l	Burns et al., 2018
Erythromycin	Antibiotic	U.S.A.	137 ng/l	Ferrer & Thurman, 2012
Metronidazole	Antibiotic	Malaysia	2.74 ng/l	Hossain et al., 2018
Sulfamethoxazole	Antibiotic	South Africa	2172 ng/l	Matongo et al., 2015
Trimethoprim	Antibiotic	South Africa	58 ng/l	Matongo et al., 2015
Ciprofloxacin	Antibiotic	Italy	14.36 ng/l	Calamari et al., 2003
Norfloxacin	Antibiotic	U.S.A.	120 ng/l	Kolpin et al., 2002
Lincomycin	Antibiotic	U.S.A.	60 ng/l	Kolpin et al., 2002
Clarithromycin	Antibiotic	Italy	8.31 ng/l	Calamari et al., 2003
Tylosin	Antibiotic	U.S.A.	40 ng/l	Kolpin et al., 2002
Sulfadiazine	Antibiotic	Italy	236 ng/l	Perret et al., 2006
Sulfadimethoxine	Antibiotic	Korea	<10-13ng/l	Choi et al., 2008
Sulfamethoxazole	Antibiotic	Luxembourg	1-22 ng/l	Pailler et al., 2009
Tetracycline	Antibiotic	Luxembourg	0.3-8 ng/l	Pailler et al., 2009

The presence and intensification of antibiotics in natural environment in the range of ng/l -µg/l may possess detrimental effect to terrestrial and aquatic ecosystem (Homem & Santos, 2011). These are extremely toxic to micro-organisms (EC_{50} below 0.1 mg/L) and toxic to algae (EC_{50} between 0.1 – 1.0 mg/L). Antibiotics like amoxicillin, erythromycin, sulfamethoxazole, ofloxacin, adversely affect the members of other trophic levels like bacteria, algae, rotifers, crustaceans and fishes present in aquatic environment. Antibiotic decreases the population of algae due to which food chain is affected and ultimately it disturbs the aquatic ecosystem (Santos et al., 2010). Presence of antibiotics in soil affects the development of plant and also reduces the number of bacteria in soil, which ultimately leads to decrease in food content for protozoans, micro-arthropods and nematodes reside in soil (Fatta-Kassinos et al., 2011). Presence of pharmaceutical drugs in aquatic environment raised the concern in recent years.

2.3.1 Effect of pharmaceutical drugs on aquatic ecosystem

Pharmaceutical drugs in the aquatic ecosystem affects growth of flora, and fauna present in it. Diclofenac, commonly used anti – inflammatory drug to reduce pain and inflammation. It inhibits the growth of algae and marine phytoplankton *Dunaliella tertiolecta* at concentration of 23 mg/l and 25 mg/l, respectively. Cytological changes were observed in gills, liver and kidneys of Brown trout (*Salmo trutta f. fario*) and rainbow trout (*Oncorhynchus mykiss*) after exposure to diclofenac at concentration of 0.5µg/l and 1µg/l respectively (Cleuvers, 2004; Schwaiger et al., 2004; Triebskorn et al., 2004). It also inhibits the growth of *Dunaliella tertiolecta*, phytoplankton at EC_{50} 185.69mg/l and above 25mg/l concentration of drug (DeLorenzo & Fleming, 2008). Similar studies have been reported on Ibuprofen, other anti-inflammatory drug, responsible for reducing the spawning and reproduction rate in fishes. It also reduces the spawning in Japanese killfish, *Oryzias latipes*, when exposed at different concentration (Flippin et al., 2007). Growth of aquatic photosynthetic organisms, duckweed plant *Lemna minor*, was affected by ibuprofen at concentration of 1-1000µg/l (Pomati et al, 2004). In another study, the toxic effect of most commonly prescribed drug paracetamol was observed on *Daphnia magna.* The EC_{50} at 48 hours was obtained as 30.1mg/l which shows the sensitivity of the species to drug (Kim et al., 2007). At EC_{50} 26µg/l, inhibition of growth was noticed on *Ceriodaphnia dubia* due to an anti-inflammatory drug, naproxen (Santos et al., 2010).

Table 2.4. Concentration of Pharmaceutical drugs in ground water

Name of the drug	Type of drug	Country	Concentration	Reference
Ibuprofen	NSAID	Serbia	92 ng/l	Petrović et al., 2014
Naproxen	NSAID	Spain	145 ng/l	Cabeza et al, 2012
Acetaminophen	NSAID	U.S.A	1.89 µg/l	Fram & Belitz, 2011
Diclofenac	NSAID	Singapore	17 ng/l	Tran et al., 2014
Salicylic acid	NSAID	Spain	26.6-620 ng/l	Lopez-Serna et al., 2013
Paracetamol	NSAID	U.S.A	380 ng/l	Barnes et al., 2008
Gemfibrozil	Lipid regulator	Spain	15.5 ng/l	Cabeza et al., 2012
Clofibric acid	Lipid regulator	Singapore	18 ng/l	Tran et., 2014
Bezafibrate	Lipid regulator	Germany	19 ng/l	Wolf & Zwiener, 2012
Carbamazepine	Antiepileptic	U.S.A	0-11 ng/l	Mceachran et al., 2016
Diazepam	Antiepileptic	Spain	35.1 ng/l	Lopez-Serna et al., 2013
Primidone	Antiepileptic	Germany	0-140 ng/l	Hass et al., 2012

Metoprolol	β-Blocker	Switzerland	0-9 ng/l	Morasch, 2013
Sotalol	β-Blocker	Germany	560 ng/l	Sacher et al., 2001
Propranolol	β-Blocker	Switzerland	0-9 ng/l	Morasch, 2013
Fluoxetine	Antidepressant	U.S.A	56 ng/l	Barnes et al., 2008
Sulfamethoxazole	Antibiotic	U.S.A.	0-21 ng/l	Mceachran et al., 2016
Sulfamethazine	Antibiotic	Spain	29.2 ng/l	Lopez-Serna et al., 2013
Ofloxacin	Antibiotic	Spain	10-367 ng/l	Lopez-Serna et al., 2013
Azithromycin	Antibiotic	China	0.2-0.7 ng/l	Tong et al., 2014
Norfloxacin	Antibiotic	Switzerland	0-10 ng/l	Morasch, 2013
Trimethoprim	Antibiotic	U.S.A	0.018 µg/l	Fram et al., 2011
Lincomycin	Antibiotic	U.S.A	320 ng/l	Barnes et al., 2008

Clofibrate, a blood lipid regulator drug alters the Zebrafish larvae body length and morphological characteristics at a concentration of 0.5 – 1.0 mg/l. It also alters the reproduction function in minnow fish (*Pimephales promelas*) by reduction in sperm motility. On the other hand, clofibric affects spawning in *Danio rerio* (Fish) at LC_{50} of 86mg/l after 48hours of exposure (Henschel et al., 1997). Growth of *Lemna minor* (Duckweed) was also inhibited at EC_{50} of 12.5mg/l after exposure of 7 days (Cleuvers, 2004). Similar studies have also observed on another lipid regulator drug, simvastatin, affects the grass shrimp (*Palaemonetes pugio*) adult and larvae shows LC_{50} as 10mg/l and 1.18mg/l respectively after 96 hours of exposure (Raldúa et al., 2008). Gemfibrozil used as blood lipid regulator has shown toxicity to *Hydra attenuate* (cnidarian), *Vibrio fischeri* (bacteria), and *Chlorella vulgaris* (algae) by inhibiting their growth and luminescence of bacteria (Quinn et al., 2008; Zurita et al., 2007).

Another important class of drugs are antibiotics which can be categorized as extremely toxic for microbes and very toxic for algae at EC_{50} lower than 0.1mg/l and in between 0.1-1.0mg/l respectively (Jones et al., 2002). A study obtained on norfloxacin revealed that it inhibits the growth of *Scenedesmus obliquus* (microalga) at EC_{50} of 38.49mg/l after exposure of 48 hours (Nie et al., 2009). A study on *synechocystis sp.* (cyanobacterium) and *Lemna minor* (dwuckweed) also noticed growth inhibition due to erythromycin at a concentration of 1-1000µg/l (Pomati et al., 2004). Toxicity of Duckweed *Lemna minor* predicted at EC_{50} of 4.92mg/l and 2.33mg/l for oxytetracycline and sulfachlorpyridazine respectively (Pro et al., 2003). Similarly, Antibiotics tiamulin, oxolinic acid and sulfamethazine shows toxicity to *Daphnia magna* at EC_{50} of 40 mg/l, 4.6mg/l and 202mg/l respectively after exposure of 48hours (Wollenberger et al., 2000; De Liguoro et al., 2009). Clarithromycin and levofloxacin antibiotics affect reproduction rate of Daphnia magna at EC_{50} of 40 and 340µg/l respectively (Yamashita et al., 2006) **(Table 2.5)**. When *Daphnia magna* and *Moina macrocopa* exposed to lower concentration (mg/l) of Neomycin, survival of adult and reproduction rate was affected at EC_{50} value of 0.74mg/l and 0.09mg/l, respectively. The growth of algae *Pseudokirchneriella subcapitata* was inhibited due to clarithromycin at EC_{50} value of 0.0020mg/l after exposure period of 72 hours (Isidori et al., 2005). It was also responsible for inducing mortality in rotifer *Brachionus calyciflorus*, fish *Oryzias latipes* and crustacean *Thamnocephalus platyurus* at LC_{50} value of 35.46mg/l, >100mg/l and 94.23mg/l respectively after exposure period of 24 hours (Isidori et al., 2005; Kim et al., 2009).

Table 2.5. Effect of pharmaceutical drugs on aquatic ecosystem

Pharmaceutical compound	Type of drug	Country	Species	Toxicity	Effects	Reference
Diclofenac	NSAID	Germany	*Desmodesmus subspicatus* (Algae)	EC_{50} at 3days 71.9mg/l	Inhibit growth	Cleuvers, 2004
Diclofenac	NSAID	Brazil	*Dunaliella tertiolecta* (Algae)	EC_{50} at 96hours 185.69µg/l	Inhibit growth	Lin et al. 2009
Diclofenac	NSAID	Germany	*Daphnia magna* (Crustacean)	EC_{50} at 48hours 68mg/l	Immobilize the species	Cleuvers, 2004
Diclofenac	NSAID	Sweden	*Salmo trout trutta fario* (Fish)	NOEC at 21days 0.5µg/l	Histopathological alterations	Hoeger et al., 2005
Diclofenac	NSAID	Germany	*Vibrio fischeri* (Bacteria)	EC_{50} at 30min 11454 µg/l	Inhibit growth	Ferrari et al., 2003
Ibuprofen	NSAID	Switzerland	*Desmodesmus subspicatus* (Algae)	EC_{50} at 7days 315mg/l	Inhibit growth	Cleuvers, 2004

Ibuprofen	NSAID	Taiwan	*Thamnocephalus platyurus* (Crustacean)	LC_{50} at 24hours 19.59mg/l	Mortality	Kim et al., 2009
Ibuprofen	NSAID	United Kingdom	*Oryzias latipes* (Fish)	LC_{50} at 96hours >100mg/l	Mortality	Pounds et al., 2008
Ibuprofen	NSAID	U.S.A.	Lemna minor (Duckweed)	EC_{50} at 7days 4.01mg/l	Inhibit growth	Pomati et al., 2004
Paracetamol	NSAID	Spain	*Vibrio fischeri* (Bacteria)	EC_{50} at 15min 567.5mg/l	Inhibit growth	Kim, et al., 2007
Paracetamol	NSAID	U.S.A.	*Daphnia magna* (Crustacean)	EC_{50} at 48hours 30.1mg/l	Immobilize the species	Kim et al., 2007
Paracetamol	NSAID	South Korea	*Scenedesmus subspicatus* (Algae)	EC_{50} at 72hours 134mg/l	Inhibit growth	Henschel et al., 1997
Paracetamol	NSAID	United Kingdom	*Brachydanio rerio* (Zebra Fish)	LC_{50} at 48hours 378mg/l	Reproduction	Henschel, et al., 1997

Paracetamol	NSAID	United Kingdom	*Tetrahymena pyriformis* (Ciliates)	EC_{50} at 48hours 112mg/l	Inhibit growth	Henschel et al., 1997
Clofibrate	Lipid regulator	France	*Danio rerio* (Zebra Fish)	LC_{50} at 96hours 0.89mg/l	Mortality	Raldúa et al., 2008
Clofibric acid	Lipid regulator	Germany	*Ceriodaphnia dubia* (Crustacean)	EC_{50} at 48hours >200000µg/l	Immobilize the species	Ferrari et al., 2003
Clofibric acid	Lipid regulator	United Kingdom	*Scenedesmus subspicatus* (Algae)	EC_{50} at 72hours 89mg/l	Inhibit growth	Henschel et al., 1997
Clofibric acid	Lipid regulator	Italy	*Vibrio fischeri* (Bacteria)	EC_{50} at 30min 100mg/l	Inhibit growth	Henschel et al., 1997
Clofibric acid	Lipid regulator	Germany	*Tetrahymena pyriformis* (Ciliates)	EC_{50} at 48hours 175mg/l	Inhibit growth	Henschel et al., 1997
Clofibric acid	Lipid regulator	Taiwan	*Danio rerio* (Fish)	LC_{50} at 48hours 86mg/l	Spawning	Henschel et al., 1997

Clofibric acid	Lipid regulator	Italy	Lemna minor (Duckweed)	EC_{50} at 7days 12.5mg/l	Inhibit growth	Cleuvers, 2004
Simvastatin	Lipid regulator	Canada	*Dunaliella tertiolecta* (Algae)	EC_{50} at 96hours 22800µg/l	Inhibit growth	DeLorenzo & Fleming, 2008
Simvastatin	Lipid regulator	Canada	*Palaemonetes pugio* (Grass shrimp)	LC_{50} at 96hours 1.18mg/l	Survival of larvae	Key et al., 2008
Levofloxacin	Antibiotic	South Korea	*Thamnocephalus platyurus* (Crustacean)	LC_{50} at 24hours >100mg/l	Mortality	Kim et al., 2009
Levofloxacin	Antibiotic	South Korea	*Oryzias latipes* (Fish)	LC_{50} at 96hours >100mg/l	Mortality	Yamashita et al., 2006
Levofloxacin	Antibiotic	South Korea	*Pseudokirchneriella subcapitata* (Algae)	EC_{50} at 96hours 1200µg/l	Inhibit growth	Yamashita et al., 2006
Norfloxacin	Antibiotic	Portugal	*Selenastrum capricornutum* (Algae)	EC_{50} at 72hours 16.6mg/l	Inhibit growth	Eguchi et al., 2004

Norfloxacin	Antibiotic	China	*Brachionus calyciflorus* (Rotifer)	LC_{50} at 24hours 29.88mg/l	Mortality	Isidori et al., 2005
Ofloxacin	Antibiotic	Swedan	*Ceriodaphnia dubia* (Crustacean)	EC_{50} at 24hours 17.41mg/l	Immobilize the species	Isidori et al., 2005
Oxolinic acid	Antibiotic	China	*Microcystis aeruginosa* (Algae)	EC_{50} at 72hours 0.180 mg/l	Inhibit growth	Holten Lützhøf et al., 1999
Ampicillin	Antibiotic	Taiwan	*Vibrio fischeri* (Bacteria)	EC_{50} at 15min 2627mg/l	Luminescence	Park & Choi et al., 2008
Lincomycin	Antibiotic	U.S.A.	*Brachionus calyciflorus* (Rotifer)	LC_{50} at 24hours 24.94mg/l	Mortality	Isidori et al., 2005
Lincomycin	Antibiotic	U.S.A.	*Thamnocephalus platyurus* (Crustacean)	LC_{50} at 24hours 30mg/l	Mortality	Isidori et al., 2005
Clarithromycin	Antibiotic	Italy	*Brachionus calyciflorus* (Rotifer)	LC_{50} at 24hours 35.46mg/l	Mortality	Isidori et al., 2005

Clarithromycin	Antibiotic	South Korea	*Oryzias latipes* (Fish)	LC_{50} at 96hours >100mg/l	Mortality	Kim et al., 2009
Clarithromycin	Antibiotic	South Korea	*Thamnocephalus platyurus* (Crustacean)	LC_{50} at 24hours 94.23mg/l	Mortality	Kim et al., 2009
Clarithromycin	Antibiotic	South Korea	*Pseudokirchneriella subcapitata* (Algae)	EC_{50} at 72hours 0.0020mg/l	Inhibit growth	Isidori et al., 2005
Erithromycin	Antibiotic	Italy	Lemna minor (Duckweed)	EC_{50} at 7days 5.62mg/l	Inhibit growth	Pomati et al., 2004
Erithromycin	Antibiotic	South Korea	*Thamnocephalus platyurus* (Crustacean)	LC_{50} at 24hours >100mg/l	Mortality	Kim et al., 2009
Erithromycin	Antibiotic	South Korea	*Oryzias latipes* (Fish)	LC_{50} at 96hours >100mg/l	Mortality	Kim et al., 2009
Erithromycin	Antibiotic	South Korea	*Selenastrum capricornutum* (Algae)	EC_{50} at 72hours 0.0366mg/l	Inhibit growth	Eguchi et al., 2004

Sulfadiazine	Antibiotic	Italy	*Microcystis aeruginosa* (Algae)	EC_{50} at 72hours 0.135 mg/l	Inhibit growth	Holten Lützhøf et al., 1999
Sulfadiazine	Antibiotic	China	*Daphnia magna* (Crustacean)	EC_{50} at 48hours 221 mg/l	Immobilize species	Yamashita et al., 2006
Sulfadimethoxine	Antibiotic	U.S.A.	*Vibrio fischeri* (Bacteria)	EC_{50} at 15min >500mg/l	Inhibit growth	Kim et al., 2007
Sulfadimethoxine	Antibiotic	U.S.A.	*Daphnia magna* (Crustacean)	EC_{50} at 48hours 248 mg/l	Immobilize species	Kim et al., 2007
Sulfadimethoxine	Antibiotic	Luxembourg	*Oryzias latipes* (Fish)	LC_{50} at 48hours >100mg/l	Reproduction	Kim et al., 2007
Sulfadimethoxine	Antibiotic	Italy	*Selenastrum capricornutum* (Algae)	EC_{50} at 72hours 2.30 mg/l	Inhibit growth	Yamashita et al., 2006
Sulfamethoxazole	Antibiotic	U.S.A.	*Vibrio fischeri* (Bacteria)	EC_{50} at 15min 78.1mg/l	Inhibit growth	Kim et al., 2007

Sulfamethoxazole	Antibiotic	U.S.A.	*Daphnia magna* (Crustacean)	EC_{50} at 48hours 189.2mg/l	Immobilize the species	Kim et al., 2007
Sulfamethoxazole	Antibiotic	Taiwan	*Oryzias latipes* (Fish)	LC_{50} at 48hours >750 mg/l	Immobilize the species	Kim et al., 2007
Sulfamethoxazole	Antibiotic	Luxembourg	*Hydra attenuate*	LC_{50} at 96hours >100 mg/l	Morphology	Quinn et al., 2008
Carbamazepine	Antiepileptic	Spain	*Daphnia magna* (Crustacean)	EC_{50} at 48hours >100mg/l	Immobolize the species	Cleuvers, 2004
Carbamazepine	Antiepileptic	U.S.A.	*Oryzias latipes* (Fish)	LC_{50} at 96hours 45.87mg/l	Mortality	Kim et al., 2009
Carbamazepine	Antiepileptic	South Korea	*Vibrio fischeri* (Bacteria)	EC_{50} at 30min >81000µg/l	Inhibit growth	Kim et al., 2009
Carbamazepine	Antiepileptic	South Korea	*Pseudokirchneriella subcapitata* (Algae)	NOEC at 96hours >100000µg/l	Inhibit growth	Cleuvers, 2004

Atenolol	β-Blocker	Finland	*Thamnocephalus platyurus* (Crustacean)	LC_{50} at 24hours >100mg/l	Mortality	Kim et al., 2009
Atenolol	β-Blocker	Sweden	*Oryzias latipes* (Fish)	LC_{50} at 96hours >100mg/l	Mortality	Kim et al., 2009
Atenolol	β-Blocker	Italy	*Desmodesmus subspicatus* (Algae)	EC_{50} at 48hours 620mg/l	Inhibit growth	Cleuvers, 2004
Atenolol	β-Blocker	Spain	*Pimephales promelas* (Fish)	NOEC at 28days 3.2mg/l	Inhibit growth	Winter et al., 2008
Metoprolol	β-Blocker	Taiwan	*Desmodesmus subspicatus* (Algae)	EC_{50} at 48hours 0.7mg/l	Inhibit growth	Brooks et al., 2003
Metoprolol	β-Blocker	Taiwan	Lemna minor (Duckweed)	EC_{50} at 7days >320mg/l	Inhibit growth	Cleuvers, 2004
Metoprolol	β-Blocker	Taiwan	*Oryzias latipes* (Fish)	LC_{50} at 48hours >100mg/l	Mortality	Huggett et al., 2002

Metoprolol	β-Blocker	Taiwan	*Hyalella azteca* (Crustacean)	LC_{50} at 48hours >100mg/l	Mortality	Huggett et al., 2002
Propranolol	β-Blocker	United Kingdom	*Desmodesmus subspicatus* (Algae)	EC_{50} at 48hours 0.7mg/l	Inihibit growth	Cleuvers, 2004
Propranolol	β-Blocker	United Kingdom	*Hyalella azteca* (Crustacean)	LC_{50} at 48hours 29.8mg/l	Mortality	Huggett et al., 2002
Propranolol	β-Blocker	South Korea	*Oryzias latipes* (Fish)	LC_{50} at 96hours 11.40mg/l	Mortality	Kim et al., 2009
Fluoxetine	Antidepressant	Canada	*Dunaliella tertiolecta*	EC_{50} at 96hours 169.81µg/l	Inhibit growth	Brooks et al., 2003
Fluoxetine	Antidepressant	Canada	*Ceriodaphnia dubia* (Crustacean)	LC_{50} at 48hours 234µg/l	Decreases reproduction rate	Brooks et al., 2003
Fluoxetine	Antidepressant	Canada	*Pimephales Promelas* (Fish)	LC_{50} at 48hours 705µg/l	spawning	Cunningham et al., 2004

Fluoxetine	Antidepressant	Canada	*Potamopyrgus antipodarum (snail)*	EC_{50} at 56days 0.81µg/l	Decreases reproduction	Nentwing, 2007
Fluoxetine	Antidepressant	Canada	*Chironomus tentans* (Midge)	LC_{50} at 10days 15.2mg/kg	Emergence	Brooks et al., 2003
Sertraline	Antidepressant	Canada	*Daphnia magna* (Crustacean)	EC_{50} at 48hours 1.3mg/l	Immobilize the species of crustacean	Minagh et al., 2009
Sertraline	Antidepressant	Norway	*Vibrio fischeri* (Bacteria)	EC_{50} at 30min 10.72mg/l	Inhibits growth of bacteria	Minagh et al., 2009
Sertraline	Antidepressant	Canada	*Oncorhynchus mykiss* (Fish)	LC_{50} at 96hours 0.32mg/l	Lethal to fish	Minagh et al., 2009
Paroxetine	Antidepressant	Norway	*Daphnia magna* (Crustacean)	EC_{50} at 48hours 2.5mg/l	Immobilize the crustacean	Cunningham et al., 2004

Another class of drugs known as antiepileptic drugs reduces activity of neuron in central nervous system (Rang et al., 1999). Carbamazepine, an antiepileptic drug produces lethal effects to Zebra fish at 43 µg/l and sub lethal effect in *Daphnia* species at 92 µg/l (Thacke, 2005). It also affects the benthic organisms which feed on the organic matter adsorbed on sediments. Otkem et al., 2005 investigated that exposure of invertebrates, *Chironomus riparus* to carbamazepine pharmaceutical through sediments, caused a blockade of population and decreased emergence with EC_{50} value of 160µg/kg. A group of drugs inhibits β-adrenergic receptors in nervous system are called as beta blockers. Atenolol, metoprolol and propranolol are the commonly used β-blockers in which propranolol is blocks the activity of β_1 and β_2 receptor while atenolol and metoprolol are specific to β_1 receptor (Rang et al., 1999). It was observed from the study that propanolol inhibits the growth of Japneses medaka at a concentration of 500µg/l (Huggett et al., 2002) while it reduces the heart rate of rainbow trout at a concentration of 70.9µg/l (Larsson et al., 2006). However, mortality of crustacean *Hyalella azteca* was observed due to propanolol and metroprolol at LC_{50} value of 29.8mg/l and >100mg/l repectively after an exposure period of 48 hours (Huggett et al., 2002).

Antidepressants are also a important class of drug which helps in different endocrine and regulatory fuctions (Daughton & Ternes, 1999). Most commonly used antidepressants are sertaline, fluoxetine, paroxetine and fluvoxamine are responsible for obstruction of reuptake of neuro-transmitter serotinin (Brooks et al., 2003). At higher concentration, fluoxetine and fluvoxamine leads to maturation of oocytes and spawning in *Dreissena polymorpha* zebra mussels (Fong, 1998). On the contrary, sertraline is highly toxic for fishes as it causes mortality in *Oncorhynchus mykiss* fish at LC_{50} of 0.32mg/l after exposing for 96 hours while for rainbow trout LC_{50} of 0.38mg/l was obtaind after exposing for the same time period (Minagh et al., 2009). At a concentration of 13.6µg/l, EC_{50} value 24µg/l and 45µg/l, deformatities in cells were reported in *Pseudokirchneriella subcapitata* due to fluoxetine after exposing for 48 hours and 96 hours, respectively (Brooks et al. 2003; Johnson et al., 2007). Reproduction of *Potamopyrgus antipodarum* (invertebrate) was decreased when exposed to fluoxetine and results in LOEC value of 69µg/l and NOEC value of 13µg/l (Péry et al., 2008). A therapeutic class of drugs that are use to eliminate the cells and proliferate unusually like cells observe in cancer are known as Antineoplastic drugs (Johnson et al., 2008). It shows carcinogenic, mutagenic, genotoxic properties and found in urine in their indigenous form (Sanderson et al., 2004). An antineoplastic

drug, cyclophosphamide inhibits growth of the *Daphnia magna* (crustacean) and *Pseudokirchneriella subcapitata* (algae) at concentration of 10-100mg/l (Grung et al., 2006). DellaGreca et al., 2007 observed the toxic effect of tamoxifen with its photoproducts on *Thamnocephalus platyurus* (crustacean) *and Brachionus calyciflorus* (rotifer) with LC_{50} of o.40-1.59mg/l and 0.95-1.31mg/l, respectively. So, it was concluded from the literature that pharmaceutical drugs present in aquatic environment may affect the growth, survival, reproduction, spawining etc. of non-target life forms. The drugs may also reach to terrestrial ecosystem through run off, urine and feces, wastewater effluents etc. and can affects its quality. So, it is necessary to study the effect of pharmaceutical drugs on terrestrial ecosystem to design the effective treatment technologies.

2.3.2 Effect of pharmaceutical drugs on terrestrial ecosystem

Pharmaceutical drugs invade the terrestrial environment from sludge of the sewage applied as fertilizer to the land, animal slurry or from the contaminated water applied for irrigation (Gielen et al., 2009). From the study, it has been documented that various categories of pharmaceutical like NSAIDs, antibiotics, antiepileptics etc. are present in terrestrial environment within range of ng/kg to g/kg which influence the properties of soil (Ternes et al., 1998; Kenney et al., 2006; Fang et al., 2012). Concentration of different drugs categorized in NSAIDs such as ibuprofen, naproxen, diclofenac and acetaminophen has been observed as 318.5ng/g, 23.79ng/g, 6.82ng/g and 1640ng/g respectively (Kinney et al., 2006; Karnjanapiboonwong et al., 2011; Chen et al. 2013) **(Table 2.6).** Similarly, higher concentration of β-blocker, warfarin has noticed as 2770ng/g in soil (Kinney et al., 2006). Norfloxacin and ofloxacin, antibiotics, shows concentration of 2160µg/kg and 898 µg/kg respectively in soil (Hu et al., 2010; Van Doorslaer et al., 2014). Pharmaceuticals shows several deleterious effects to soil, soil microbes, soil fauna and flora (Harrow et al., 2011). The crops growing on the soils that are irrigated with retrieved water can able to uptake pharmaceuticals, which consequently, inhibits the growth of crop and results in decline in production of crop (Herkoltz et al., 2010; Karnjanapiboonwong et al., 2011; Qiu et al., 2013). Sometimes pharmaceuticals may get accumulate in palatable part of crops causing harmful effects to human health. It may disrupt the endocrine system of humans and hindered the growth of embryonic cells of humans (Qin et al., 2015).

Table 2.6. Concentration of pharmaceutical drugs in terrestrial ecosystem

Pharmaceutical compound	Type of drug	Concentration	Reference
Ibuprofen	NSAID	318.5 ng/g	Karnjanapiboonwong et al., 2011
Naproxen	NSAID	23.79 ng/g	Chen et al., 2013
Diclofenac	NSAID	6.82 ng/g	Chen et al., 2013
Acetaminophen	NSAID	1640 ng/g	Kinney et al., 2006
Triclosan	Antiseptic	8.16 ng/g	Karnjanapiboonwong et al., 2011
Carbamazepine	Antiepileptic	549 ng/g	Kinney et al., 2006
Primidone	Antiepileptic	3.3 ng/g	Chen et al., 2011
Clofibric acid	Lipid regulator	4.27 ng/g	Ternes et al., 2007
Fluoxetine	Antidepressant	376 ng/g	Kinney et al., 2006
Bisphenol A	Endocrine distruptor	31 ng/g	Chen et al., 2013
Warfarin	β-Blocker	2770 ng/g	Kinney et al., 2006
Estrone	Steroid hormones	135.9 ng/g	Karnjanapiboonwong et al., 2011
17β-estradiol (E2)	Steroid hormones	3.33 ng/g	Xu et al., 2009

Azithromycin	Antibiotic	1.3-158 µg/kg	Li et al., 2013
Norfloxacin	Antibiotic	2160 µg/kg	Hu et al., 2010
Ofloxacin	Antibiotic	898 µg/kg	Van Doorslaer et al., 2014
Ciprofloxacin	Antibiotic	0.68 ng/g	Karnjanapiboonwong et al., 2011
Oxytetracycline	Antibiotic	6.2 ng/g	Chen et al., 2011
Sulfadimethoxine	Antibiotic	22.7 µg/kg	Lillenberg et al., 2010
Sulfadiazine	Antibiotic	91000 µg/kg	Martínez-Carballo et al., 2007
Enrofloxacin	Antibiotic	2-200 µg/l	Nowara et al., 1997
Tylosin	Antibiotic	1250 µg/kg	Pan & Chu, 2017b
Sulfadoxine	Antibiotic	9.1 µg/kg	Dolliver et al., 2007
Trimethoprim	Antibiotic	60 ng/g	Kinney et al., 2006
Tetracycline	Antibiotic	2683 µg/kg	Pan & Chu, 2017b
Doxycycline	Antibiotic	728 µg/kg	Liu et al., 2016
Chlortetracycline	Antibiotic	764000 µg/kg	Massé et al., 2014
Lincomycin	Antibiotic	2.6 µg/kg	Ding et al., 2011

Various has been reported the presence of pharmaceuticals in soil and plants but they primarily focus on antibiotics. It was reported that an antibiotic penicillin and oxytetracycline hydrochloride decreases the biomass of bacteria present in the soil at a concentration of 10µg/g (Colinas et al., 1994). Activities of soil microorganisms like biodegradation, nitrification, respiration and enzymatic activities may also get disturbed due to presence of pharmaceuticals in soil. Study documented on sulfamethoxazole and ciprofloxacin revealed that they may inhibit the respiration at concentration of 150µg/kg (Waller et al., 2009; Liu et al., 2009; Girardi et al., 2011). Similarly, it has been observed that the concentration of triclosan, an antibiotic, at above 1mg/kg may affect nitrification process in sandy soil which may cause disturbance of nitrogen cycle in soil (Waller et al., 2009). On the other hand, it was investigated that Sulphamethoxazole inhibits the growth of bacterial species *Pantoea agglomerans* and *Pseudomonas aeruginosa* at EC_{50} of 0.34mg/l and 2.98mg/l after 24 hours of exposure time (Tappe et al., 2008). Several antibiotics may also affect the growth pattern in plants and seed germination in crops. A study done by 48 observed the inhibition of growth and seed germination in *Medicago sativa* (Alfalfa), *Dacus carota* (carrot) and *Lactuca sativa* (Lettuce) due the amoxicillin and Chlortetracycline at concentration of 0.001–10 mg/l. In the similar study, death of the *Zea mays* (Maize) was also observed due to sulfadiazine at 10mg/kg and 200 mg/kg (dry weight) of spiked soil (Michelini et al., 2012). Sensitivity of rice was observed to sulfamethoxazole at EC_{10} of 0.1mg/l. On the contrary, seed germination of cucumber was inhibited with EC_{50} of >300mg/l after exposing to an antibiotic drugs, tetracycline and chlortetracycline (Liu et al., 2009). An anti-inflammatory drug, ibuprofen shows reduction in quantum efficiency of photosystem II and photochemical quenching coefficient on Sorghum bicolor (Great millet) at concentration of 83mg/kg (González-Naranjo et al., 2015). Another study observed the reduction in development and growth of *Dacus carota* (carrot) after exposure to an antidiabetic drug, Metformin at concentration of 10mg/kg (Eggen et al., 2011). Various studies have also been noticed noxious effect of pharmaceuticals on soil fauna like earthworms, nematodes etc. An antibiotic triclosan affects rate of reproduction in invertebrate species, *Enchytraeus albidus*, *Folsomia candida* and *Eisenia andrei* at 0.6-7.0mg/kg concentration in soil while at the same concentration sensitivity was higher for species of earthworm, *Eisenia andrei* for triclosan (Amorim et al., 2010). The ecological function of soil mainly dependent on species of earthworms which may contain 60-80% of soil biomass and it was observed that after exposure for a long time, triclosan affects antioxidative enzymatic activities of glutathione-S-

transferase and catalase (Lin et al., 2010). It was also evaluated from the study that Sulphadiazine, Sulphapyridine, Sulphamethazine and Sulphamethoxazole influence the growth, length and movement of the body of *Caenorhabditis elegans* (nematode) after exposure of 24-96 hours with EC_{10} value of 0.00131mg/l at 96 hours (Yu et al., 2011).

Pharmaceuticals present in the soil may reach to surface water through irrigation when get cumulated in surface of the soil. These may also enter into ground water through leaching and affects its quality. Overall, pharmaceuticals drugs present in aquatic and terrestrial ecosystem, directly or indirectly reach to water resources and degrade its quality. So, effective treatment technologies are required to treat the contaminated water for its future use.

2.4 Treatment of pharmaceutical wastewater

The treatment of pharmaceutical wastewater is troublesome because of its variation in volume, composition, quantity, raw material and recalcitrant nature (Carballa et al., 2008). Pharmaceutical manufacturing industries along with hospitals, sewage treatment plants and also unused drugs are the fundamental sources of pharmaceutical wastewater in the ecosystem (Andersson & Huges, 2014). So, it is a challenge to treat and adopt an effective methodology for treating such a complex wastewater. Various treatment methods such as conventional and advanced methods and their comparison are discussed below.

2.4.1 Conventional treatment

Conventional treatment methods used for the pharmaceutical wastewater include physicochemical and biological treatment methods. Earlier treatment of wastewater using biological method was most commonly used and economical method (Kulik et al., 2008) but it was found that these methods are not that much effective for the removal of persistent constituents present in wastewater (Clara et al., 2005). Biological methods are further classified as aerobic and anaerobic processes. Activated sludge method, membrane batch reactors and sequential batch reactors are included in aerobic methods (LaPara et al., 2002) (Noble, 2006) (Chang et al., 2008) (Chen et al., 2008) (Deegan et al., 2011) while anaerobic methods include anaerobic film reactors, anaerobic sludge reactors, and anaerobic filters (Gangagni et al. 2005, Enright et al. 2005). Anaerobic treatment has more potential to treat high-strength wastewater compared to aerobic process with less energy input, operational cost, requirement of nutrients, sludge yield, recovery

of biogas, and requirement of space. However, anaerobic processes are not as effective in treating the pharmaceutical wastewater that carries recalcitrant xenobiotic compounds, which are non-biodegradable to microbial mass within the conventional treatment (Fountoulakis et al., 2008; Deegan et al., 2011). The other treatment technologies used for treatment of pharmaceutical wastewater are physico-chemical treatment methods such as membrane separation (Gonzalez-Brambila et al., 2006; Fazal et al., 2015; Tian et al., 2015; Shahbeig et al., 2016; Wang et al., 2018), activated carbon adsorption (Chang et al., 2015; Akhtar et al., 2015; Aljeboree & Alshirifi, 2018; Coimbra et al., 2019; Macías-García et al., 2019), air stripping (Chen et al., 2019) etc. In adsorption process adsorbents are used to degrade the drugs in pharmaceutical wastewater. In industries, adsorbents get exhausted frequently and the continual replacement or regeneration of adsorbent makes the treatment costly. Another problem with this process is discard of spent adsorbent loaded with toxic pollutants (Kibbey et al., 2007). Precipitation and coagulation processes can be used to remove suspended particulate matter, grease and oil along with some definite compounds and act as pre-treatment option to improve the wastewater biodegradability (Parmar & Upadhyay, 2013; Sahu & Chaudhari, 2013; Shirafkan et al., 2016). Several coagulants such as alum, lime, ferric chloride and ferrous sulfate can be used but studies have revealed that ferric chloride shows more efficiency in removing BOD_5 and COD. This process is useful in decreasing the COD load at less cost, but the main drawback with this process is that it can be used only for secondary treatment (Cheng et al., 2007). These methods are responsible for transferring the pollutant from one phase to another rather than destroying them completely (Elmolla et al. 2010). On the other hand, certain advanced physical and chemical treatment methods have got relatively higher removal efficiency and improve rate kinetics. These methods are collectively classified as Advanced oxidation processes (AOPs)

AOPs are found to be the most effective treatment technology for completely mineralizing the pollutants to inorganic compounds, CO_2 and water without the formation of secondary pollutant (Andreozzi et al., 1999; Comninellis et al., 2008; Poyatos et al., 2010; Oller et al., 2011; Oturan et al., 2014; Kanakaraju et al., 2018).

2.4.2 Advanced oxidation processes (AOPs)

AOPs act as low cost, easy to operate and effective option for treatment of pharmaceutical wastewater and can also be coupled with biological or conventional physico-chemical processes to design cost effective solutions. AOPs are based on generation of highly reactive hydroxyl

radical, which can rapidly oxidize the target pollutants non-selectively (Balcioglu et al., 2001; Bhatkhande et al., 2002; Neyens & Baeyens, 2003; Gonze et al., 2003; Sarria et al., 2004; José et al., 2010; Catalkaya & Kargi 2007; Gomes et al., 2005; Tai et al., 2002; Shin et al., 2008; Chelliapan & Sallis, 2013). Hydroxyl radicals have oxidation potential of 2.80 V vs NHE, second only to Fluorine (Glaze & Kang, 1989; Haag & Yao, 1992; Gogate & Pandit, 2004a,b; Pera-Titus et al., 2004; Devipriyas & Yesodharan, 2005; Pignatello et al., 2006; Comninellis et al., 2008; Shannon et al., 2008; Wang & Xu, 2012; Muruganandham, et al., 2014). There are various technologies included in AOPs such as Fenton, photo-Fenton, ultrasonication, photo-catalysis, etc., which differ in mechanism of radical generation (Kim, & Ihm, 2011). It was also reported that the combinations of AOPs are more efficient in removal of organic compounds than that generated with individual techniques (Mendez-Arriagad et al., 2009). Various technologies included in AOPs are discussed below:

2.4.2.1 Photocatalysis

Among the various AOPs, photocatalytic oxidation process is regarded as a promising technique for treatment of pharmaceutical wastewater due to its non-toxic nature, absence of mass transfer limitation, relatively cost-efficient, chemically stability, and it can even be operated at ambient temperature (Elmolla & Chaudhuri, 2010; Sharma et al., 2015, Sharma et al., 2016). During photocatalysis, reaction is stimulated in the presence of photons and a catalyst. Homogenous and heterogenous photocatalysis are the two main classes of photocatalysis. In homogenous, catalyst and the substrate both appear in same phase while in heterogenous, process move at the periphery of two phases aqueous or gaseous phase and solid photocatalyst phase (Ku & Hseih, 1992; Kansal et al., 2007; Brillas et al., 2009; Mishra et al., 2010; Almeida et al., 2011; Smykalova et al., 2019). Various photocatalysts which can be used for treatment of persistent pollutants are iron (III) oxide (Fe_2O_3), zinc oxide (ZnO), tungsten trioxide (WO_3), Titanium dioxide (TiO_2), Zirconia (ZrO_2), and Vanadium oxide (V_2O_5) (Kudo et al., 2009). A photocatalyst can be considered as ideal when it has properties like photoactivity, biological and chemical inertness, stability toward photo corrosion, suitability towards visible or near UV light, low cost, lack of toxicity, etc. (Bhatkhande et al., 2001). Among various photocatalysts, TiO_2 and ZnO are found to be the most efficient catalysts for degrading recalcitrant pollutant. Titanium dioxide (TiO_2) is a mixture of anatase and rutile forms and possesses the properties like photostability, non-toxicity, inexpensive, photoreactive and chemical and biological inertness (Friedmann et al.

2010). At room temperature, ZnO is an n-type of semiconductor, which possess a broad band gap of 3.2 eV and binding energy of 60 meV. It also provides good biocompatibility, piezoelectric characteristics and also the photochemical stability (Benhebal et al., 2010). Photocatalytic performances ZnO and TiO_2 are expected to be similar as both possess have same band gap energy (Lee et al., 2016). Some of the factors like charge-transfer dynamics, morphology, and surface interactions regulate the performance of semiconductors (Kamat et al., 2002). Photocatalysis is initiated when the photocatalyst particle gets excited with quantum of light. When the photons illuminated on the surface of TiO_2, electrons (e^-) present in the valence band gets excited to conduction band leaving behind a hole (h^+) in the valence band (Reaction 2.1) **(Fig. 2.2).** Water molecules or hydroxyl ions adsorbed on TiO_2 surface further combine with photogenerated valence band to produce strong oxidant hydroxyl radicals (Reaction 2.2 and 2.3). Organic molecules adsorbed on surface of catalyst reacts with hydroxyl radical through abstraction of hydrogen atom or electron to form organic cations radical (Reaction 2.4). Under UV illumination, on the interface of the particle reaction of the holes is more rapid than electrons and it accommodate excess of electrons. It is necessary to intercept the recombining of electrons with holes by removing the excess of electrons so that oxidation rection gets complete. Further, formation of superoxide ions radicals takes place by combining the electrons with most readily accessible molecular oxygen (Reaction 2.5). Under acidic conditions, superoxide ion combined with proton to form hydroperoxide radical and further reaction of hydroperoxide radical with electron of conduction band forms hydroperoxide ion. Electrons from conduction band split the hydrogen peroxide to yield hydroxyl ions and hydroxyl radicals (Reaction 2.6). Hydroxyl radicals combines with valence band holes to generate more hydroxyl radicals (Elmolla & Chaudhuri, 2010).

$TiO_2 + h\upsilon \rightarrow TiO_2 (e^- + h^+)$……..2.1
$h^+ + H_2O \rightarrow H^+ + \cdot OH$……..2.2
$h^+ + OH^- \rightarrow \cdot OH$……2.3
Organics + $\cdot OH \rightarrow$ Degradation Products…….2.4
$e^- + O_2 \rightarrow \cdot O_2^-$……2.5
$H_2O_2 + e^- \rightarrow \cdot OH + OH^-$……...2.6

In recent years, several studies have been focused on use of nano-sized TiO_2 and ZnO photo-catalysts in the form of nanorods, nanospheres, thin porous films, nano fibers and nanowires for treatment of recalcitrant compounds in wastewater because of their high activity, low-cost and

environmentally safe nature. Various researchers have studied the degradation of pharmaceutical drugs using photocatalysis and observed complete degradation of drugs. Safari et al., (2015) studied the degradation of tetracycline antibiotic using TiO_2 photocatalysis and also added H_2O_2 to enhance the reaction. It was observed that the TiO_2 photocatalysis could efficiently degrade tetracycline at maximum concentration of 1.0mg/l while addition of H_2O_2 reduces the time duration to completely degrade the tetracycline. Similarly, degradation of Metronidazole was studied by Farzadkia et al., (2015) **(Table 2.7)**. and this study reported that with increase in dose of TiO_2, increases degradation of Metronidazole and the maximum degradation was achieved at 0.5g/l at

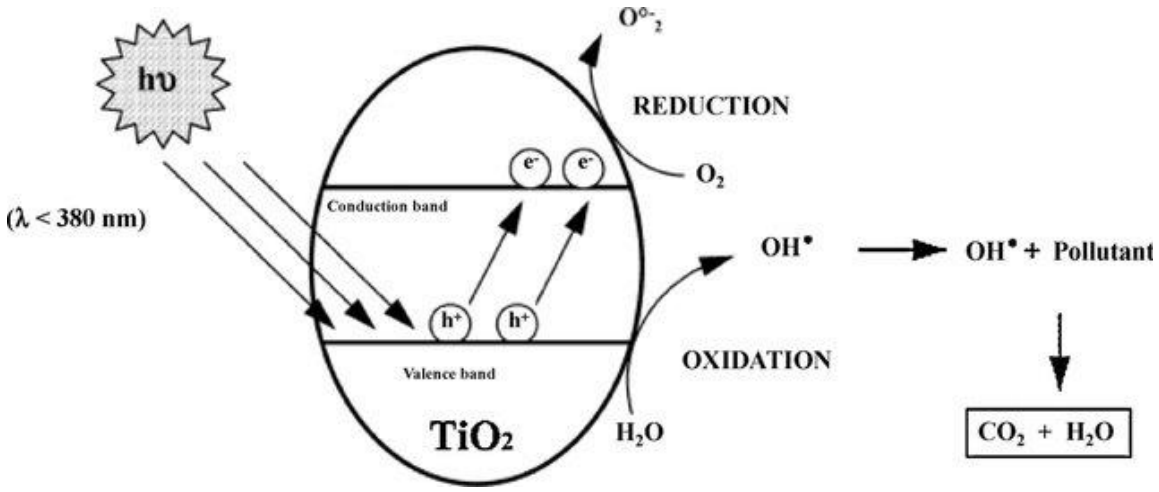

Figure 2.2. Mechanism of photocatalysis (source: Ghaly et al. 2011)

neutral pH within 180 minutes. Kaur et al., (2016) synthesized Bi_2WO_6 nano cuboids and studied the photocatalysis process using the synthesized Bi_2WO_6 nano cuboids to degrade levofloxacin and observed that more than 80% degradation was achieved within 150 minutes of reaction time. All such studies have confirmed that photocatalysis has got a significant potential towards treatment/mineralization of pharmaceutical compounds.

Table 2.7. Degradation of pharmaceutical drugs by photocatalytic treatment

Name of the drug	Conditions	Degradation efficiency	Reference
Diclofenac	Initial drug concentration:5-80mg/l TiO_2 loading: 0.2-1.6g/l; Source of UV: fluorescent lamp: 125W (350nm)	COD removal-85% at 0.8g/l within 120min of reaction time	Rizzo et al., 2009
Ibuprofen	Initial drug concentration: 5-20mg/l; TiO_2 loading: 50-3000mg/l; pH: 3.0-10; H_2O_2: 0.07–1.4mM	80% degradation within 120min of reaction time; TiO_2: 250mg/l; Initial drug concentration: 5mg/l; H_2O_2: 1.4mM	Achilleos et al., 2010
Carbamazepine	Initial drug concentration: 5-20mg/l; TiO_2 loading: 50-3000mg/l; pH: 3.0-10; H_2O_2: 0.07–1.4mM	79% degradation within 120min; TiO_2: 100mg/l; initial drug concentration: 5mg/l; H_2O_2: 1.4mM	Achilleos et al., 2010
Acetaminophen	Initial drug concentration: 25–100 μM, TiO_2 loading: 0.25–1.0 g/l, pH: 3–11	Degradation: around 95% within 100min of reaction time at 100 μM of drug concentration and TiO_2 loading: 1g/l	Zhang et al., 2008
Paracetamol	Initial concentration: 20mg/l; TiO_2 nanotubes; pH: 2.5, 4.5, 6.5, 8.5 and 10.5	Degradation: 99% within 100min reaction time at pH 6.5	Lozano-Morales et al., 2019
Cetirizine	Initial drug concentration: 5-25mg/l; TiO_2 dosage: 0.1–0.5 g/l; pH: 3–11, Time: 30–140 min	Degradation: 95.38% within 420min reaction time; TiO_2 dosage: 2.32g/l; drug concentration: 15mg/l; pH 3.35;	Talwar et al., 2019

Clofibric acid	Initial drug concentration: 1.5-30mg/l; TiO_2 dosage: 0.1-1.0g/l; pH:	Degradation: 100% at 1.5g/l drug concentration within 30min of reaction time; TiO_2 dosage: 1g/l	Favier et al., 2019
Oxolinic acid	Initial drug concentration: 20mg/l; TiO_2 dosage: 0.2-1.5 g/l; pH: 7.5-11	Degradation: 100% within 30min at pH 7.5 and TiO_2 1.0g/l	Giraldo et al., 2010
17 β-Estradiol	Initial drug concentration: 1µM; Hg-Xe lamp; TiO_2 dosage: 1.0 g/l	Degradation: 100% within 30min of reaction time	Ohko et al., 2002
Cephalexin	Initial drug concentration: 50mg/l; TiO_2 dosage: 0.25–1.75 g/l; pH: 3–8.5	Degradation: 80%; TiO_2 1.0 g/l; H_2O_2 0.15 ml and UV intensity of 25 W/m^2	Bansal et al., 2016
Amoxicillin	Initial drug concentration: 10-50mg/l; TiO_2 dosage: 300-600mg/l; H_2O_2 concentration: 100-200mg/l; pH: 3,7 and 11	Degradation: 80%, AMX - 30mg/l, TiO_2 dosage - 450mg/l, H_2O_2 concentration - 150 mg/l and pH – 7.0	Verma & Haritash, 2020
Ofloxacin	Initial drug concentration: 4-128mg/l; TiO_2 dosage: 8-128mg/l; H_2O_2 concentration: 8-128mg/l; pH: 3,6 and 10	Degradation: 89.3% within 60 min of reaction time; TiO_2 dosage: 128mg/l; addition of H_2O_2 1.68 mmol/l increased degradation efficiency to 97.8%.	Peres et al., 2015
Tetracycline	Initial drug concentration: 27, 55, 74, and 103 mg/l; TiO_2 dosage: 0.25-5mg/l; H_2O_2 concentration: 50-200mg/l; pH: 5-11	Degradation: 83% within 120min of reaction at initial drug concentration 55mg/l; TiO_2 dosage: 1g/l; pH: 5.0 and after addition of H_2O_2 concentration of 100mg/l, complete degradation was attained within 30min of reaction time	Safari et al., 2015

Metoprolol	Initial drug concentration: 50mg/l; TiO_2 dosage: 0.4g/l; pH: 9	Degradation: 100% within 240min at pH 9	Romero et al. 2013
Atenolol	Initial drug concentration: 4.5-30mg/l; TiO_2 dosage: 50 and 1000mg/l; pH: 4.8, 7.0, 9.0	Degradation: 75% at 20mg/l drug concentration; pH 9 and TiO_2 50mg/l	Tammaro et al. 2017
sulfamethazine	Initial drug concentration: 10-70mg/l; TiO_2 dosage: 1.0g/l; ZnO: 1.0g/l pH: 4.8	Degradation: more than 90% using ZnO and 35% using TiO_2 within 60min at 50mg/l of drug concentration	Kaniou et al. 2005
Chloramphenicol	Initial drug concentration: 50mg/l; TiO_2 dosage: 0.25-4g/l	Degradation: 100% within 90min of reaction time at TiO_2 1g/l.	Chatzitakis et al. 2008
Lincomycin	Initial drug concentration: 10, 20 and 50mg/l; TiO_2 dosage:400mg/l pH: 5.7 and 6.0	Degradation: 100% within 180min of reaction time at 50mg/l of drug concentration	Addamo et al. 2005
Tamoxifen	Initial drug concentration: 5-50mg/l; TiO_2 dosage: 0.4g/l pH: 10	Degradation: 100% degradation within 60min at 20mg/l of drug concentration	Yurdakal et al. 2007
Norfloxacin	Initial drug concentration: 0.15-0.5mM; TiO_2 dosage: 0.5-3g/l pH: 4-11	Degradation: 100% with 80min of reaction time at 0.25mM; TiO2: 1g/l and pH 10.4	Haque & Muneer, 2007

2.4.2.2 Fenton's treatment

Fenton process is another AOP which can efficiently degrade the pollutants. Fenton process preferably works at pH range of 2.0-4.0. The process involves the reaction of Fe^{2+} and H_2O_2 to generate hydroxyl radicals under acidic conditions as shown in Eq. (2.7) (Merli et al., 2003; Kavitha & Palanivelu, 2004; Bautista et al. 2008; Bagal & Gogate, 2014). Fe^{3+} regenerates Fe^{2+} by reacting with an excess of H_2O_2 and $^{\cdot}OOH$ as shown in Eq. (2.8) and (2.9) (Rozas et al., 2010).

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + OH^{-} + OH^{\cdot} \quad \text{.....2.7}$$

$$Fe^{3+} + H_2O_2 \rightarrow Fe^{2+} + HOO^{\cdot} + H^{+} \quad \text{.....2.8}$$

$$Fe^{3+} + HOO^{\cdot} \rightarrow Fe^{2+} + O_2 + H^{+} \quad \text{.....2.9}$$

Several studies reported the limitations of Fenton process like high hydrogen peroxide cost, iron sludge produced during process require additional treatment, storage risk, require neutralization of treated solution before disposal etc. (Bagal et al., 2014). To overcome the disadvantages of Fenton process, photo- assisted Fenton reaction can be used. Photo-Fenton process as compared to dark Fenton reaction leads to rapid mineralization as well as higher rate of reaction (Vilar et al., 2012).

The photo-Fenton process enhances the production of hydroxyl radicals by photo-reduction of Fe^{3+} to Fe^{2+} and photolysis of peroxide as shown in Eq. (2.10) and (2.11) (Shima et al., 2014).

$$Fe(OH)_2 + h\upsilon \rightarrow Fe^{2+} + {}^{\cdot}OH \quad \text{.....2.10}$$

$$H_2O_2 + h\upsilon \rightarrow 2{}^{\cdot}OH \quad \text{.....2.11}$$

Several researchers have reported **(Table 2.8)** that the application of solar light as compared to UV lamps is more economical and better alternative for the treatment of recalcitrant pollutants (Luna et al., 2014). It was also reported by several researchers that the Ferrioxalate (FeOx) can also be used for degradation of organic pollutants in photo-Fenton process. Ferrioxalate strongly absorbs between 250 and 500nm and has high quantum efficiency so, it is highly suitable for solar applications (Trovó et al., 2008). During the past few years electrochemical advanced oxidation processes (EAOPs) has become more popular among the

AOPs as these are more effective for degradation of refractory organic compounds. EAOPs are involved in production of strong oxidants like sulfate or hydroxyl radicals (in situ) in water medium. Various technologies involved in EAOPs are anodic Fenton, electro-Fenton and anodic oxidation. The degradation of compounds in EAOPs is carried out through direct electrolysis or indirect electrolysis. In direct electrolysis, there is direct exchange of electrons between the compounds and anodic surface and the participation of other substances is nil. In indirect electrolysis, there is reformation of electroactive species which behaves as a mediator for exchanging the electrons between the compounds and electrode. Efficiency of EAOPs can be increased by adding some external sources like UV light in photo-electro-Fenton or ultrasound in sono-electro-fenton or by combining it with other processes for improving degradation (Oturan et al., 2018). Anodic oxidation is based on direct EAOPS in which origin of hydroxyl radicals takes place through the oxidation of water over the highly oxygen developing anodic surface (Panizza & Cerisola, 2009). Some of the electrode materials like platinum, Boron doped diamond (BDD) etc. are considered as efficacious materials for electrode. In doped diamond, at the time of electrolysis, the area where the discharge of water takes place, the BD anodes encourage the generation of hydroxyl radicals which ultimately degrade the compounds with high current efficiency as shown in Eqs. (2.12) and (2.13).

$$BD + H_2O \rightarrow BDD(\bullet OH) + H^+ + e^- \quad \text{.....2.12}$$

$$BD(\bullet OH) + R \rightarrow BDD + CO_2 + H_2O \quad \text{.....2.13}$$

The degradation of antibiotic Trimethoprim (TMP) was studied by González et al. (2011) reported complete degradation of TMP at flow rate 1.25cm^3min^{-1}, pH 3.0 and the current density of 207 mA/cm^2. BDD can also be effective for degradation real pharmaceutical effluent. Based on experimental study done by Domínguez et al., (2012), almost complete removal of TOC was observed for real pharmaceutical effluent and the parameters such as flow rate and current density show maximum degradation within residence time of 77 minutes. Degradation of amoxicillin (AMX) was carried out using nanoscale zero-valent iron (nZVI) as a catalyst. It was observed that around 25% AMX was degraded using nZVI while more than 85% AMX was degraded using nZVI/H_2O_2 within 25 minutes at nZVI 500mg/l, H_2O_2 6.6 mM, pH 3.0 and AMX 50 mg/l. (Zha et

al., 2014). Electro-Fenton process is indirect EAOPs in which production of hydrogen peroxide is carried out in-situ on the cathode surface in acidic medium. Then the Fenton reaction takes place by combining the electrolytically produced hydrogen peroxide and externally added ferrous ions. Production of ferric ions takes place which further undergoes cathodic reduction and leads to regeneration of ferric ions as shown in Eqs. (2.15), (2.16), (2.17), and (2.18). During Electro-Fenton process pH remains under control because of production of protons at anode and production of carboxylic acids; while in conventional Fenton's process pH is not controlled because of the production of hydroxyl ions in water. Electro-AOP was categorized into two types on the basis of catalyst physical nature: Homogenous and Heterogenous process. In homogenous process, iron like ferrous sulfate and ferric chloride are used in soluble form as a catalyst while in heterogenous process solid catalysts are used which are slightly soluble or insoluble in water.

$$BDD + H_2O \rightarrow BDD(\bullet OH) + H+ + e - \text{.....} 2.15$$

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + OH^- + HO^{\bullet} \text{.....} 2.16$$

$$Fe^{3+} + e^- \longrightarrow Fe^{2+} \text{.....} 2.17$$

$$2H_2O \rightarrow O_2 + 4H^+ + 4e^- \text{.....} 2.18$$

Electro-Fenton (EF) and anodic oxidation (AO) processes using platinum (Pt) and BDD anodes and carbon felt cathode was used to study the degradation of ketoprofen which is a non-steroidal anti-inflammatory drug. It was observed that rate of degradation was increased with increase in applied current and complete mineralization was achieved with Pt, BDD anodes and carbon felt cathode Feng et al. (2014) Electro-Fenton process is advantageous as it is highly efficient in degradation, no sludge production, regeneration of ferrous ion is more and also production hydrogen peroxide is in-situ.

Table 2.8. Degradation of pharmaceutical drugs by Fenton's treatment

Name of the drug	Process used	Conditions	Degradation efficiency	Reference
Naproxen	Fenton and photo-Fenton	Fenton: Initial drug concentration: 100mg/l; H_2O_2 concentration: 300-800µl; Fe^{2+}: 200-1000µl; pH: 3.0-7.0; Photo-Fenton: Fe^{2+} 500 µl; H_2O_2 : 400 µl; pH: 3.0	Fenton: 81.92% degradation within 30min of reaction time; Fe^{2+} 500 µl; H_2O_2: 400 µl; pH: 3.0: Photo-Fenton: 83.43% within 30min of reaction	Herghelegiu1 et al., 2018
Sulfathiazole	Fenton and photo-Fenton	Initial drug concentration: 47µmol/l; Fe^{2+}: 47-188µmol/l; H_2O_2: 469-1970 µmol/l: pH: 3.0	Fenton: 84% degradation within 8min of reaction time; Fe^{2+}: 192µmol/l; H_2O_2: 1856 µmol/l at pH: 3.0 Photo-Fenton: 95% degradation within 8min of reaction time; Fe^{2+}: 157µmol/l; H_2O_2: 1219 µmol/l at pH: 3.0	Velásquez et al., 2014
Paracetamol	Fenton	Initial drug concentration: 100mg/l; H_2O_2 concentration: 28	100% degradation within 150min of reaction time; H_2O_2: 28mM; Fe_3O_4: 1g/l at pH 2.6	Velichkova et al., 2013

		and 153mmol/l; Fe_3O_4: 1 and 6g/l; pH: 2.6		
Diclofenac	Photo-Fenton	Initial drug concentration: 100mg/l; H_2O_2 concentration: 200-400mg/l; Fe^{2+}: 0.05mM; pH: 3.7-6.5	100% degradation within 60min reaction time; Fe^{2+}: 0.05mM; H_2O_2; 20mM; pH: 3.7	Pearez-estrada et al., 2005
Carbamazepine	Fenton	Initial drug concentration: $2.11x10^{-5}$mol/l; H_2O_2 concentration: $0\text{-}16.8x10^{5}$mol/l; Fe^{2+}: $0\text{-}1.68x10^{5}$mol/l; Fe^{3+}: $0\text{-}1.68x10^{5}$mol/l pH: 2.5-4.5	100% degradation at H_2O_2: $1.39x10^{-4}$ mol/l Fe^{2+}: $1.25x10^{-5}$mol/l; Fe^{3+}: $1.68x10^{-5}$mol/l pH: 3	Domínguez et al., 2012
Metoprolol	Photo-Fenton	Initial drug concentration: 20mg/l; H_2O_2 concentration: 0.0-105mg/l; Fe^{2+}: 0.0-3.15mg/l; pH: 2.9	Complete mineralization within 150min of reaction time at Initial drug concentration: 20mg/l; H_2O_2 concentration: 95mg/l; Fe^{2+}: 2.8mg/l; pH: 2.9	Veloutsou et al., 2014
Ciprofloxacin	Fenton	Initial drug concentration: 20mg/l; H_2O_2 concentration:26-51mM; Fe^{2+}: 5-10mM; pH: 3.0	Around 75% degradation within 45min of exposure at H_2O_2 : 26mM; Fe^{2+}: 5mM and pH 3.0	Rakhshandehroo et al., 2018

Doxycycline	Fenton	Initial drug concentration: 100mg/l; H_2O_2 concentration:2.9-26.5mM; Fe^{2+}: 0.09–2.1mM; pH: 5.0	100% degradation within 10min of reaction time at H_2O_2: 18mM; Fe^{2+}: 0.44mM	Borghi et al., 2015
Chloramphenicol	Photo-Fenton	H_2O_2 concentration: 0.044–0.088mM; Fe^{2+}: 0.016–0.064mM; pH: 5.8-7.7	79% degradation within 20min of reaction time at H_2O_2: 0.088mM; Fe^{2+}: 0.048mM; pH: 5.8	Ricardo et al., 2018
Oxacillin	Photo-Fenton	Initial drug concentration: 203µmol/l; H_2O_2 concentration: 0.09-10mM; Fe^{2+}: = 0.0036–0.09mM; pH: 6.0	100% degradation within 20min of reaction time: H_2O_2: 10mM; Fe^{2+}: 0.09mM	Giraldo-Aguirre et al., 2017
Trimethoprim	Photo-Fenton	Initial drug concentration: 0.0689 mmol/l; H_2O_2 concentration:0.03-5mM; Fe^{2+}: = 0.03-2mM; pH: 2.5-4.5	99% degradation within 6min of reaction time: H_2O_2: 0.09mM; Fe^{2+}: 0.09mM; pH: 4.56	Wang et al., 2019
Ampicillin	Solar Photo-Fenton	Initial drug concentration: 100 µg/l; H_2O_2 concentration:25-100mg/l; Fe^{2+}: = 5mg/l; pH: 3.0,8.0	100% degradation within 20min of reaction at H_2O_2: 75mg/l; Fe^{2+}: 5mg/l; pH: 3.0	Ioannou-Ttofa et al., 2019
Tinidazole	Photo-Fenton(U	Initial drug concentration: 202 µM; H_2O_2 concentration:500,900,	Photo-Fenton: 100% degradation within 60min of reaction time at	Velo-Gala et al., 2017

	V)and Solar photo-Fenton	1500µM; Fe^{2+}: = 90,180,360µM; pH: 3.0,8.0	H_2O_2 : 100 µM; Fe^{2+}: 90µM and pH: 3.0 Solar photo-Fenton: around 98% degradation within 60min of reaction time; H_2O_2 : 500 µM; Fe^{2+}: 360µM and pH: 3.0	
Mitoxantrone	Photo-Fenton (Fe^{3+}, FeOx and UV/H_2O_2)	Initial drug concentration: 0.07mmol/l; Photo-Fenton: Fe^{2+}: 0.54, mmol/l; H_2O_2: 18.8 mmol/l at pH 3.0	UV/H_2O_2: 90% mineralization; FeOx: 82%; Fe^{3+}: 77%	Cavalcante et al., 2013
Ibuprofen	Electro-Fenton	Initial drug concentration: 0.2mM; Electrolytes (Na_2SO_4): 0.05M; Current: 50-500mA; pH: 3.0	Degradation: 100% in 50min of reaction time; current: 50mA	Loaiza-Ambuludi et al., 2013
Chloroquine	Electro-Fenton	Initial drug concentration: 34-250mg/l; Electrolyte (Na_2SO_4): 0.05M; current: 20-200mA/cm^2; Fe^{2+}: 5-20mg/l; pH: 3.0-12.0	Degradation: 100% within 180min of reaction time; Initial drug concentration: 125mg/l; Electrolyte (Na_2SO_4): 0.05M; Fe^{2+}: 10mg/l; current: 60mA/cm^2; pH: 3.0	Midassi et al., 2020

Metformin	Electro-Fenton	Initial drug concentration: 1.25mM; Electrolyte (Na_2SO_4): 0.05M; current: 100-400mA; Fe^{2+}: 0.1-0.3mM; pH: 2-4	Degradation: 99.5% within 27min of reaction time; current: 300mA; Fe^{2+}: 0.1mM; pH; 3.0	Orata et al., 2019
Ketoprofen	Electro-Fenton	Initial drug concentration: 0.198 mM; Electrolyte (Na_2SO_4): 0.05M; current: 100–2,000 mA; Fe^{2+}: 0.05-1mM; pH: 3.0,7.5 and 10.0	Degradation: 100% within 30min of reaction time; Current: 300mA; Fe^{2+}: 0.1mM; pH: 3.0	Feng et al., 2014
Sulfamethoxazole	Solar photo-Fenton	Initial drug degradation: 50mg/l; H_2O_2: 30-210mg/l; Fe^{2+}: 2.6,5.2, 10.4mg/l	Degradation: 100% within 16min of reaction time; H_2O_2: 30mg/l; Fe^{2+}: 2.6mg/l	Trovo et al., 2009
Amoxicillin	Fenton	Initial drug degradation: 10-200mg/l; H_2O_2: 10-500mg/l; Fe^{2+}: 0-50mg/l;pH: 3.5	Degradation: 100% degradation within 2.5min reaction time; Initial drug degradation: 105mg/l; H_2O_2: 255mg/l; Fe^{2+}: 25mg/l	Ay & Kargi, 2010

2.4.2.3 Ultrasonic Treatment

Ultrasound removes pollutants without the generation of contaminants and can be regarded as a 'green' technology. Under the periodic pressure variations, acoustic cavitation implies the formation and subsequent expansion of micro-bubbles which leads to production of ·OH radicals (Li et al., 2010; Eren, 2012). Ultrasound carries out acoustic cavitation mainly above 20 kHz. When ultrasound irradiation propagates in solution, a sequence of compression and rarefaction waves occurs. Cavitation bubbles are formed which increase in size and reach to an unsteady size at sufficient high power causing the bubble to collapse violently. At high temperature and pressure of 2000ºC and 200 atm, respectively, the auxiliary liberation of heat leading to formation of 'hotspots' within the reaction mixture **(Fig. 2.3)**. At these extreme conditions of temperature and pressure, the bond of dissolved gases, organic substances and water vapors gets ruptured and ultimately leads to generation of hydroxyl radical from water dissociation as indicated in Eq. 2.19.

$$H_2O +))) \rightarrow \cdot H + \cdot O \quad \text{.....2.19}$$

The perhydroxyl radical is formed in presence of oxygen as shown in Eq. 2.20.

$$\cdot H + O_2 \rightarrow \cdot OOH \quad \text{.....2.20}$$

The radicals which are fabricated disperse in the suspension while at the same time hydrogen peroxide liberated from the incorporation of ·OOH and ·OH radicals Eq. 2.21 and 2.22.

$$2\cdot OH \rightarrow H_2O_2 \quad \text{.....2.21}$$

$$2\cdot OOH \rightarrow H_2O_2 + O_2 \quad \text{.....2.22}$$

There are three zones which can be characterized in cavitation process bulk of dissolution, supercritical interface, and bulk liquid zone (Mendez-Arriaga, et al., 2009). The details of the process are as given below

- Bulk of dissolution: In this zone, at the interior of bubble cavity i.e. gaseous zone, degradation of hydrophobic and volatile molecules takes place through hydroxyl radicals and pyrolysis.
- Supercritical interface: This zone is the interface of bubble (gas) and liquid. The hydroxyl radicals generated in the bubble react with the hydrophobic molecules at the interface region to degrade them.
- Bulk liquid zone: The radicals which are formed at the interface of bubble and liquid are migrate to form secondary sonochemical reactions. The pathway of sonochemical degradation of molecules mainly depends upon its solubility, activity of surface and its volatility (Pilli et al., 2011).

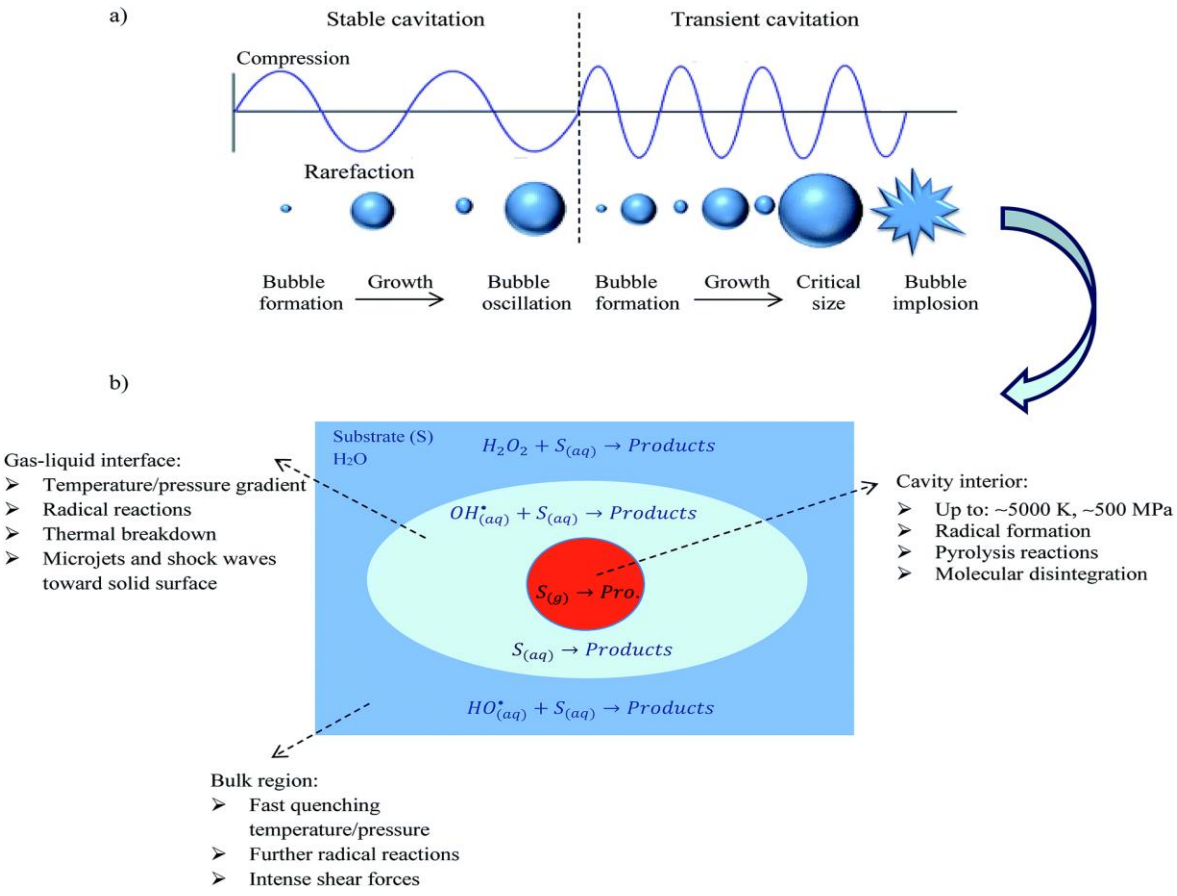

Figure 2.3 Principle of Ultrasonication process (Pirsaheb & Moradi, 2020)

At lower frequency, in the range of 20-40kHz, the bubbles formed are big in size and long-lasting and also there is recombination and scavenging of •OH through another radicals in cavity of bubble as well as at the interface of bubble and liquid leading to ejection of smaller quantity of •OH to bulk solution. Therefore, this condition leads to degradation of hydrophobic and volatile compounds as these can readily diffuse into cavity of the bubble or interface region (González-García et al., 2010). Several studies have been reported on degradation of drugs from lower to higher frequencies (Isariebel et al., 2008; Méndez-Arriaga et al., 2008; Matouq & Tagawa, 2014) and it was concluded that ultrasonication is mainly dependent upon transducer and molecules to be degraded.

The degradation of pharmaceutical drugs such as diclofenac, AMX, carbamazepine individually and by mixing them with urban wastewater effluent was studied by (Naddeo et al., 2009). The initial substrate concentration was varied from 2.5-10mg/L and pH was varied from 3.0-11.0. It was observed that at lower frequency, with or without mixing the samples in wastewater, low frequency sonication can efficiently degrade the compounds by generating the hydroxyl radical and it acts as better pretreatment option for biological and other oxidation processes. The degradation of amoxicillin using high frequency ultrasonic waves (2.4MHz) and without ultrasonic waves was studied by (Matouq & Tagawa, 2014) **(Table 2.9)**. The concentration of amoxicillin and concentration of outlet wastewater effluent was selected to be similar in pharmaceutical industry as 50 and 100ppm. The rate of degradation of antibiotic amoxicillin was increased when ultrasound waves and H_2O_2 were applied together. It was observed that the ultrasound waves double the degradation of amoxicillin than without ultrasonic waves.

Ultrasonication is considered to be one of the effective technology but the individual use of ultrasonication process has some limitation over degrading the compounds. So, combining the ultrasonication with other AOPs such as photocatalysis (Sonophotocatalysis), Fenton (Sono-Fenton) and photo-Fenton (Sono-photo-Fenton) significantly improves the degradation efficiency of the pharmaceuticals. In sonophotocatalysis process, a semiconductor photocatalyst is combined with ultrasonication in the presence of UV irradiation to generate more hydroxyl radicals. The degradation of pharmaceuticals is primarily obtained as a result of synergistic effect due to ultrasonication and photocatalysis. Ultrasonication process in combination with photocatalysis frequently clean surface of photocatalyst to maintain the action of photocatalyst for relatively

longer duration of time and also able to degrade hydrophobic as well as hydrophilic compounds and ultimately increase the process efficiency (Madhavan et al., 2010).

In the sono-Fenton process, combination of ultrasound and Fenton process results in synergistic effects and also responsible for reducing the time of treatment and cost of chemicals which ultimately increase the effectiveness of the process. Hydrogen peroxide produced in the ultrasound process combined with Fe^{2+} to generate $^{\bullet}OH$ that may attack the target compound (Eq. 2.23). Ultrasound may also be responsible for increasing disintegration of $Fe\text{-}OOH^{2+}$ into hydroperoxyl radicals and Fe^{2+} (Eq. 2.24) (Ma, 2012).

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + OH^- + {}^{\bullet}OH \quad \text{2.23}$$

$$Fe\text{-}OOH^{2+} +))) \rightarrow Fe^{2+} + {}^{\bullet}OOH \quad \text{2.24}$$

Furthermore, formation of hydrogen radicals ($^{\bullet}H$) occurs through water sonolysis which is further combined with either ferric ion, hydrogen peroxide, hydroxyl radical or hydroperoxyl radicals to generate ferrous ion, hydroxyl radicals, water or hydrogen peroxide respectively as per the equations given below (Vaishnave et al., 2012).

$$Fe^{3+} + {}^{\bullet}H \rightarrow Fe^{2+} + H^+ \quad \text{2.25}$$

$$^{\bullet}H + H_2O_2 \rightarrow {}^{\bullet}OH + H_2O \quad \text{2.26}$$

$$^{\bullet}OH + {}^{\bullet}H \rightarrow H_2O \quad \text{2.27}$$

$$^{\bullet}H + {}^{\bullet}OOH \rightarrow H_2O_2 \quad \text{2.28}$$

Finally, ferrous ion originated from Eq. 2.24 and 2.25 combines with hydrogen peroxide as observed in Fenton process.

When the semiconductor catalyst coupled with ultrasound in the Fenton process (Sono-photo-Fenton), the degradation efficiency increases in the presence of UV irradiation due to synergistic effect. This will lead to generation of more hydroxy radicals and regeneration of ferrous ions. Low frequency ultrasound with catalyst may enhance mixing and reduces limitation of mass transfer, increases the active sites of catalyst by reducing its particle size and also responsible in frequent cleaning of catalyst surface (Gogate et al., 2002).

Table 2.9. Degradation of pharmaceutical compounds by Ultrasonic treatment

Name of drug	Process used	Conditions	Degradation efficiency	Reference
Diclofenac	Sonolysis	Initial drug concentration: 15, 30, 70, 130µM; frequency: 577, 861, 1145 kHz; pH: 3.0, 5.7, 9.0; Temperature: 25^{o}C	Degradation: 100% within 60min of reaction time at drug concentration: 30µM; frequency: 861kHz; pH: 5.7,	Güyer & Ince, 2011
Acetaminophen	Sonolysis	Initial drug concentration: 33–1323µM/l; ultrasonic power: 20-60W; pH; 3-12; frequency: 600kHz	Degradation: 46% within 60min of reaction time at drug concentration: 83µM; ultrasonic power: 60W; pH: 5.6	Villaroel et al., 2014
Paracetamol	Sono-photocatalysis	Initial drug concentration: 0.03-0.12mM; ultrasonic power: 16,35, 55mW/ml; Frequency: 213kHz	Degradation: 40.2x 10^{-7} drug concentration: 0.09mM; TiO_2: 1g/l; ultrasonic power: 55mW/ml	Jagannathan et al., 2013
Ciprofloxacin	Sono-Fenton	Initial drug concentration: 100mg/l; Frequency: 580,862kHz; pH: 3.0; H_2O_2: 0-28.4mM; Temperature: 30^{o}C	Degradation: 99% within 15min of reaction time; frequency; 580kHz; H_2O_2/Fe^{2+}ratio: 6; H_2O_2: 28.4mM	Labrada et al., 2019
Tetracycline	Sonocatalysis (TiO_2/H_2O_2)	Initial drug concentration: 25-100mg/l; H_2O_2: 20-	Degradation: 100% within 75min of reaction time at drug	Hoseini et al., 2013

		100mg/l; TiO_2: 100-500mg/l; frequency: 35kHz; pH: 4.0-9.0	concentration: 75mg/l; TiO_2: 250mg/l; pH: 5.5; H_2O_2: 100mg/l	
Carbamazepine	Sonolysis and Sono-photocatalysis (TiO_2/UV)	Initial drug concentration: 10mg/l; power: 130-640W/l; TiO_2: 100mg/l	Snolysis: 50% degradation within 90min of reaction time; power; 640W/l Sono-photocatalysis; 82% within 120min of reaction time	Jelic et al., 2013
Naproxen	Sono-Fenton	Initial drug concentration: 4.80-30.72mg/l; Fe^{2+}: 0.49-4.86mg/l; H_2O_2: 0.0176-176mmol/l; pH: 3.0-5.3	Degradation: 100% within 10min of reaction time; H_2O_2: 9.98mmol/l; Fe2+; 4.83mg/l; pH: 3.0	Lan, et al., 2012
Sulfadiazine	Sonolysis and Sono-Fenton	Initial drug concentration: 25,50,70mg/l; frequency: 574, 860, 1134kHz; pH: 3-11; Fe^{2+}: 2-20mg/l; H_2O_2: 120,671, 1220mg/l	Sonolysis: 90% degradation within 120min of reaction time at drug concentration: 25mg/l; frequency: 574kHz; pH; 5.5 Sono-Fenton: 99% degradation within 15min of reaction time; Fe^{2+}: 20mg/l; H_2O_2: 1220mg/l	Lastre-Acosta et al., 2014

Ibuprofen	Sonolysis	Initial drug concentration: 2-21mg/l; frequency: 200-400kHz; power; 20-80W; pH: 3.0-11.0	Drug: 98% degradation within 30min of reaction time at 21mg/l drug concnetration; frequency: 300kHz; power: 80W; pH: 3.0	Méndez-Arriaga et al., 2008
Atenolol	Sonolysis	Initial drug concentration: $1–50\times10^{-6}d/m^3$; frequency: 200,350,620kHz, 1MHz; power: 20 to 80W; pH: 4-8	Degradation:100% within 60min of raction time at $10^{-5}mol/dm^3$; Frequency: 350kHz; power: 50W; pH: 4.0	Nejumal et al., 2014
Amoxicillin	Sonophotocatalysis (UV and Solar)	Initial drug concentration: 30mg/l; TiO_2: 450mg/l; H_2O_2: 150mg/l; pH: 7.0 Frequency: 40kHz	Degradation: 80% within 150min of reaction time at 30mg/l drug concentration	Verma & Haritash, 2020
Amoxicillin	Sono-Fenton and Sono-photo-Fenton	Initial drug concentration:10mg/l; Fe^{2+}: 30mg/l; H_2O_2: 375mg/l; pH: 3.0	Sono-Fenton: 100% degradation within 20min of reaction time Sono-photo-Fenton: 100% degradation within 6min of reaction time	Verma & Haritash, 2019

2.5 Management of pharmaceutical wastewater

As discussed earlier, the wastewater generated from pharmaceutical manufacturing industry is heterogenous and enormous in quantity. So, the treatment of such a complex wastewater needs effective disposal and management technologies. The major constituents of pharmaceutical wastewater are the residual drugs which pose high COD, BOD like surfactants, antibiotics, volatile organic compounds (VOCs), and hormones and consequently leads to ecosystem imbalance. From the studies it was concluded that the antibiotics are leading drug that are used to cure diseases and now -a-days not only wastewater but also the disposal of unused drugs are responsible for generating ARB and ARGs. These ARB and ARGs are carried to surface water, ground water system and pose threat to human life. Sometimes, pharmaceutical wastewater mixes with STPs or with the wastewater discharged from treatment units which makes it more complex and challenging to treat it efficiently. Segregating the components of waste for the purpose of recovery increase the overall cost of the treatment process. Individual treatment approaches lead to generation of undiscovered issues related to treatment of wastewater and introduce different kind of wastewater which is difficult to treat. Waste from pharmaceuticals are divided into two classes in order to introduce effective treatment technologies and for developing a global policy to minimize the waste in an eco-friendly manner:

- Waste produced from pharmaceutical industries and secondary waste generated from recycling and treatment operations.
- Waste obtained from domestic sources and hospitals which extensively responsible for polluting sewage system.

Various physical, chemical and advance treatment technologies like autoclaving, adsorption, AOPs etc. are used to handle such a hazardous waste as discussed below.

2.5.1 Incineration

This method is mainly selected for disposing the sludge at high temperature. It involves the burning of waste in open environment without taking any measures to control the spreading of disease-causing microbes and ash disposal. The ash generated through burning of waste is further buried in landfill. It reduces the volume of waste and toxicity of waste by converting it to ash and consequently reduces the volume of waste, cost and its impact on landfill (Lee & Huffman, 1996). This is not an eco-friendly technique as it involves transfer of

contaminants of water to air and sometimes results in emission of dioxins, mercury and furans into the environment (Insa et al., 2010; Jiang et al., 2012). According to Central Pollution Control Board (CPCB), in India, incinerator must be comprising of scrubber to control the air pollution and the ash produced from incinerators should be disposed in a designated landfill. So, the use of such kind of incinerator increases the operational and investment cost (Jaseem et al., 2017).

2.5.2 Autoclaving

This method can be used as a substitute of incineration method. It involves the suspension of microbial growth on waste, and harmful chemicals under high temperature. Antibiotic residues contain high organic load which need to be treated using autoclave. The temperature requires to carry out the process is varying from 121-163^{o}C (Lee et al., 2004; Windfeld & Brooks, 2015). The waste treated from autoclave does not contain infectious waste and can be discharged directly to municipal solid waste landfill. Autoclave method is more beneficial than incineration method as it does not generate the toxic contaminants from PVC and other toxic chemicals like dioxins, furans, and mercury etc. It generates the waste from steam for eliminating the microbes without burning the waste directly which looks like untreated waste, therefore sometimes treated and untreated waste get mixed and dumped to landfill. Because of this problem, the waste from autoclave has to be pretreated using incineration before disposing it finally and this will ultimately increase the energy use and disposal cost of the process (Klangsin & Harding, 1998; Windfeld & Brooks, 2015; Rajbongshi et al., 2016). Another problem with this method is that it has not efficiently reduces the volume of the waste for landfill while the incinerators has the efficiency to reduce the original waste volume to 70-80% (Verma, 2014). In spite of higher efficiency of autoclaving, it needs to sterilize supercritical fluid for further treatment which is quite toxic (Hossain et al., 2011). So, developing an economical treatment method for treatment of pharmaceutical waste is difficult task.

2.5.3 Land filling

This method can be considered as an optional method for disposing the pharmaceutical waste. In Landfill, disposal of sludge waste is carried out by burying the waste and this is one of the common method applied in many countries. According to biomedical waste rules, landfills are also used to discard unused medicines, chemical waste, ash from incineration and cytotoxic drug etc. (Vilar et al., 2011). Unused or empty quarries, pits or

mining voids were used as a landfill. It is one of the economical methods for waste disposal if the landfill is well established and designed properly. But it leads to production of gases such as CO_2 and methane which generates odor issues and affect vegetation (Jiang et al., 2012). It also results in contamination of water resources through leaching and not able to nullify the harmful effects generated due to hazardous substances present in waste. The pharmaceutical residues get bioaccumulate in the leachate and may reach to ground water through leakage which makes the landfill more dangerous to water resources. So, the landfill should be design in such a way that it can overcome the problem of leachate and generation of noxious gases. For leachate problem, plastic or clay lining material can be used (Schwarzbauer et al., 2002; Wang et al., 2003). When the waste get deposit over landfill, it should be covered to obstruct the entry of vermin and should be compacted to enhance its stability as well as density. Gas extraction system can be installed for the extraction of gases and perforated pipes are used for pumping the gas which can be be further burn for the generation of electricity (Pratyusha et al., 2012).

2.5.4 Waste minimization

Waste minimization is the reduction of waste or stoppage of waste from production level. Minimization of waste can be achieved by reusing the products, designing of reusable or refill products and by avoiding use of disposable things, using less material for package purpose (Windfeld & Brooks, 2015; Rajbongshi et al., 2016). Reduction of waste at source level can be achieved using three methods: Reformulation of product, Substitution of material and Modification of Process. Product reformulation reduces the toxicity and volume of the pharmaceutical waste through substituting the raw material in the process. However, this process extends the time for testing and redevelopment of drug. the properties effect of the drug produced from reformulation is same as actual drug (Sreekanth et al., 2014). On the other hand, material substitution process replaces the hazardous material to non-hazardous material used in manufacturing of drugs and results in reduction of toxicity, hazardous residual material and volume (Institute for Local Self-Reliance, 1986). But the coating of tablet leads to emission of volatile organic compounds which should be controlled by installing air quality equipment (Waymant & Miller, 1987). This increases the cost of the overall process. In process medication, generation of waste minimize through modification of process or modernization. Modification of process can be attained by doing changes in equipment of the process and operational parameters. Whereas in modernization updated control mechanisms are installed or levels of control are increased. This increases the efficiency of the reactor and minimizes

the formation of byproduct. Incomplete chemical reactions lead to the generation of waste in the process. Sedimentation, corrosion and crystallization causes deposition of fouling and consequently increases generation of waste and reduces operational efficiency. Fouling deposition can be obstructed by increase in agitation process or by modifying operational temperature (ICF technology, 1987).

2.5.5 Recycling and recovery

Recycling and recovery involve elimination of impurities present in waste to achieve pure material, reusing of waste directly and recovery of secondary material for using separately for other process. Recycling process has been primarily used for organic waste however recovery of energy is suspended in it (Freeman & Eby, 1987). The purity of the material recovered from manufacturing process is high and requires strict regulation for controlling the quality of products. For example, Ammonium chloride use in process can be recovered using evaporation (Patterson & Minear, 1974). Pharmaceutical manufacturing process generate byproducts such as sodium sulphate and ammonium sulphate. Sodium sulphate is concentrated and dried for further use in glass industry while ammonium sulphate can be use as material for fertilizer. This process is advantageous for environment as it controls the use of raw substances (Freeman & Eby, 1987; Fried & Stockton, 1973). The waste generated from fermentation process can be use as feeding material for animals, amendment of soil and as fertilizer (EPA 1983). The recycling of solvent waste can be improved by reducing the concentration of solids in waste, by recording composition and methods from waste generated and by segregating the solvent waste. Solvent waste segregation involves segregation of aliphatic from aromatic, chlorinated from non-chlorinated, freon from methylene chloride solvent (Cue & Zhang, 2009). The recycling can be done on-site or off-site depending on operational cost, expertise needed and capital investment. On-site treatment of waste reduces the cost and accountability for transporting the waste off-site, reduces requirements for reporting and lowers unit cost required for the use of raw material. But this can increase the maintenance and operational cost, risk for workers and operational training. On the other hand, off-site recycling is used for small quantity generators. It can be performed for the facilities at commercial level. This method of recycling is more beneficial when the volume of the waste is small and on-site treatment is not available (Ozkan, 2013; Taghipour et al., 2014).

2.5.6 Constructed wetlands

Constructed wetlands can be used to treat the wastewater containing pharmaceuticals. These can be categorized as: vertical subsurface flow wetland, horizontal subsurface flow wetland, surface free water wetland and hybrid wetland. In the surface free water wetland, wastewater flows freely at shallow depth planted accommodated with vegetation above the water-resistant bottom and packed with a layer of substrate while the flow of water is horizontal across the substrate. The water is fed from inlet zone and collected from outlet zone in the wetland. In case of vertical subsurface flow wetland, dosage of wastewater has given on the surface which further flows vertically from the vegetation planted in the wetland. The hybrid wetlands are made by combining the two or more wetlands to improve the efficiency of treatment (Li et al., 2014; Ilyas et al., 2020). The evaluation of removal efficiency of constructed wetland is significant criteria for evaluating its performance. On the basis of removal efficiency in constructed wetlands, pharmaceuticals can be classified as hardly removable, low removable, moderately removable and readily removable. Ampicillin, lincomycin and erythromycin show removal efficiency less than 20% and can be categorized as hardly removable. The removal efficiency of pharmaceuticals varies from 20-50% can be categorized as low removable and includes amoxicillin, diclofenac, clarithromycin, sotalol, carbamazepine and ketoprofen. In case of moderately removable, the efficiency of pharmaceuticals such as naproxen, ibuprofen, gemfibrozil and doxycline may vary from 50-70% while efficiency of removal may increase more than 70% for readily removable pharmaceuticals. Atenolol, metoprolol, tetracycline, acetaminophen, furosemide, sulfamethoxazole, sulfamethazine, and sulphapyridine are readily removable drugs (Matamoros et al., 2007; Zhang et al., 2008; Matamoros et al., 2008; Hijosa-Valsero et al., 2011; Hussain & Prasher, 2011; Hussain et al., 2012; Anderson et al., 2013; Ávila et al., 2013; Carvalho et al., 2013). In constructed wetlands, plants play a major role in removal of organic pollutants. The plants do not have transporters to carry the organic compounds like pharmaceuticals from roots of the plant to tissues. However, these compounds can be translocated through diffusion process. Several researchers reported different plant species for removal of pharmaceutical drugs using constructed wetlands. *Typha latifolia*, *Typha angustifolia* and *Phragmites australis* are common species used in constructed wetlands for removal of drugs (Dordio et al., 2009a; Xian et al., 2010). The removal efficiency is higher in *Typha spp*. than *Phragmites australis* due to higher rate of transpiration of *Typha spp.* (Zarate Jr et al., 2012; Li et al., 2014). However, the major disadvantage associated with constructed wetland is that it requires large space to carry out the process (Llorens et al., 2009).

2.5.7 Zero discharge approach and biopharmaceuticals

Zero discharge approach is the green approach in which process is designed to eliminate all the waste produced during treatment processes. Although the zero discharge is difficult to achieve but the green pharmacy can be used to make it possible. In this approach, firstly the process involved in production of product has been observed to make it innoxious. Then the production of products has been attained using lesser energy, fewer steps, reducing the production of by products to make it biodegradable and eco-friendly (Lapkin & Constable, 2008; Pal & Dey, 2013; Pal & Nayak, 2015). Biopharmaceutical is also a green approach in which biotechnology is used to generate pharmaceutical drugs. This process uses microbes and biocatalysts peculiarly enzymes for the production of substances used for making drugs. This is an economical and eco-friendly method as it minimizes the use of synthetic catalyst (Zaks & Dodds, 1997). Several noxious pharmaceutical compounds that cannot be treated from conventional treatment plants can be converted into biodegradable form using biocatalytic processes (Tao & Xu, 2009). Pregabalin, levetiracetam, paroxetine, simvastatin and atorvastatin are the examples of small molecules of pharmaceuticals which are synthesized using biopharmaceuticals. Application of these processes may results elimination of hazardous chemical reactions. However, risk of pharmaceutical waste can be avoided using less material and less energy in manufacturing process to reduce the generation of waste (Hu et al., 2006). So, to minimize the waste and threat from pharmaceuticals we should switch over to green technologies.

CHAPTER 3
MATERIALS AND METHODS

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3.1 Collection of Pharmaceutical wastewater

The real industrial pharmaceutical wastewater of AMX producing batch was collected from Euro Healthcare pharmaceutical industry located in industrial area of Bhagwanpur, Uttrakhand, India. The treated and untreated wastewater **(Fig. 3.1)** was collected in pre-rinsed HDPE cane (50L) and stored in refrigerator at 4°C temperature until analysed. The industrial wastewater had residual concentration of 210 mg/l of AMX, after treatment through in-house effluent treatment plant (ETP). The initial characterization of wastewater was done for pH, Electrical conductivity (EC), TDS, and COD according to the methods prescribed by APHA. All the chemicals used for analysis were analytical grade (AR); and the solutions/reagents were prepared using Type I ultrapure water.

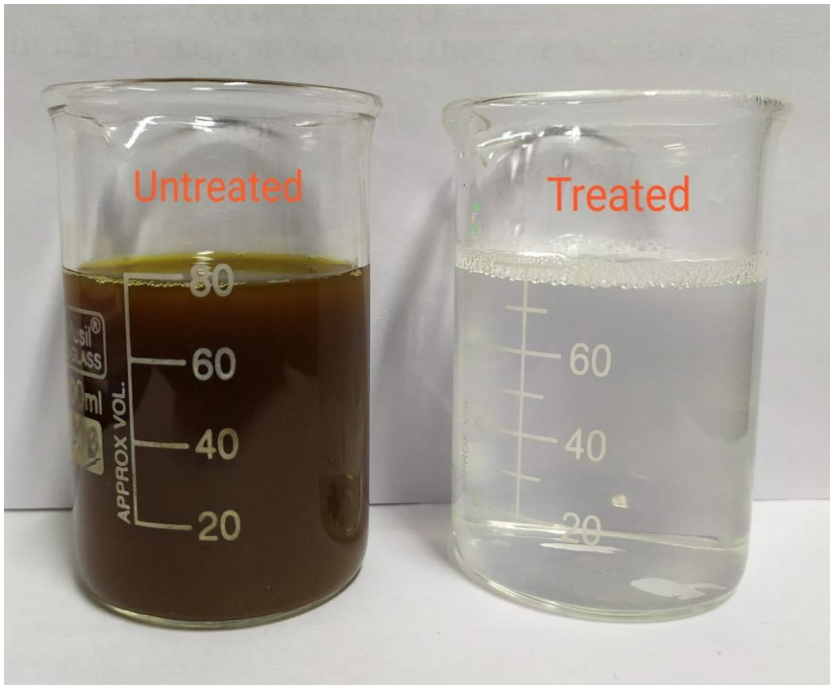

Figure 3.1 Difference in appearance between untreated and treated (in-house ETP) effluent used in the present study

As the real wastewater collected from industry was from AMX manufacturing batch, so to compare the results of AMX in wastewater with pharmaceutical drug, AMX was selected as model compound for further study on degradation.

Another drug selected for study was Atenolol, a β-blocker drug as the problems related to cardiac and hypertension have been increasing now-a-days which consequently leads to increase in use of these drugs. The detail of each drug selected for study is discussed below.

3.1.1 Amoxicillin (AMX)

AMX is primarily used as semi synthetic penicillin which belongs to β-lactam group of antibiotics, and particularly responsible for obstruction of bacterial cell wall synthesis (Verma & Haritash, 2020). Chemically AMX can be defined as (2S,5R,6R)-6-[[(2R) -2-Amino-2-(4-hydroxyphenyl) acetyl] amino] -3,3dimethyl-7-oxo-4-thia-1-aza-bicyclo [3.2.0] heptane-2--carboxylic acid as shown in **Fig. 3.2**. AMX is moderately soluble in ethanol (around 96%) and water while insoluble in oils. It also shows dissolving properties in diluted solution of hydroxides of alkali and diluted acids. Half-life of elimination of AMX is around 1-1.5hours and it mainly eliminates from urine (Kaur et al., 2011). The mechanism of action of AMX is to hinder the synthesis of peptidoglycan of bacterial cell wall (Pan et al., 2008). It was also reported that around 70% of the antibiotics used worldwide comes under the category of β-lactams (Längin et al., 2009). It is mainly used to treat infections from bacteria such as pasteurellosis, furunculosis and streptococcosis. AMX is dominantly used in human and veterinary medicine, and on the basis of its consumption, WHO designated it as one of the extremely significant antimicrobial drug. Absorption of AMX is very fast and it remains unchanged when defecated from the body (Umamaheswari et al., 2019). Several authors have reported notable concentration of AMX in effluents of manufacturing unit, surface water, effluents from ETP units, effluent of sewage treatment plant, and other environmental compartments as well (Trovo´et al., 2011; Dimitrakopoulou et al., 2012). AMX can give rise to ARB even at low concentration.

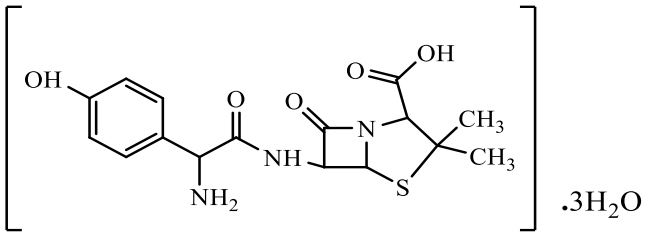

Figure 3.2. Chemical structure of amoxicillin (AMX)

3.1.2 Atenolol (ATL)

β-blockers are one of the important class of PCs which are mainly prescribed for cardiovascular diseases and to cure disorders like cardiac arrhythmias, hypertension and angina pectoris. These are aromatic compounds having multi-functional groups, lower vapor pressure, soluble in water and ionizable (Liu & Williams, 2007). Among β-blockers, $\beta 1$ receptor antagonist, ATL which are widely used for cardiovascular diseases have been selected for the present study. In India, it was predicted by World Health Report 2002 that the heart diseases are going to be rise by 2025 which will ultimately increase the use of β- Blockers. β- Blockers attacks β-adrenergic receptors by preventing the activity of adrenaline and noradrenaline predominantly in heart. These drugs are found in excessive quantities in discharges from urban wastewater treatment plants (El-Hanaf et al., 2014). Trace concentration of ATL has been detected in municipal sewage and surface water (Hapeshi et al., 2010). ATL is ecotoxic for freshwater species and also inhibits the growth of human embryonic cells. After the process of disinfection, ATL also retains phytotoxic activity at the time of chlorination (Bhatia et al., 2017). Several studies reported that conventional treatment technologies such as activated carbon, membrane technologies and activated sludge fail to completely degrade ATL. It also persists in the environment for a longer duration like other PACs because these prevail against natural attenuation and biological degradation (Tammaro et al., 2017). ATL is mainly excreted as parent compound from human body as only around 50% of orally taken drug is absorbed. Chemically, ATL is defined as benzeneacetamide (2-[4-(2-Hydroxy-3-isopropylamino-propoxy)-phenyl]-acetamide) and the chemical structure of ATL is shown in **Fig. 3.3**. The molecular formula and moleculare weight of ATL is $C_{14}H_{22}N_2O_3$ and 266,33 (C 63,13%, H 8,33%, N 10,52%, O 18,02%) respectively. The solubility of ATL in water is 26.5mg/ml at 37◦C (Hapeshi, et al., 2010).

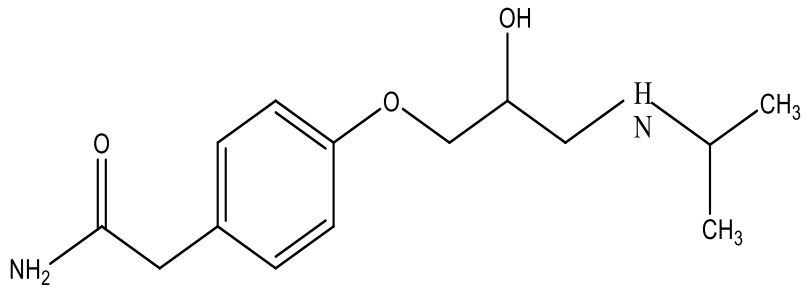

Figure 3.3. Chemical structure of ATL

3.2 Chemicals used for the study

The analytical grade (AR) amoxicillin trihydrate (99.5%) and ATL was purchased from Sigma-Aldrich, India and synthetic solution of AMX was prepared in ultrapure Type-I water. Ferrous sulphate ($FeSO_4.7H_2O$) (99.5%) used for Fenton experiments was purchased from SRL chemicals, India and Hydrogen peroxide (H_2O_2) (30% w/v) used in Fenton and photocatalysis experiment was also obtained from SRL chemicals, India. Sodium hydroxide (NaOH) and Sulphuric acid (H_2SO_4) used for pH adjustments were purchased from CDH, India. TiO_2 - P25 (Anatase to Rutile ratio - 80:20) which was used as catalyst in photocatalysis experiments was purchased from Evonik, India. HPLC grade acetonitrile, methanol and phosphate buffer were used for HPLC analysis. Ultrasonication (Labman Scientific Instruments LMUC –9) with frequency 40 kHz was used for Sono-photocatalysis, Sono Fenton and Sono-photo-Fenton experiments. To obtain the reproducibility of results, each experiment was conducted in triplicates.

3.3 Analytical Techniques

3.3.1 UV-Vis spectrophotometer

The absorption spectrum of AMX and ATL was plotted in the wavelength range of 190 nm to 1100 nm over a double beam UV-Vis spectrophotometer (Lab India make UV 3092 model) **(Fig. 3.4)** and the wavelength of maximum absorption (λ_{max}) was obtained at 227 nm and 224nm respectively.

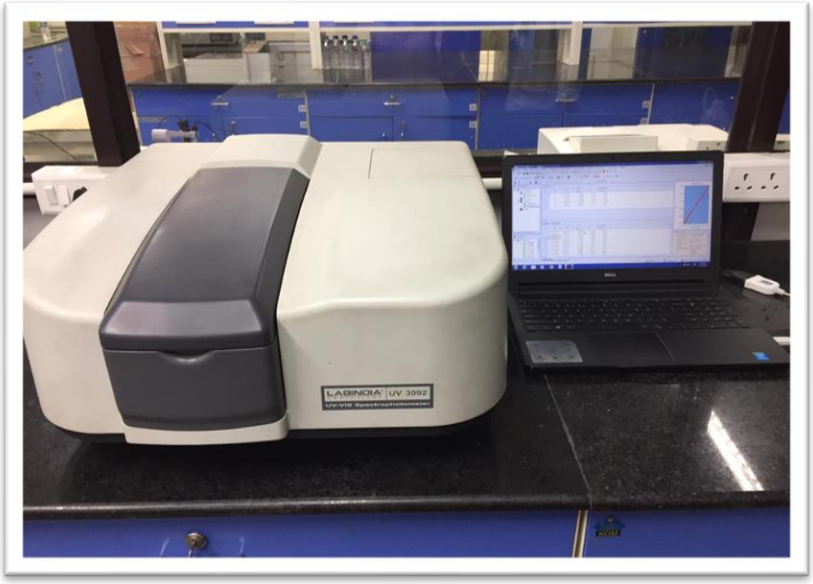

Figure 3.4. Double beam UV-Vis Spectrophotometer (Lab India make) used for determining the concentration of drugs in the present study

The degradation profile of each drug was determined at a regular interval of time till the residual concentration got stabilized. The percent degradation of AMX and ATL was calculated using following relation:

$$\text{Degradation (\%)} = \left[\frac{(Ci - Cf)}{Ci}\right] \times 100$$

Where, C_i is initial concentration of AMX or ATL (mg/l)

C_f is final concentration of AMX or ATL (mg/l)

3.3.2 High Pressure Liquid Chromatography (HPLC) system

Under optimized conditions, the real industrial pharmaceutical wastewater and ATL was further analyzed using HPLC (Shimadzu make, Japan) **(Fig. 3.5)** to inspect the formation of intermediates.

The conditions for analysis of AMX and real pharmaceutical wastewater were mobile phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV Detector at a wavelength of 227nm; sample injection volume: 10µl; flow rate: 0.5ml/min .The conditions for degradation analysis of ATL were mobile phase: water (pH adjusted with 2.5 phosphate buffer) /methanol (80/20) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 224nm; sample injection volume: 10µl; flow rate: 0.6ml/min .

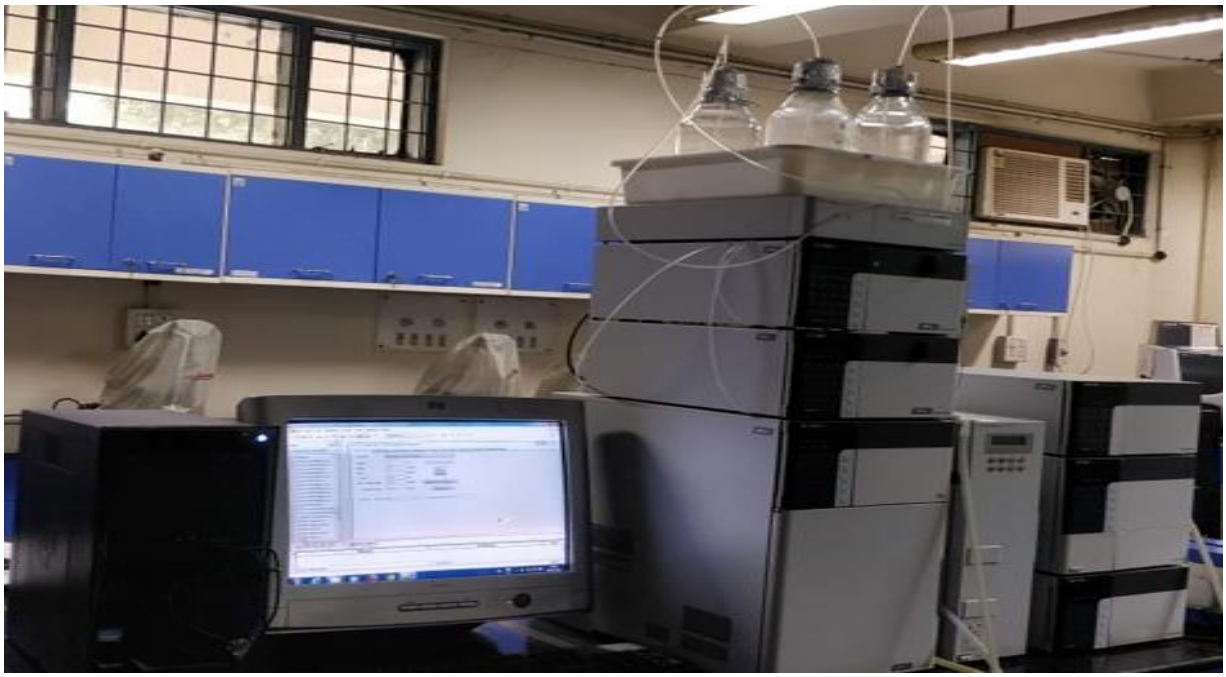

Figure 3.5. HPLC system (Shimadzu make) used for analysis of intermediates and concentration of pharmaceutical drugs

3.4 Photocatalysis Experiment

For photocatalytic and solar photocatalytic experiments, UV illumination was given by keeping the sample in UV-chamber and solar light, respectively. A UV chamber with 8 UV tubes (Philips- 36 W power of each tube) was designed to perform photocatalytic experiments. The

details of experimental set up are given in **Fig. 3.6**. The UV chamber had cumulative source intensity of 672 W/m^2 (at a distance 10cm) over the synthetic and real wastewater for its effective treatment of AMX and ATL. The intensity of the source was calculated by dividing the net power generated per unit area (W/m^2) with a distance of 10 cm between the source of light and the surface of exposed solution. The experiments were performed at varying initial concentration of AMX and ATL in 200 ml aqueous solution in a glass beaker having capacity of 500 ml. The pH of the solution was adjusted using H_2SO_4 and NaOH. Thereafter, varying dosages of TiO_2 and H_2O_2 were added; and the solution was placed over magnetic stirrer with 200 rpm for continuous stirring. During the reaction, O_2 was continuously supplied using an air sparger. The sample volume of 5 ml was withdrawn at regular interval of 30 minutes using pre-rinsed syringe and filtered through 0.45 µm membrane filter. The concentration of AMX and ATL was determined using UV-Vis spectrophotometer at 227 nm wavelength till the residual concentration got stabilized. Photocatalytic degradation without H_2O_2 and sono-photocatalytic oxidation were conducted at the optimized conditions of photocatalysis with H_2O_2 in case of AMX while the treatment of AMX in real wastewater was investigated using the optimized conditions of AMX degradation. In case of ATL, the optimized values of photocatalytic experiments were further utilized to perform photocatalysis with H_2O_2, solar photocatalysis, Sono-photocatalysis, and solar sono-photocatalysis experiments. Sono-photocatalytsis and solar sono-photocatalysis experiments were performed by placing the Ultrasonication unit under UV chamber and solar light, respectively.

Figure 3.6. Experimental setup for photocatalytic degradation of AMX and ATL

3.5 Fenton Treatment

Fenton treatment was performed with a sample volume of 200 ml taken in a 500 ml beaker and placed over magnetic stirrer for continuous stirring at 200 rpm. The experiment set up of Fenton is shown in **Fig. 3.7**. The pH of the solution was kept in a range of 2.5-4.0. The varying concentration of $FeSO_4.7H_2O$ and H_2O_2 were added with working concentration of AMX and ATL. The samples (5 ml) were extracted using a pre-rinsed syringe and then filtered it through a 0.45 µm membrane filter. The samples were extracted and analysed at a regular interval of 30 seconds for AMX and 1min in case of ATL for 0-5 minutes and later after every 5 minutes for determining AMX and ATL concentration using UV-visible spectrophotometer at a wavelength of 227 nm till the residual AMX and ATL concentration was stabilized. Throughout the reaction, O_2 was provided by sparger. The optimized values obtained from the Fenton process were then utilized for photo-Fenton, solar photo-Fenton, sono-Fenton, and sono-photo-Fenton to determine the effect of combined techniques towards AMX and ATL degradation. For photo-Fenton and solar photo-Fenton experiments, required amount of UV illumination was provided by keeping solution under UV chamber and solar light. On the other hand, sono – Fenton experiments were carried out in an ultrasonicaton unit (40 kHz); whereas for the sono-photo-Fenton, ultrasonicator was kept in UV chamber. The results of different processes were compared with Fenton process to check enhancement in the rate of degradation. The schematic representation of photo-fenton and sono-photo-fenton experiment is shown in **Fig. 3.8**.

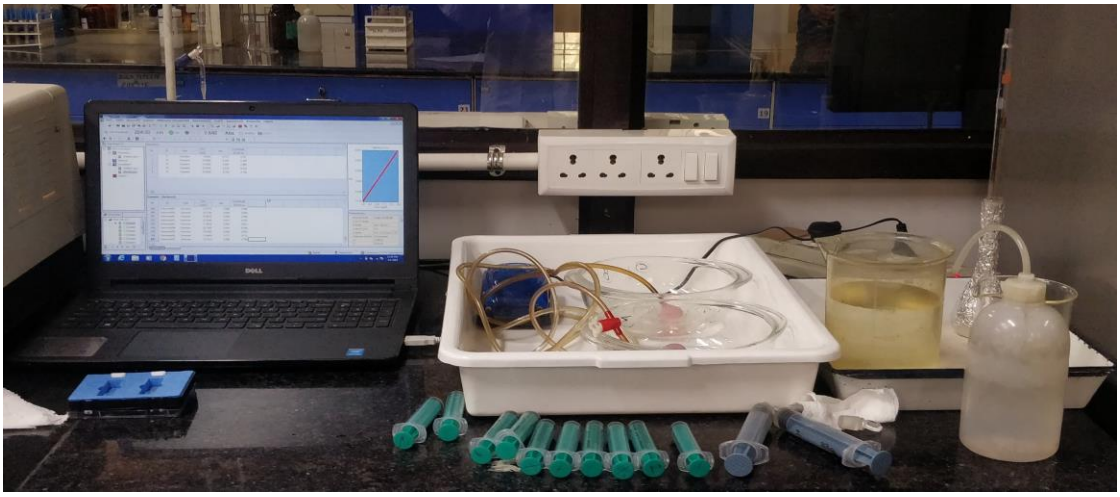

Figure 3.7. Experimental setup for Fenton treatment of AMX and ATL

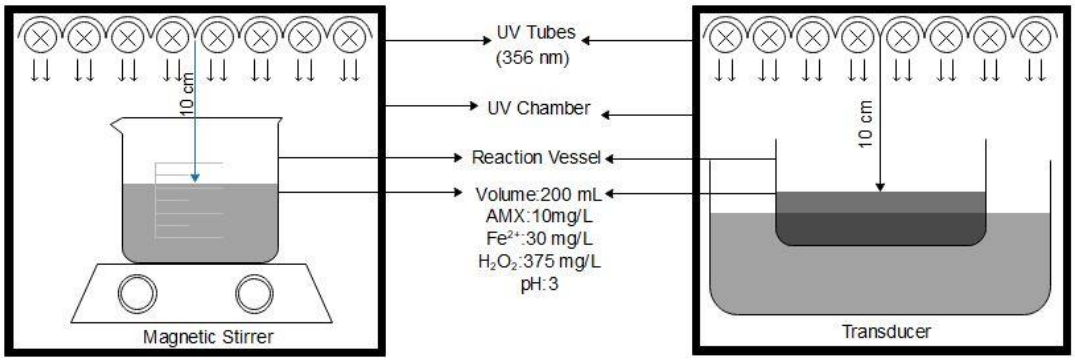

Figure 3.8. Schematic representation of a) photo-Fenton b) sono-photo-Fenton treatment

3.6 Experimental conditions for AMX degradation

3.6.1 Photocatalysis with H_2O_2 and integrated processes

The experiments for photocatalysis with H_2O_2 were performed at initial AMX concentration of 10, 30, and 50 mg/l. The TiO_2 dosage was varied from 50-600mg/l (50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600 mg/l) while the concentration of H_2O_2 was varied as 50-600mg/L (50, 75, 150, 225, 300, 375, 450, 525, 600 mg/l). The pH for degradation was varied in the range of 5.0-9.0 (5.0, 6.0, 7.0, 8.0, 9.0). To accomplish the effective degradation of AMX using photocatalysis with H_2O_2, the working solution was placed in a UV chamber. The photocatalytic and sono-photocatalytic degradation of AMX was carried out at initial AMX concentration of 30mg/l, TiO_2 dosage 450mg/l and pH 7.0. The degradation study was carried out in a UV chamber for photocatlytic experiments while sono-photocatalytic experiments were performed by placing the ultrasonic bath inside the UV-chamber.

3.6.2 Fenton and Photo-Fenton Treatment

In order to achieve the effective degradation of AMX, the initial concentration of AMX was taken as 10mg/l, pH was varied within range of 2.5-4.0, concentration of $FeSO_4$ and H_2O_2 was varied as 10-40 mg/l (10,20,30,40mg/l) and 150-600 mg/l (150, 300mg/l, 375mg/l, 450mg/l, 600mg/l) **(Table 3.2)**. For photo-Fenton treatment, experiments were performed inside the UV chamber at initial AMX concentration-10mg/l, $FeSO_4$-30mg/l, H_2O_2-375mg/l at pH-3.0.

Table 3.1. Experimental conditions for photocatalysis of AMX

	AMX		
Factor	**Photocatalysis with H_2O_2**	**Photocatalysis**	**Sono-photocatalysis**
Initial AMX concentration	10-50 mg/l (10, 30, 50mg/l)	30mg/l	30 mg/L
TiO_2	50-600mg/l (50,100,150,200,250,300,350,400,450, 500,550,600 mg/L)	450mg/l	450 mg/L
H_2O_2	50-600mg/l (50,75,150,225,300,375,450,525,600 mg/L)	-	150mg/L
pH	5.0-9.0 (5.0,6.0,7.0,8.0,9.0)	7.0	7.0
Source of light	UV chamber having 8 tubes (Philips 36 W)	UV chamber having 8 tubes (Philips 36 W)	UV chamber having 8 tubes (Philips 36 W)

Source Intensity	672 W/m^2	672 W/m^2	672 W/m^2
Replicates	03 for each experiment	03 for each experiment	03 for each experiment
Chemicals	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)
TiO_2 P 25	Evonik, India (anatase to rutile ratio 80:20)	Evonik, India (anatase to rutile ratio 80:20)	Evonik, India (anatase to rutile ratio 80:20)
Filters	Fresh, sterilized, 0.45µm	Fresh, sterilized, 0.45µm	Fresh, sterilized, 0.45µm
Solvent	Ultrapure (Type-I) water	Ultrapure (Type-I) water	Ultrapure (Type-I) water
Instrument used	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm), HPLC (Shimadzu-UFLC)	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm), HPLC (Shimadzu-UFLC)	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm), HPLC (Shimadzu-UFLC), Ultrasonication bath (40KHz)

3.6.2.1 Sono-Fenton and Sono-photo-Fenton Treatment

The operating parameters to investigate the maximum degradation of AMX were taken as initial AMX concentration-10mg/l, pH-3.0 while concentration of $FeSO_4$ and H_2O_2 were consider as 30mg/l and 375mg/l respectively at pH-3.0. Reaction was accomplished by placing ultrasonication bath as shown inside UV chamber. The degradation of AMX using sono-Fenton was achieved at initial AMX concentration 10mg/l, $FeSO_4$ 30mg/l, H_2O_2 375mg/l and pH 3.0.

3.7 Experimental conditions for real pharmaceutical wastewater

3.7.1 Photocatalysis and integrated processes

The operating conditions for Photocatalysis, solar photocatalysis, sono-photocatalysis and solar sono-photocatalysis for treatment of real wastewater were the conditions optimised for synthetic wastewater *i.e.* AMX concentration-30mg/l, TiO_2 - 450mg/l, H_2O_2 -150mg/l at pH -7.0 **(Table 3.3)**. Sono-photocatalysis and solar sono-photocatalysis experiments were executed by placing the ultrasonication bath under UV chamber and solar light respectively for UV illumination, as performed earlier for synthetic wastewater.

3.7.2 Fenton and Fenton-integrated treatment

The real pharmaceutical wastewater experiments using Fenton were investigated at pH 3.0 and initial wastewater concentration 10mg/l while the distinct concentration of $FeSO_4$ and H_2O_2 were employed as 10-50mg/l (10, 20, 30, 40, 50 mg/l) and 150-360mg/l (150, 210, 240, 270, 300, 330, 360 mg/l) respectively **(Table 3.4)**. The optimized conditions obtained from Fenton treatment was were used to perform photo-Fenton, solar photo-Fenton, Sono-Fenton, sono-photo-Fenton and solar sono-photo-Fenton. At optimized conditions, initial wastewater concentration was 10mg/l, $FeSO_4$- 10mg/l, H_2O_2- 270mg/l and pH-3.0. For Photo-Fenton and solar photo-Fenton, UV illumination is given by UV chamber and solar light in case of photo-Fenton and solar photo-Fenton respectively. Sono-Fenton, sono-photo-Fenton and solar sono-photo-Fenton experiments were performed using ultrasonication bath (40KHz). In case of sono-photo-Fenton, ultrasonication bath was placed inside the UV chamber. On the other hand, for solar sono-photo-Fenton experiment UV illumination was provided by placing the ultrasonication bath under solar light.

Table 3.2. Experimental conditions for Fenton treatment of AMX

	AMX			
Factors	**Fenton**	**Photo-Fenton**	**Sono-Fenton**	**Sono-photo-Fenton**
Initial AMX concentration	10mg/L	10mg/L	10mg/L	10mg/L
$FeSO_4$	10-40mg/L (10,20,30,40mg/L)	30mg/L	30mg/L	30mg/L
H_2O_2	150-600mg/L (150,375,600mg/L)	375mg/	375mg/L	375mg/L
pH	2.5-4.0 (2.5,3.0,3.5,4.0)	3.0	3.0	3.0
Source of light	-	UV chamber having 8 tubes (Philips 36 W)	-	UV chamber having 8 tubes (Philips 36 W)
Source Intensity	-	672 W/m^2	-	672 W/m^2
Replicates	03 for each experiment	03 for each experiment	03 for each experiment	03 for each experiment
Chemicals	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)

Solvent	Ultrapure (Type-I) water	Ultrapure (Type-I) water	Ultrapure (Type-I) water	Ultrapure (Type-I) water
Instrument used	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm); **HPLC** (Shimadzu-UFLC) mobile phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 227nm;	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm); **HPLC** (Shimadzu UFLC) mobile phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 227nm;	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm); **HPLC** (Shimadzu-UFLC) mobile phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 227nm; **Ultrasonic bath** (Labman scientific instruments LMUC –9) with frequency 40 kHz	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm); **HPLC** (Shimadzu UFLC) mobile phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 227nm; **Ultrasonic bath** (Labman scientific instruments LMUC –9) with frequency 40 kHz

Table 3.3. Experimental conditions for treatment of real pharmaceutical wastewater using photocatalysis and integrated processes

	Real pharmaceutical wastewater			
Factors	**Photocatalysis**	**Solar photocatalysis**	**Sono-photocatalysis**	**Solar sono-photocatalysis**
Initial wastewater concentration	30 mg/l	30 mg/l	30 mg/l	30 mg/l
TiO_2	450 mg/l	450 mg/l	450 mg/l	450 mg/l
H_2O_2	150mg/l	150mg/l	150mg/l	150mg/l
pH	7.0	7.0	7.0	7.0
Source of light	UV chamber having 8 tubes (Philips 36 W)	Solar irradiation	UV chamber having 8 tubes (Philips 36 W)	Solar irradiation
Source Intensity	672 W/m^2	672 W/m^2	672 W/m^2	672 W/m^2
Replicates	03 for each experiment	03 for each experiment	03 for each experiment	03 for each experiment
Chemicals	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)
TiO_2 P 25	Evonik, India	Evonik, India	Evonik, India	Evonik, India

	(anatase to rutile ratio 80:20)	(anatase to rutile ratio 80:20)	(anatase to rutile ratio 80:20)	(anatase to rutile ratio 80:20)
Filters	Fresh sterilized 0.45µm	Fresh sterilized 0.45µm	Fresh sterilized 0.45µm	Fresh sterilized 0.45µm
Solvent	Ultrapure (Type-I) water	Ultrapure (Type-I) water	Ultrapure (Type-I) water	Ultrapure (Type-I) water
Instrument used	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm); **HPLC** (Shimadzu-UFLC) mobile phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 227nm;	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm); **HPLC** (Shimadzu-UFLC) mobile phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 227nm;	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm); **HPLC** (Shimadzu-UFLC) mobile phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 227nm; **Ultrasonic bath** (Labman scientific instruments LMUC –9) with frequency 40 kHz	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm); **HPLC** (Shimadzu-UFLC) mobile phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 227nm; **Ultrasonic bath** (Labman scientific instruments LMUC –9) with frequency 40 kHz

Table 3.4. Experimental conditions of Fenton and integrated processes for treatment of real pharmaceutical wastewater

	Real pharmaceutical wastewater					
Factors	**Fenton**	**Photo-Fenton**	**Solar photo-Fenton**	**Sono-Fenton**	**Sono-photo-Fenton**	**Solar photo-Fenton**
Initial wastewater concentration	10mg/l	10mg/l	10mg/l	10mg/l	10mg/l	10mg/l
$FeSO_4$	10-50mg/l (10,20,30,40,50 mg/l)	10mg/l	10mg/l	10mg/l	10mg/l	10mg/l
H_2O_2	150-360mg/L (150,210,240,270,300,330,360 mg/L)	270mg/l	270mg/l	270mg/l	270mg/l	270mg/l
pH	3.0	3.0	3.0	3.0	3.0	3.0

Source of light	-	UV chamber having 8 tubes (Philips 36 W)	Solar irradiation		UV chamber having 8 tubes (Philips 36 W)	Solar iradiation
Source Intensity	-	672 W/m^2			672 W/m^2	
Replicates	03 for each experiment	03 for each experiment	03 for each experiment	03 for each experiment	03 for each experiment	03 for each experiment
Chemicals	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)
Solvent	Ultrapure (Type-I) water	Ultrapure (Type-I) water	Ultrapure (Type-I) water	Ultrapure (Type-I) water	Ultrapure (Type-I) water	Ultrapure (Type-I) water
Analysis	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm); **HPLC** (Shimadzu-UFLC) mobile	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm); **HPLC** (Shimadzu-UFLC) mobile	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm); **HPLC** (Shimadzu-UFLC) mobile	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm); **HPLC** (Shimadzu-UFLC) mobile	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm); **HPLC** (Shimadzu-UFLC) mobile	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 227nm); **HPLC** (Shimadzu-UFLC) mobile

	phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 227nm.	phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 227nm.	phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 227nm.	phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 227nm; **Ultrasonic bath** (Labman scientific instruments LMUC –9) with frequency 40 kHz	phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 227nm; **Ultrasonic bath** (Labman scientific instruments LMUC –9) with frequency 40 kHz	phase: water/acetonitrile (60/40) under isocratic conditions; column: C 18, 4.6 x 250mm, 5µm reverse phase; detector: UV at a wavelength of 227nm; **Ultrasonic bath** (Labman scientific instruments LMUC –9) with frequency 40 kHz

3.8 Experimental conditions for degradation Atenolol

The operating parameters used to investigate the photocatalytic degradation of ATL were initial concentration of ATL, amount of TiO_2 and pH **(Table 3.5)**. Addition of H_2O_2 to enhance the photocatalytic degradation was also evaluated. Sono-photocatalytic degradation was also observed at the same operating conditions to compare the degradation efficiencies of different processes. Degradation of ATL was also determined using Fenton and integrated processes. To achieve the degradation of ATL using Fenton parameters varied were initial concentration of ATL, $FeSO_4$, H_2O_2 and pH.

3.8.1 Photocatalysis and integrated processes

3.8.1.1 Photocatalysis and solar photocatalysis

The parameters varied to achieve the photocatalytic degradation of ATL under UV light were initial concentration of ATL 10-40mg/l (10, 25, 40mg/l), TiO_2 300-600mg/l (300, 450, 600mg/l), pH 3.0-11.0 (3.0, 7.0, 11.0). Solar photocatalysis experiments were performed at initial ATL concentration 10mg/l, TiO_2 450mg/l and pH 3.0 under solar light.

3.8.1.2 Photocatalysis with H_2O_2

The effect of H_2O_2 was studied at initial concentration of ATL- 10mg/l, TiO_2 450mg/l, pH 3.0 and H_2O_2 was varied between 0.5mM-1.5mM (0.5, 1.0 and 1.5 mM). All the experiments were performed under UV illumination (365nm).

3.8.1.3 Sono-photocatalysis and solar sono-photocatalysis

Both the experiments, sono-photocatalysis as well as solar sono-photocatalysis, were performed by keeping the aqueous solution inside the ultrasonicat bath. Furthermore, Ultrasonication apparatus bath was placed under UV chamber and solar light to achieve degradation using sono-photocatalysis and solar sono-photocatalysis, respectively. Degradation of ATL was observed at initial concentration of ATL 10mg/l, TiO_2 450mg/l and pH 3.0.

Table 3.5. Experimental conditions of Atenolol for photocatalysis

	Atenolol (ATL)				
Factors	**Photocatalysis**	**Photocatalysis with H_2O_2**	**Solar photocatalysis**	**Sono-photocatalysis**	**Solar sono-photocatalysis**
Initial ATL concentration	10-40 mg/L (10,25,40 mg/L)	10mg/l	10mg/l	10mg/l	10mg/l
TiO_2	300-600 mg/L (300,450,600mg/L)	450mg/l	450mg/l	450mg/l	450mg/l
pH	3-11(3,7,11)	3.0	3.0	3.0	3.0
H_2O_2	-	0.5mM - 1.5mM (0.5,1.0,1.5mM)	-	-	-
Source of light	UV chamber having 8 tubes (Philips 36 W)	UV chamber having 8 tubes (Philips 36 W)	Solar irradiation	UV chamber having 8 tubes (Philips 36 W)	Solar irradiation
Source Intensity	672 W/m^2	672 W/m^2		672 W/m^2	
Replicates	03 for each experiment	03 for each experiment	03 for each experiment	03 for each experiment	03 for each experiment
Chemicals	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)
TiO_2 P 25	Evonik, India	Evonik, India	Evonik, India	Evonik, India	Evonik, India

	(anatase to rutile ratio 80:20)	(anatase to rutile ratio 80:20)	(anatase to rutile ratio 80:20)	(anatase to rutile ratio 80:20)	(anatase to rutile ratio 80:20)
Filters	Fresh sterilized 0.45µm	Fresh sterilized 0.45µm	Fresh sterilized 0.45µm	Fresh sterilized 0.45µm	Fresh sterilized 0.45µm
Solvent	Ultrapure (Type-I) water	Ultrapure (Type-I) water	Ultrapure (Type-I) water	Ultrapure (Type-I) water	Ultrapure (Type-I) water
Instrument Used	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 224nm); **HPLC** (Shimadzu UFLC) (mobile phase: Methonol (80%) and phosphoric acid (pH=2.5) in water (20%), running in isocratic conditions; Flow rate 0.6 mL min^{-1}; λ_{max} 224nm	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 224nm); **HPLC** (Shimadzu UFLC) (mobile phase: Methonol (80%) and phosphoric acid (pH=2.5) in water (20%), running in isocratic conditions; Flow rate 0.6 mL min^{-1}; λ_{max} 224nm	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 224nm); **HPLC** (Shimadzu UFLC) (mobile phase: Methonol (80%) and phosphoric acid (pH=2.5) in water (20%), running in isocratic conditions; Flow rate 0.6 mL min^{-1}; λ_{max} 224nm	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 224nm); **HPLC** (Shimadzu UFLC) (mobile phase: Methonol (80%) and phosphoric acid (pH=2.5) in water (20%), running in isocratic conditions; Flow rate 0.6 mL min^{-1}; λ_{max} 224nm; **Ultrasonic bath** (Labman scientific instruments LMUC – 9) with frequency 40 kHz	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 224nm); **HPLC** (Shimadzu UFLC) (mobile phase: Methonol (80%) and phosphoric acid (pH=2.5) in water (20%), running in isocratic conditions; Flow rate 0.6 mL min^{-1}; λ_{max} 224nm; **Ultrasonic bath** (Labman scientific instruments LMUC – 9) with frequency 40 kHz

3.8.2 Fenton and Fenton integrated treatment of ATL

Degradation of ATL using Fenton reaction was investigated by varying the initial ATL concentration between 10-40mg/l (10, 25, 40mg/l), $FeSO_4$ – 5.0-50mg/l (5, 27.5, 50mg/l), H_2O_2 – 100-500mg/l (100, 300, 500mg/l) at pH-3.0 **(Table 3.6)**. For photo-Fenton experiment, reaction was done inside UV chamber while for solar photo-Fenton experiment reaction was done by placing the solution under solar light. Degradation of ATL was estimated at initial ATL concentration 10mg/l, $FeSO_4$ 27.5mg/l, H_2O_2 100mg/l at pH-3.0. Degradation of ATL using sono-Fenton was achieved using initial ATL concentration 10mg/l, $FeSO_4$ 27.5mg/l, H_2O_2 100mg/l and pH-3.0 under ultrasonic bath. The degradation of ATL was investigated using sono-photo-Fenton and solar sono-photo-Fenton at initial ATL concentration 10mg/l, $FeSO_4$ 27.5mg/l, H_2O_2 100mg/l and pH-3.0. Ultrasonication bath was kept under UV chamber for sono-photo-Fenton while solar light and ultrasonic bath was used for solar sono-photo-Fenton.

3.9 Approaches used for experiments

There are two different strategies which are used to optimize the process parameters:

- One-factor-at-a-time (OFAT) - Traditional approach
- Design of experiments (DOE) – Statistical approach

3.9.1 OFAT

One variable was studied at a time keeping other factors constant on the basis of experimental response. This approach ignored the interactive effects between the variables and also increases the number of experiments which is ultimately time consuming and added expenses for chemicals used in experiments (Bezerra, et al, 2008). This approach used only two observation at a time of the experiment to determine the response of various factors (Czitrom, 1999). In the present study, degradation of AMX using photocatalysis with H_2O_2 and Fenton was observed by varying one factor at a time and keeping another variable constant. The degradation study for photocatalysis with H_2O_2 was carried out by varying the factors such as initial AMX concentration, TiO_2 dosage, H_2O_2 concentration and pH.

Table 3.6. Experimental conditions for Atenolol using Fenton and integrated processes

	Atenolol (ATL)						
Factors	**Fenton**	**Photo-Fenton**	**Solar photo-Fenton**	**Sono-Fenton**	**Solar Sono-Fenton**	**Sono-photo-Fenton**	**Solar Sono-photo-Fenton**
Initial ATL concentration	10-40mg/l	10mg/l	10mg/l	10mg/l	10mg/l	10mg/l	10mg/l
$FeSO_4$	5-50mg/L (5, 27.5, 50 mg/L)	27.5mg/l	27.5mg/l	27.5mg/l	27.5mg/l	27.5mg/l	27.5mg/l
H_2O_2	100-500mg/L (100,300,500 mg/L)	100mg/l	100mg/l	100mg/l	100mg/l	100mg/l	100mg/l
pH	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Source of light		UV chamber having 8 tubes (Philips 36 W)	Solar irradiation		Solar irradiation	UV chamber having 8 tubes (Philips 36 W)	Solar irradiation
Source Intensity		672 W/m^2				672 W/m^2	

Replicates	03 for each experiment	03 for each experiment	03 for each experiment	03 for each experiment	03 for each experiment	03 for each experiment	03 for each experiment
Chemical	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)	Analytical grade (AR)
Solvent	Ultrpure (Type-I) water	Ultrpure (Type-I) water	Ultrpure (Type-I) water	Ultrpure (Type-I) water	Ultrpure (Type-I) water	Ultrpure (Type-I) water	Ultrpure (Type-I) water
Analysis	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 224nm); **HPLC** (Shimadzu UFLC) (mobile phase: Methonol (80%) and phosphoric	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 224nm); **HPLC** (Shimadzu UFLC) (mobile phase: Methonol (80%) and phosphoric	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 224nm); **HPLC** (Shimadzu UFLC) (mobile phase: Methonol (80%) and phosphoric acid (pH=2.5) in water (20%),	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 224nm); **HPLC** (Shimadzu UFLC) (mobile phase: Methonol (80%) and phosphoric	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 224nm); **HPLC** (Shimadzu UFLC) (mobile phase: Methonol (80%) and phosphoric acid (pH=2.5) in water (20%),	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 224nm); **HPLC** (Shimadzu UFLC) (mobile phase:	**Double beam UV-Vis spectrophotometer** (UV 3092 model) (λ_{max} 224nm); **HPLC** (Shimadzu UFLC) (mobile phase: Methonol (80%) and phosphoric

	acid (pH=2.5) in water (20%), running in isocratic conditions; Flow rate 0.6 mL min^{-1}; λ_{max} 224nm	acid (pH=2.5) in water (20%), running in isocratic conditions; Flow rate 0.6 mL min^{-1}; λ_{max} 224nm	running in isocratic conditions; Flow rate 0.6 mL min^{-1}; λ_{max} 224nm	acid (pH=2.5) in water (20%), running in isocratic conditions; Flow rate 0.6 mL min^{-1}; λ_{max} 224nm; **Ultrasonic bath** (Labman scientific instruments LMUC –9) with frequency 40 kHz	running in isocratic conditions; Flow rate 0.6 mL min^{-1}; λ_{max} 224nm; **Ultrasonic bath** (Labman scientific instruments LMUC –9) with frequency 40 kHz	Methanol (80%) and phosphoric acid (pH=2.5) in water (20%), running in isocratic conditions; Flow rate 0.6 mL min^{-1}; λ_{max} 224nm; **Ultrasonic bath** (Labman scientific instruments LMUC –9) with frequency 40 kHz	acid (pH=2.5) in water (20%), running in isocratic conditions; Flow rate 0.6 mL min^{-1}; λ_{max} 224nm; **Ultrasonic bath** (Labman scientific instruments LMUC –9) with frequency 40 kHz

On the other hand, in case of Fenton treatment for degradation of AMX, initial concentration of AMX was kept constant while other variables like pH, concentration of $FeSO_4$ and H_2O_2 were varied. It was noticed from the experiments that this method is time consuming, increases number of experiments and avoid the interaction between the factors.

3.9.2 DOE

For developing the correlation between the parameters and their interspecific effects, Response Surface Methodology (RSM) was employed. RSM helps in assessing relations between the variables for optimisation and design of experiments. Subsequently, to make the model comprehensive and holistic, Box-Behnken design (BBD) was adopted. Compared to other types of RSM designs, BBD provides estimation in the quadratic model without sacrificing with the simplicity of the model. Minitab 16 Statistical Software was used for the codification of independent variables and the analysis of response for optimisation of the design. The following equation was used to derive the relation between dependent (Y) and independent variables (Xi).

$$Y = b_o + b_1X_1 + b_2X_2 + b_3X_3 + b_{12}X_1X_2 + b_{13}X_1X_3 + b_{23}X_2X_3 + b_{11}X_1X_1 + b_{22}X_2X_2 + b_{33}X_3X_3$$

Table 3.7. Design of experiments

	Amoxicillin (AMX)		**Atenolol (ATL)**	
	Photocatalysis	**Fenton**	**Photocatalysis**	**Fenton**
Software Used	Minitab 16	Minitab 16	Minitab 16	Minitab 16
Design Used	Box-Behnken	Box-Behnken	Box-Behnken	Box-Behnken
Number of Runs	27	27	15	15
Number of variables	4	4	3	3
Independent factors	• X_1 AMX conc.(10-50mg/l) • X_2 TiO_2 (300-600mg/l) • X_3 H_2O_2(100-200mg/l) • X_4 pH (3.0-11)	• X_1 AMX conc.(10-50mg/l) • X_2 FeSO4 (20-40 mg/l) • X_3 H_2O_2(150-600mg/l) • X_4 pH (2.5-3.5)	• X_1 ATL conc.(10-40mg/l) • X_2 TiO_2 (300-600mg/l) • X_3 pH (3.0-11)	• X_1 AMX conc.(10-40mg/l) • X_2 $FeSO_4$ (5.0-50 mg/l) • X_3 H_2O_2(100-300mg/l)
Response Variables	Degradation of AMX [Y]	Degradation of AMX [Y]	Degradation of ATL [Y]	Degradation of ATL [Y]

The confidence limit was set at 95% for the regression analysis and the analysis of variance. The quality of fit was analysed by estimating the value of R^2. Regression Analysis was done to determine the coefficients and the design was later optimized. The experiments related to AMX degradation and optimization of variable parameters was performed using synthetic effluent of AMX. Optimization and validation of parameters were also studied using synthetic effluent of ATL. Experimental conditions for each process have been discussed below **(Table 3.7)**.

3.9.2.1 Experimental conditions for AMX

There were 27 number of runs with 4 variables obtained for photocatalysis and Fenton experiments. Degradation of amoxicillin [Y] was considered as response variable for both the processes. The independent factors for photocatalysis and Fenton processes were varied as X_1 AMX conc.(10-50mg/L), X_2 TiO_2 (300-600mg/L), X_3 H_2O_2(100-200mg/L), X_4 pH (3.0-11) and X_1 AMX conc.(10-50mg/L), X_2 $FeSO_4$ (20-40 mg/L), X_3 H_2O_2(150-600mg/L), X_4 pH (2.5-3.5).

3.9.2.2 Experimental conditions for ATL

To optimize and validate the photocatalysis and Fenton process, 15 runs with 3 variables were attained from BBD design. The achieve the effective degradation of ATL, X_1 ATL conc.(10-40mg/L), X_2 TiO_2 (300-600mg/L), X_3 pH (3.0-11) and X_1 AMX conc.(10-40mg/L), X_2 FeSO4 (5.0-50 mg/L), X_3 H_2O_2(100-300mg/L) variables were taken as independents factors for photocatalysis and Fenton processes, respectively.

CHAPTER 4
RESULTS AND DISCUSSION

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RESULTS AND DISCUSSION

4.1 Characterization of real pharmaceutical wastewater

The investigation of physico-chemical characteristics of wastewater shows pH 7 at 25 °C temperature which is according to standards described by CPCB. The color of the treated wastewater was transparent with unpleasant odour. The TDS, EC and salinity of wastewater were 261mg/l, 534 µs/cm, 0.309ppt respectively as shown in **Table 4.1**. The permissible limit given by CPCB for COD and BOD_5 is 250mg/l and 100mg/l, respectively, while the observed values for COD and BOD_5 are 360mg/l and 200mg/l which are higher than permissible limit. The industrial wastewater had residual concentration of 210 mg/l of AMX after treatment through in-house effluent treatment plant (ETP) of the industry.

4.2 Assessment of Toxicity of pharmaceutical wastewater

The toxicity of the wastewater was evaluated on the basis of previous studies that have already been discussed in literature. There are various studies which have discussed about the toxicity of amoxicillin on various species of fishes, algae and invertebrates. In the present study, the initial concentration of AMX in wastewater was determined as 210mg/l and inference about toxicity on each species according to concentration determined in present study is discussed in detail as given below **(Table 4.2)**.

Toxicity to Fish - The LC 50 value for *Oryzias latipes* is 1000mg/l (Park & Choi, 2008) at 96 hours which is non-toxic according to the concentration of AMX found in the present study. The different volumes of AMX containing wastewater (0.2%, 0.3%, 0.4%, 0.5% and 0.6%) have been used by Xie et al., 2017 to test the toxicity on Zebra fish for time duration of 24 hours, 48 hours,72 hours and 96 hours. The toxicity on Zebra fish increased with increase in volume of AMX wastewater and it concluded LC_{50} value at 96 hours was 40.74%. It was inferred that the concentration 210mg/l is non-toxic to the Zebra fish, as reported in the present study.

Table 4.1 Physico-chemical Characterization of treated pharmaceutical wastewater (Batch of AMX production)

Parameter	Unit	Value	APHA Method used	CPCB standards for pharmaceutical effluent
pH	-	7.1	4500-(H+ B)	6.5-8.5
Temperature	^{o}C	25	2550 (B)	-
Color	-	Transparent*	2120 (B)	-
Odour	-	Unpleasant*	2150 (B)	-
TDS	mg/L	261	2540 (C)	-
EC	µs/cm	534	2510 (B)	-
Salinity	ppt	0.309	2520 (B)	-
COD	mg/L	360	5220 (C)	250
BOD_5	mg/L	200	5210	100
AMX concentration	mg/L	210	HPLC	-

***** Based on physical observation

Another study (Umamaheswari et al., 2019) reported on fish *Labeo rohita* revealed that when fish was exposed to AMX concentration 0.5mg/l and 1.0mg/l for 35days, it affected the hematological/biochemical/electrolytes/enzymological parameters of fish. On the basis of this study, the concentration is toxic to *Labeo rohita*, as observed for the present study

Toxicity to Algae- The toxicity test of Amoxicillin within the range of 50ng/l to 50mg/l was investigated on Cyanophyta *Synechococcus leopolensis* and EC_{50} at 96hours was obtained as 2.22µg /l. So it was concluded that the concentration found in present study is toxic to *Synechococcus leopolensis* (Andreozzi et al., 2004)

AMX concentration of 0.0009–0.0038 mg/l was used to study toxicity on cyanobacteria *Microcystis aeruginosa* species of algae. It was reported that the value of LC_{50} was 0.0037mg/l (Holten Lutzhøf et al., 1999). Based on the AMX concentration in the present study, the treated effluent is reported to be toxic to cyanobacteria.

Furthermore, toxicity on algae *Rhodomonas salina* and *Selenastrum capricornutum* was also tested for AMX concentration of 5-500mg/l and 2.5-250mg/l, respectively. The LC_{50} value for *R.salina* and *S. capricornutum* was determined as 3.108mg/l and 250mg/l, respectively (Holten Lutzhøf et al., 1999). Based on the reported results, the effluent used in present study stands toxic to *R.salina* and *S. capricornutum* algal species.

Toxicity to Invertebrates- The clam *Ruditapes philippinarum* and the mussel *Mytilus galloprovincialis* are the two bivalve species which were taken for the study by Matozzo et al. (2016) and subjected to study haemoctyic parameters to AMX concentrations 100, 200 and 400 mg/L for 1, 3 and 7 days. It was revealed that the same concentration of AMX significantly affect haemocyte proliferation, total haemocyte count (THC), pH of haemolyph, micronuclei formation and lactate dehydrogenase (LDH). AMX concentration of 210mg/l in treated effluent used for the present study toxic to the aquatic invertebrates.

Toxicity to Zooplankton- The effect in rate of reproduction and survival on two species of rotifers *Brachionus calyciflorus* and *Brachionus havanaensis* was studied by Gonza´lez-Pe´rez et al., 2016. The concentration of AMX within the range of 50-200µg/l affects the reproduction and survival rate of the species. The effluent used in the present study is reported to be toxic to the zooplanktons explained to this concentration.

4.3 Photocatalytic degradation of AMX

In order to observe the degradation of AMX, experiments were performed using photocatalysis with H_2O_2, photocatalysis without H_2O_2, and sono-photocatalysis. The effect of photocatalysis and combination of photocatalysis with sonication was studied by varying the concentration of AMX, TiO_2, H_2O_2, and pH. The details of each parameter are discussed in sections given below.

Table 4.2. Assessment of Toxicity of AMX (210mg/l) to different life -forms

Species	Toxicity related detail	Inference from present study (Ci - 210 mg/L)	Reference used
Oryzias latipes (Fish)	LC_{50} at 96 hours 1000mg/L	Non-toxic	park et al., 2008
Zebra fish (Fish)	LC_{50} at 96 hours 40.74%	Non-toxic	Xie et al., 2017
Synechococcus leopolensis (Algae)	EC_{50} 2µg/L	Toxic	Andreozzi et al., 2004
Labeo rohita (Fish)	1 and 0.5 mg/L concentrations affect the hematological/biochemical/electrolytes/enzymological parameters of fish	Toxic	Umamaheswaria et al., 2019
Microcystis aeruginosa (Algae)	LC_{50} 0.0037mg/L	Toxic	Lutzholft et al., 1999
Rhodomonas salina (Algae)	LC_{50} 3.108mg/L	Toxic	Lutzholft et al., 1999
Selenastrum capricornutum (Algae)	LC_{50} 250mg/L	Toxic	Lutzholft et al., 1999
Ruditapes philippinarum (Clam) and *Mytilus galloprovincialis* (Mussel)	Affects total haemocyte count (THC) at 100-400 µg/L	Toxic	Matozzo et al., 2016
Rotifers Brachionus calyciflorus and *Brachionus havanaensis*	Affects survival and reproduction at 50-200 µg/L	Toxic	Gonza´lez-Pe´rez et al., 2016

4.3.1 Effect of AMX concentration

Although the concentration of AMX in municipal wastewater is observed in a relatively lower range (ng/L-mg/l); but it may be quite high in pharmaceutical effluent; and to devise a

potentially effective method for degradation, the concentration of AMX was varied from 10-50 mg/l in both the approaches *i.e.* OFAT and BBD. At lower concentration (10mg/l) of AMX, there was maximal degradation in comparison to 30 mg/l **(Fig. 4.3)** and 50 mg/l as shown in **Fig. 4.1**. With increase in concentration of AMX, the degradation was decreasing but the maximum degradation of 65% was achieved at 10 mg/l AMX level (TiO_2-250 mg/l; Time of treatment 150 minutes) **(Fig. 4.2)**. Further, increase in concentration results in slight decrease in degradation. When the concentration of AMX was lower, the active sites present on surface of catalyst were sufficient, while at higher concentration all the active sites present on surface of catalyst are loaded by molecules of AMX. So, binding to active sites and availability of oxidizing •OH radicals reduces from change of lower to higher initial concentration of AMX. Since the reaction rate kinetics remains higher at lower concentration of AMX, correspondingly higher removal was observed. In a similar study, Klauson et al., (2010) varied the AMX concentration from 1-100 mg/l and reported optimum concentration of AMX from 10-25 mg/l. The findings of this study are, therefore, in line with the earlier reports present in literature.

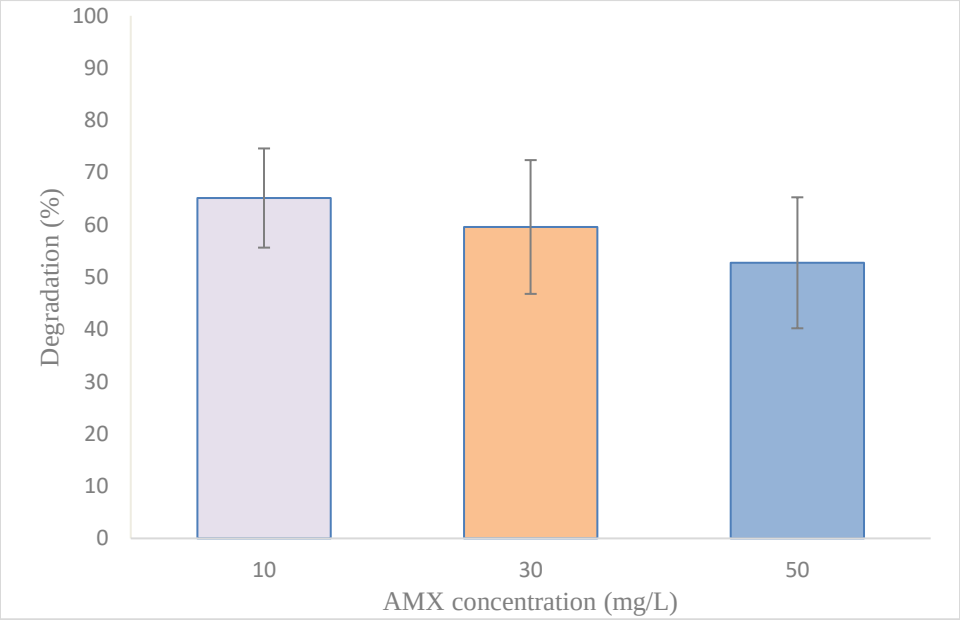

Figure 4.1. Effect of initial AMX concentration on its percent degradation

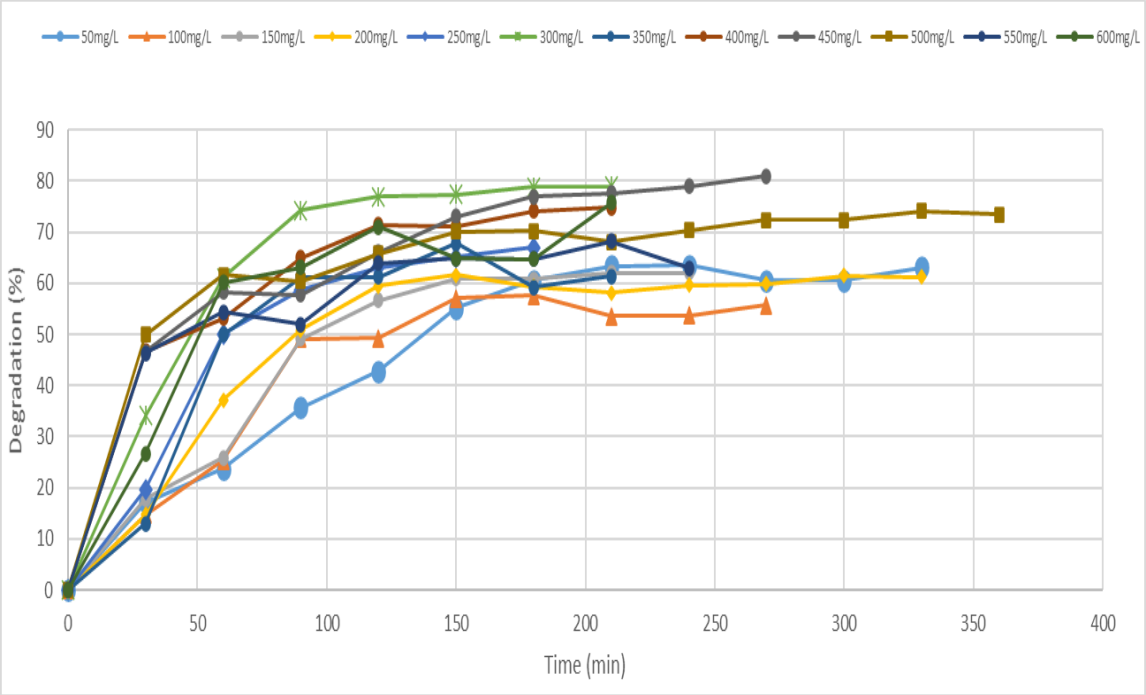

Figure 4.2. Effect of initial AMX concentration on its percent degradation at 10mg/L

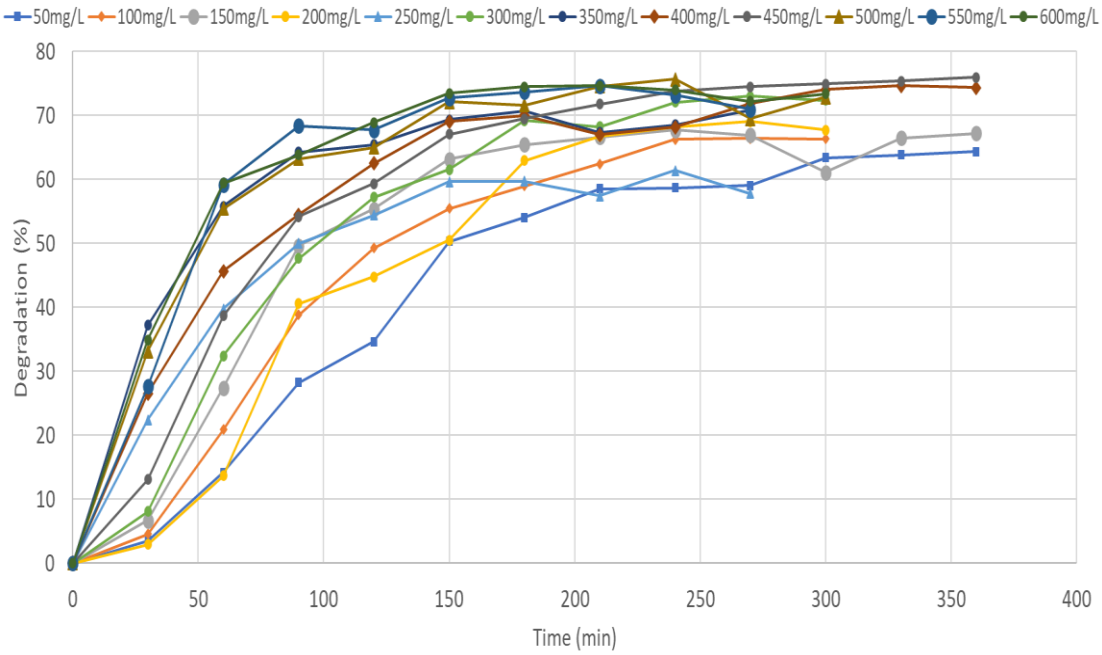

Figure 4.3. Effect of initial AMX concentration on its percent degradation at 30mg/L

4.3.2 Effect of catalyst (TiO_2) loading

TiO_2 P25 was used as catalyst for AMX degradation because it is highly active compared to other catalysts. The concentration of TiO_2 was varied from 50mg/l to 600mg/l and 300mg/l to 600mg/l in OFAT approach and BBD respectively. At lower dose of 300 mg/l, TiO_2 showed slightly less rate of degradation while at medium (450 mg/l) and higher level (600 mg/l), around 75% degradation of AMX was achieved **(Fig. 4.4)**. Degradation of AMX increased with increase in TiO_2 concentration from 300 mg/l to 450 mg/l but there was insignificant enhancement in rate of degradation at higher concentration of 600 mg/l. This may be attributed to the reduction in light penetration, deposition of TiO_2, increase in scattering of light and agglomeration at higher concentration of TiO_2. Several researchers (Elmolla & Chaudhari 2010) reported degradation of

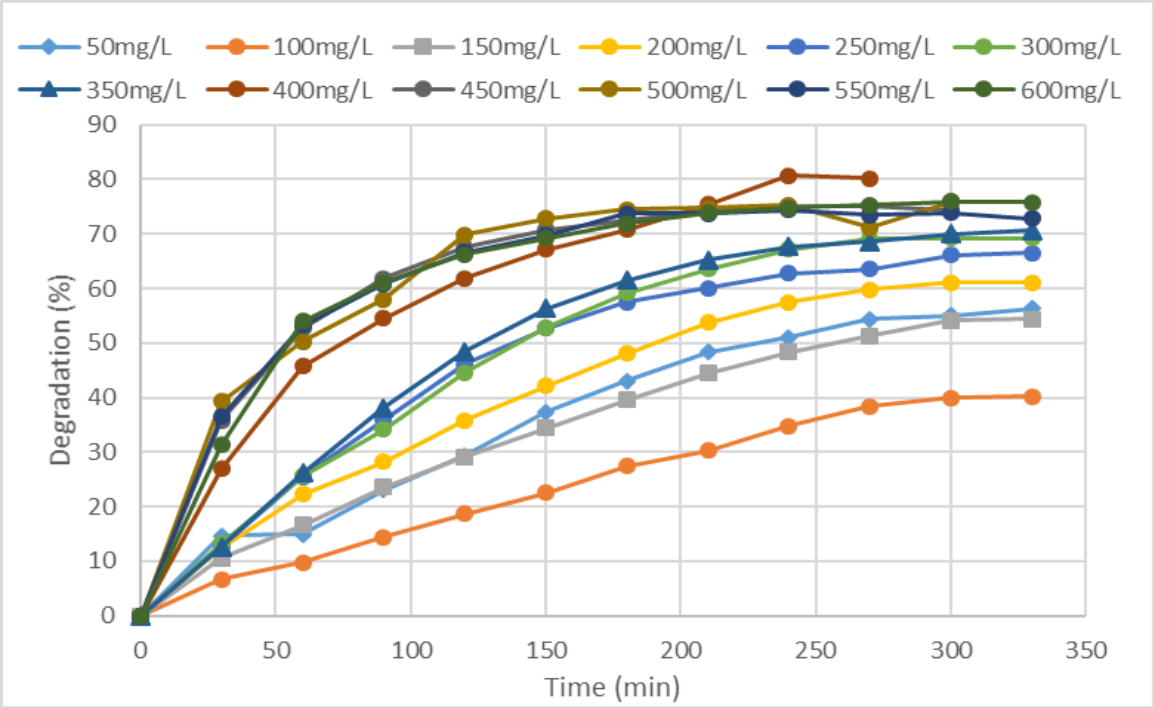

Figure 4.4. Effect of catalyst dose on percent degradation of AMX

AMX using TiO_2 as catalyst but concentration of TiO_2 was higher as compared to this study. Therefore, the optimization of dose of TiO_2 can help reduce the amount as well as cost of TiO_2 involved in photocatalytic degradation of AMX. Although maximal removal efficiency of

around 72% was observed for TiO_2 range of 300 - 600 mg/l, the rate kinetics was relatively higher for TiO_2 dose of 450 mg/l and 500 mg/l which may be particularly useful for treating relatively larger volumes of wastewater.

4.3.3 Effect of H_2O_2 concentration

When H_2O_2 is added to photocatalytic process, it increases the production of $^{\bullet}OH$ radicals and therefore enhances the rate of degradation. In photocatalytic process, H_2O_2 performs binary functions in order to generate $^{\bullet}OH$ radicals. Firstly, it act as acceptor of photo-excited electrons from conduction band of semiconductor (TiO_2 P25) to generate more $^{\bullet}OH$ as per reaction (4.1). Further it generates the $^{\bullet}OH$ radicals as per reaction (4.2) (Elmolla & Chaudhari, 2010; Safari et al., 2015).

$$H_2O_2 + e^- \rightarrow {}^{\bullet}OH + OH^- \quad \text{.....4.1}$$

$$H_2O_2 + O_2^{\bullet -} \rightarrow {}^{\bullet}OH + OH^- + O_2 \quad \text{.....4.2}$$

To examine the effect of addition of H_2O_2 in photocatalytic process, concentration of H_2O_2 was varied from 100 to 200 mg/l in BBD design and 50mg/l to 600mg/l in OFAT approach. The experimental results show that with increase in concentration of H_2O_2, degradation of AMX increase and maximum degradation of AMX was achieved at 150 mg/l. At concentration of 150mg/l, 80% degradation of AMX was achieved within 270 minutes. Although antecedent literature reports an increase in rate of oxidation of pollutants with addition of H_2O_2, there was an insignificant improvement in rate of photocatalytic degradation of AMX after addition of H_2O_2 in the present study **(Fig. 4.5)**.

4.3.4 Effect of pH

In order to investigate the effect of pH on degradation of AMX, experiments were performed at pH 5.0, 6.0 ,7.0,8.0 and 9.0 in OFAT approach while in BBD design pH was varied as 3.0,7.0 and 11. The effect of pH can be interpreted through distribution of charge on catalyst surface, compound's capacity to get adsorbed and dissociate, and the oxidative potential of the catalyst valence band (Safari et al., 2015). When the pH of solution/wastewater AMX was acidic, both TiO_2 and AMX were positively charged.

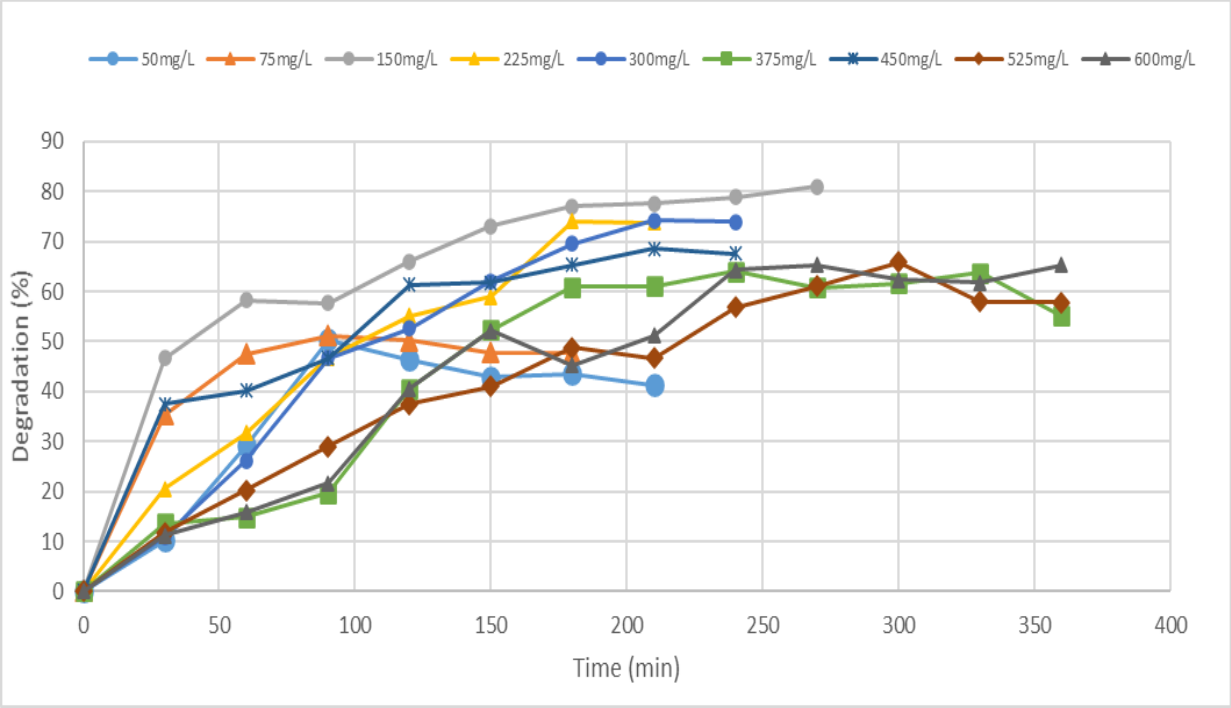

Figure 4.5 Effect of H_2O_2 on percent degradation AMX

So, the adsorption of AMX on TiO_2 was reduced. The degradation of AMX at acidic pH was higher as compared to neutral pH which may be attributed to hydrolysis of antibiotics as observed in antecedent study of Elmolla & Chaudhari, (2010). When the pH was alkaline, both TiO_2 and AMX were negatively charged. So, the repulsive forces were generated between TiO_2 and AMX. Relatively higher degradation was observed at neutral pH due to generation of more $^{\bullet}OH$ radicals. On the surface of TiO_2, hydroxyl ions were present which get oxidized to form $^{\bullet}OH$ radicals (Yang et al., 2008). The maximum degradation for AMX was achieved at pH 5.0 in OFAT approach while rate of reaction was higher at pH 7. On the other hand, maximum degradation of AMX was evaluated in BBD design. At pH 7, degradation of AMX was slightly higher than the pH 3.0 and pH 11. This may be due to the reason that at neutral pH, both AMX and TiO_2 were in neutral in charge, and there were no repulsive forces between them. Similar reports of higher degradation of antibiotics (ofloxacin) at around neutral pH (6.0) have highlighted the role of pH in photocatalytic degradation (Peres et al., 2015). Maximum degradation was achieved at AMX 10 mg/l, TiO_2 450 mg/l, H_2O_2 150 mg/l and pH 7 using OFAT approach **(Fig. 4.6)**.

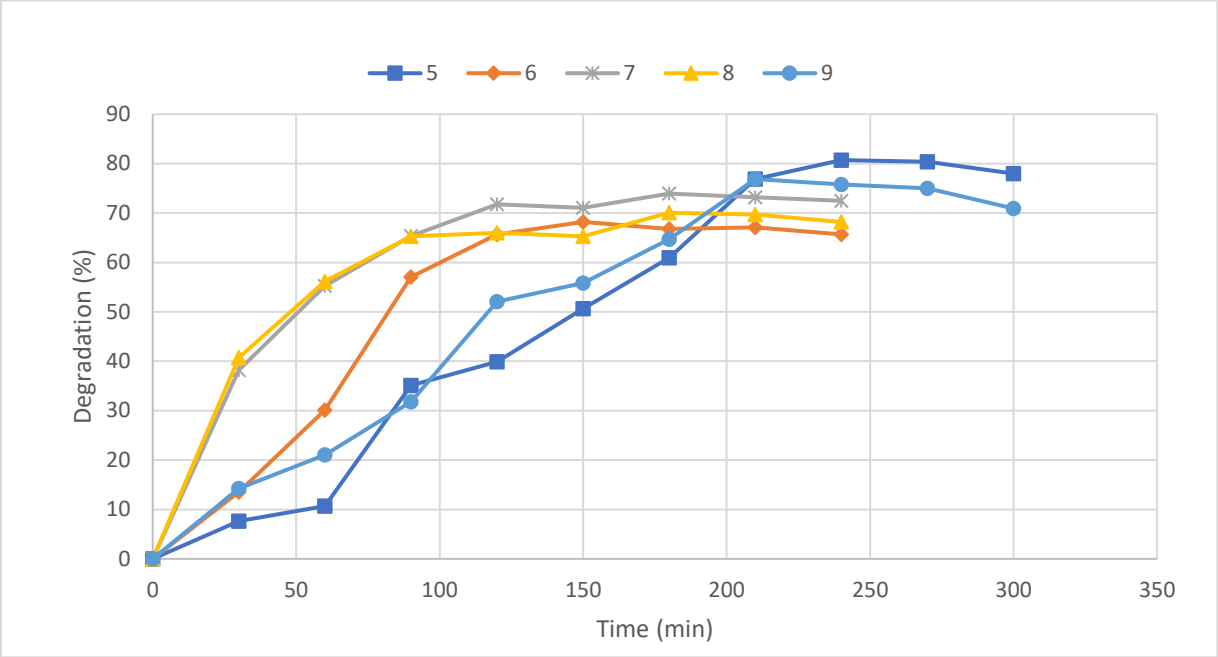

Figure 4.6. Effect of pH on percent degradation of AMX

4.3.5 Statistical analysis, Optimization and Validation of model

The parameters for degradation of AMX were optimized using the BBD design as well. The most critical parameters which affect the degradation of AMX are initial AMX concentration (X_1), TiO_2 loading (X_2), H_2O_2 concentration (X_3), and pH (X_4). Minimum and maximum levels for the parameters were ranged as 10-50mg/l for X_1, 300-600mg/l for X_2, 100-200mg/l for X_3 and 3-11 for X_4 and the results obtained from all the 27 runs are given in **Table 4.3**. The following equation (4.3) was obtained from regression analysis to evaluate the effect of independent variables on percent degradation (Y):

$$Y = - 68.5715 + 3.23\ X_1 + 0.126\ X_2 + 0.52\ X_3 + 6.31\ X_4 - 0.027\ X_1X_1 - 0.0001\ X_2X_2 - 0.007\ X_3X_3 - 0.3212\ X_4X_4 - 0.001\ X_1X_2 - 0.0054\ X_1X_3 - 0.0373\ X_1X_4 - 0.002\ X_2X_3 - 0.001\ X_2X_4 - 0.0045\ X_3X_4 \quad \text{.....4.3}$$

Where, Y is percent degradation, X_1 is AMX concentration, X_2 is TiO_2 concentration, X_3 is H_2O_2 concentration and X_4 is pH. The synergistic or antagonistic effect of each parameter on AMX degradation was explained by the positive or negative sign given before each term (Moosavi and Tavakoli, 2016). Actual values of percent degradation of AMX obtained from experiments were

compared with predicted values (obtained from model) of percent degradation as given in **Table 4.3** and **Fig. 4.7**. The adequacy of the model was further illustrated by analysis of variance (ANOVA) as shown in **Table 4.4**. The F value and P value indicate the significance of the regression model. The higher F-value of 5.34 for the model indicates that the model is efficient ($P<0.05$ for 95% confidence level). The regression coefficient (R^2) of 87% implies the fit of model. It was observed from **Table 4.4** that the quadratic terms X_1, X_2, X_3, X_4, X_1^2, X_2^2, X_3^2, X_4^2 show significant positive and negative effect on AMX degradation, respectively. Response surface plots were used **(Fig. 4.9)** to study interaction among the parameters; and further, each parameter was optimized for AMX degradation. The optimized values for maximum AMX degradation illustrated by model was AMX 30 mg/l, TiO_2 450 mg/l, H_2O_2 150 mg/l and pH 7 **(Fig. 4.8)**. At optimized conditions, 80% degradation was achieved with 270 minutes.

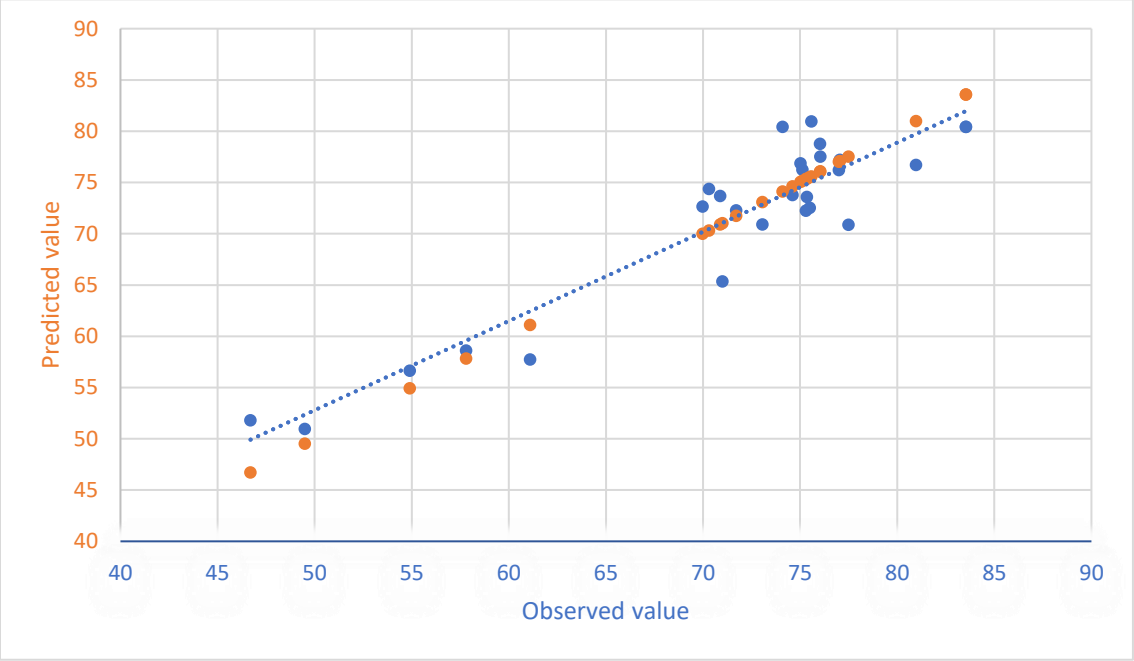

Figure 4.7. Relationship of predicted and observed values for degradation (%) of AMX

Table 4.3. Box-Behnken Design matrix and response factor results for degradation of AMX

	X1	X2	X3	X4	Degradation (%)	
Run	**AMX (mg/l)**	**TiO_2 (mg/l)**	**H_2O_2(mg/l)**	**pH**	**Predicted**	**Observed**
1	30	450	100	11	73	**70**
2	50	450	150	3	77	75
3	30	600	150	3	74	75
4	30	450	200	11	74	70
5	10	600	150	7	59	58
6	30	450	150	7	80	84
7	30	600	100	7	77	81
8	50	600	150	7	77	77
9	10	450	150	3	52	47
10	50	450	150	11	71	77
11	30	300	150	3	72	75
12	10	450	200	7	65	71
13	30	450	200	3	76	77
14	30	600	200	3	77	76

15	30	300	100	7	73	76
16	30	450	150	7	80	74
17	30	300	150	11	72	71
18	30	300	200	7	78	76
19	50	450	100	7	81	76
20	50	450	200	7	74	75
21	10	300	150	7	57	55
22	30	450	150	7	80	83
23	50	300	150	7	76	75
24	30	450	100	3	71	73
25	10	450	100	7	51	49
26	10	450	150	11	58	61
27	30	600	100	3	74	71

Table 4.4. Results of ANOVA-test for response percent degradation

Source	Coefficient	Degrees of freedom	F-ratio	P-value
Model	-68.5715	14	5.74	0.002
X_1 (AMX)	3.2331	1	23.85	0.000
X_2 (TiO_2)	0.1265	1	1.39	0.261
X_3 (H_2O_2)	0.5204	1	2.61	0.132
X_4 (pH)	6.3100	1	3.44	0.089
X_1 X_1	-0.0274	1	25.70	0.000
X_2 X_2	-0.0001	1	1.12	0.310
X_3 X_3	-0.0007	1	0.65	0.436
X_4 X_4	-0.3212	1	5.65	0.035
X_1 X_2	-0.0001	1	0.01	0.925
X_1 X_3	-0.0054	1	4.74	0.050
X_1 X_4	-0.0373	1	1.43	0.256
X_2 X_3	-0.0002	1	0.30	0.495
X_2 X_4	-0.0001	1	0.00	0.989
X_3 X_4	-0.0045	1	0.13	0.725

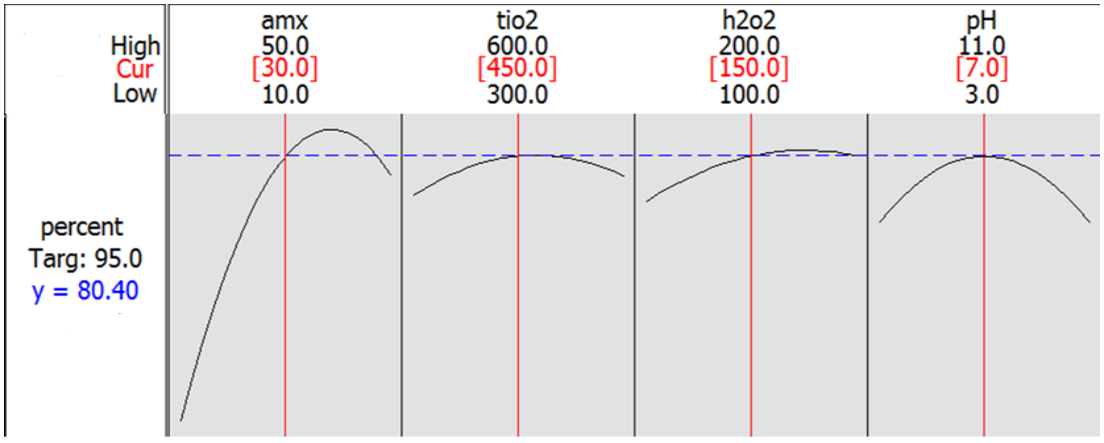

Figure 4.8. Optimization plot for photocatalytic degradation of AMX (AMX 30mg/L, TiO_2 450mg/L, H_2O_2 150mg/L, pH 7)

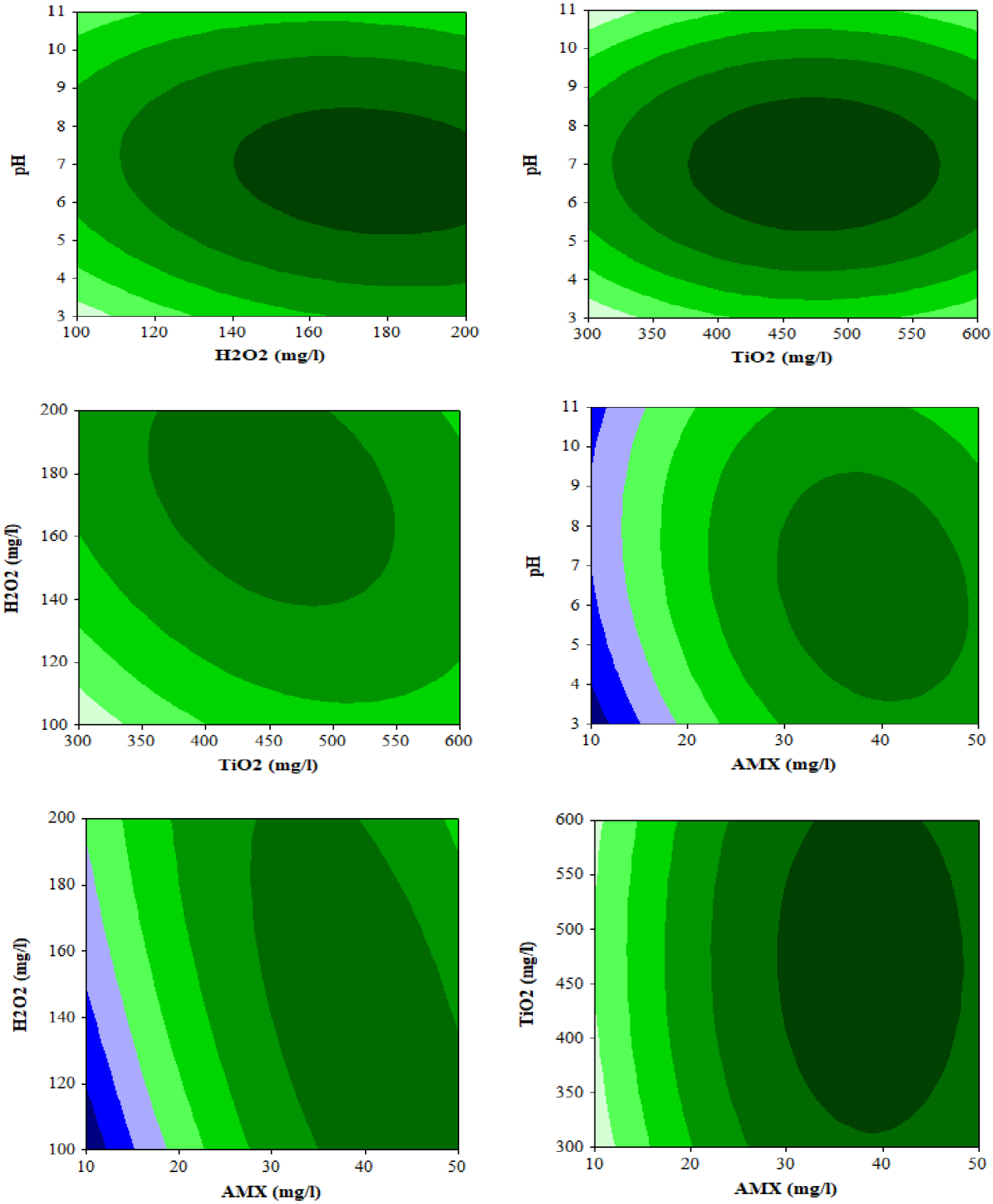

Figure 4.9. Response surface plots of percent degradation of amoxicillin under different sets of conditions

4.3.6 Comparison of Photocatalysis, Photocatalysis with H_2O_2 and Sono-photocatalysis

Maximum degradation for AMX was obtained using photocatalysis with H_2O_2 at AMX 30 mg/l, TiO_2 450 mg/l, H_2O_2 150 mg/l and pH 7. The same optimized conditions were further used to study the degradation pattern of AMX using photocatalysis and sono-photocatalysis. The results revealed that there was no significant improvement in maximal degradation or rate of degradation when photocatalysis was amended with H_2O_2 **(Table 4.5)**. Although the rate of degradation was enhanced in sono-photocatalysis process and more than 50% degradation was achieved within 30 minutes but reaction rate got slow after 30 minutes **(Fig. 4.10)** stabilizing at almost same maximal removal. This may be attributed to fact that at lower frequency, in the long-lived bubble, scavenging of $^{\bullet}OH$ radicals occurred with hydroperoxyl radical (reaction 4.4) (Lim et al., 2011)

$$^{\bullet}OH + {\bullet}OOH \rightarrow H_2O + O_2 \quad \text{.....4.4}$$

Another study (Matouq et al. 2014) reported degradation of AMX at higher frequency of 2.4 MHz. The reaction rate was enhanced using H_2O_2 and maximum degradation of 70% was observed at the same frequency.

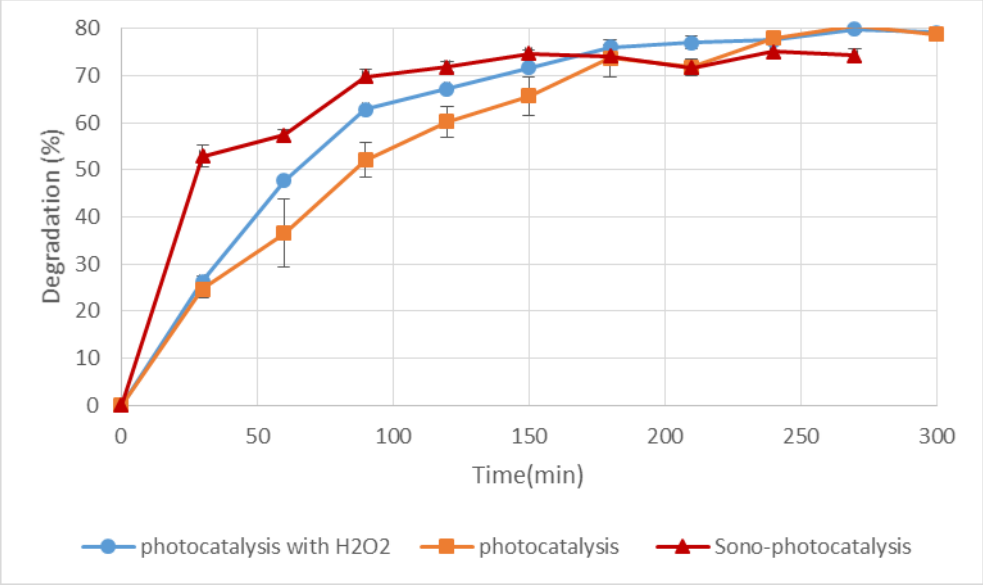

Figure 4.10. Comparison of Photocatalysis, Photocatalysis with H_2O_2 and Sono-photocatalysis towards degradation of AMX

Table 4.5. Comparison of photocatalysis and photocatalysis integrated processes (AMX)

Processes	Conditions	Time (min)	Degradation (%)
Photocatalysis	UV (365nm) AMX:30mg/L TiO_2: 450mg/L pH: 7.0	270	80
Photocatalysis with H_2O_2	UV (365nm) AMX:30mg/L TiO_2: 450mg/L; H_2O_2: 150mg/L; pH: 7.0	210	83
Sono-photocatalysis	UV (365nm) Ultrasound: 40kHz AMX:30mg/L TiO_2: 450mg/L; H_2O_2: 150mg/L; pH: 7.0	240	75

4.3.7 Comparison of Photocatalysis, Solar- photocatalysis, Sono-photocatalysis and Solar sono-photocatalysis for treatment of real pharmaceutical wastewater

The initial characterization of wastewater shows pH 7.0, EC 534 µS/cm, TDS 261 mg/l and COD 360 mg/l. The degradation of pharmaceutical wastewater was investigated at initial concentration of 30 mg/l AMX after diluting the real wastewater, TiO_2 450 mg/l, H_2O_2 150 mg/l and pH 7.0. It was observed that within 10 minutes of reaction time, around 50% degradation was achieved in sono-photocatalysis and solar sono-photocatalysis as shown in **Fig. 4.11**; while at the same time very less (≈15%) degradation was achieved in photocatalysis and solar photocatalysis.

After 30 minutes, more that 80% degradation was found in sono-photocatalysis and solar sono-photocatalysis and more that 50% degradation was found in photocatalysis and solar-photocatalysis. This increase in rate of degradation in sono-photocatalysis and solar sono-photocatalysis was attributed to the fact that combination of photocatalysis and sonolysis shows synergistic effect which ultimately enhance the production of hydroxyl radical and increase the rate of reaction. The rate of reaction get slower after 30 min and 95% degradation was achieved in solar sono-photocatalysis after 90 min; photocatalysis (150 min) and around 90% degradation was achieved in solar photo-catalysis and sono-photocatalysis after a period of 180 min (Table 4.6). HPLC analysis confirmed that AMX degradation of about 80% was achieved by optimized photocatalysis without formation of any major intermediates **(Fig. 4.12)**.

Table 4.6. Comparison of photocatalysis and photocatalysis integrated processes in real pharmaceutical wastewater

Processes	Conditions	Time (min)	Degradation (%)
Photocatalysis	UV (365nm) AMX:30mg/L TiO_2: 450mg/L; pH: 7.0	150	95
Solar Photocatalysis	UV (Sunlight) AMX:30mg/L TiO_2: 450mg/L; pH: 7.0	180	90
Sono-photocatalysis	UV (365nm) Ultrasound: 40kHz AMX:30mg/L TiO_2: 450mg/L pH: 7.0	180	90
Solar Sono-photocatalysis	UV (Sunlight) Ultrasound: 40kHz AMX:30mg/L TiO_2: 450mg/L pH: 7.0	180	95

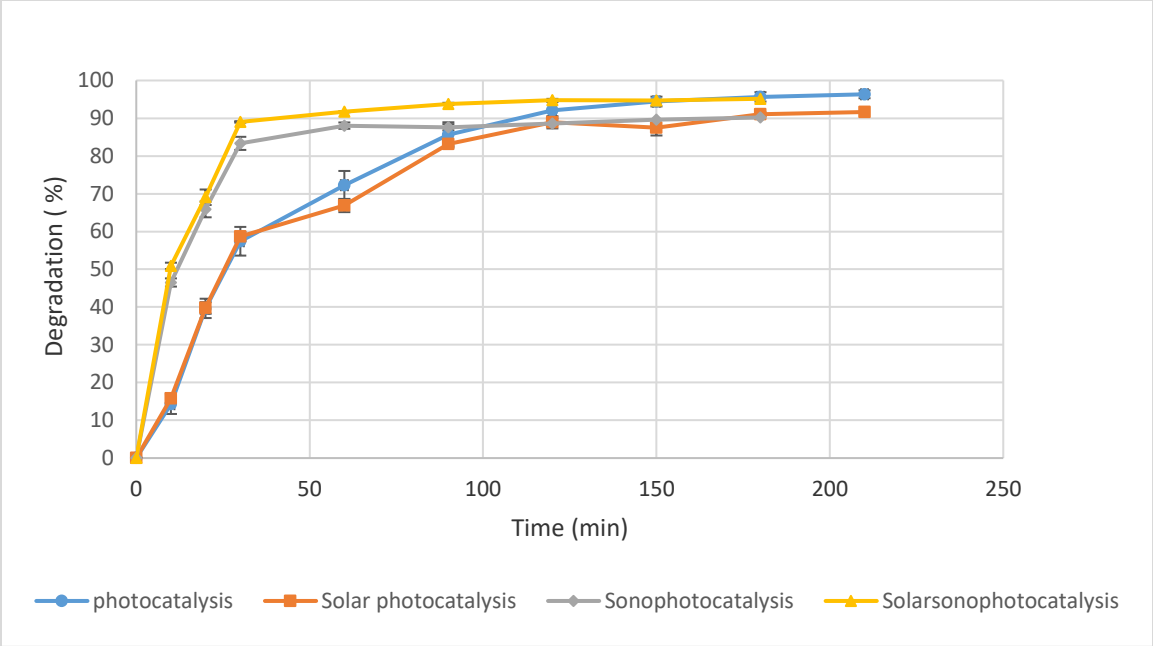

Figure 4.11. Comparison of Photocatalysis, Solar- photocatalysis, Sono-photocatalysis and Solar sono-photocatalysis in real pharmaceutical wastewater

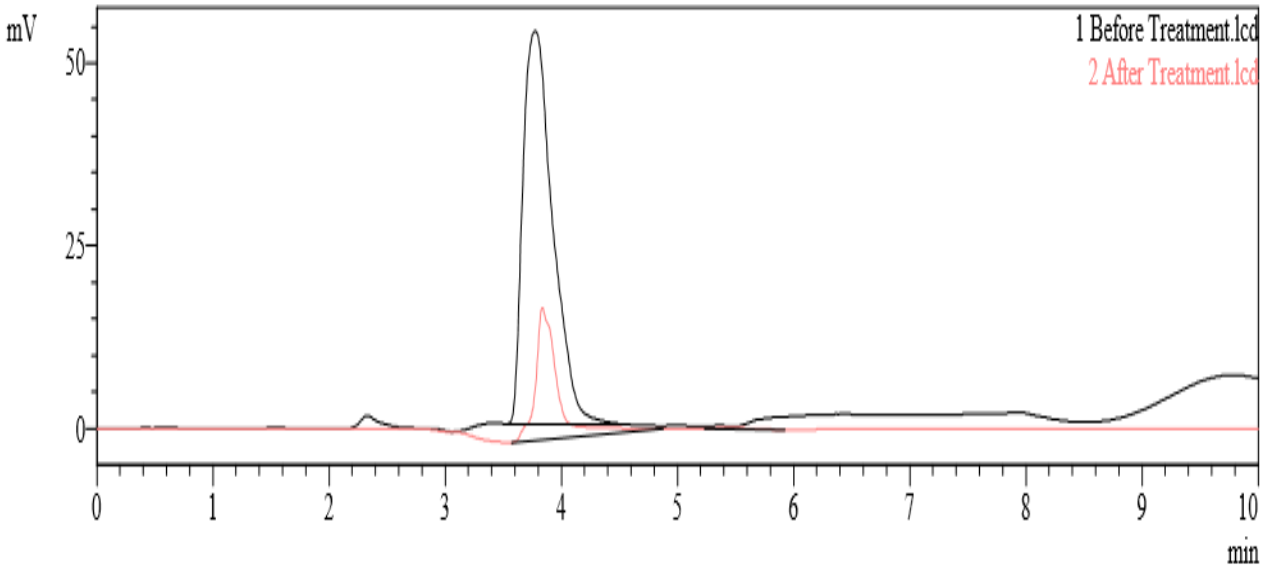

Figure 4.12. HPLC chromatogram of untreated and photocatalytically treated wastewater for degradation of AMX

4.4 Degradation of AMX using Fenton treatment

Degradation of AMX was observed in the experiments undertaken with Fenton and integrated Fenton integrated processes. Significant increase in rate of degradation was observed in case of integrated processes. The degradation specific details (pH, $FeSO_4$, H_2O_2, light source etc.) of the experiments are discussed in detail in the sections given below.

4.4.1 Effect of AMX concentration

The initial concentration of AMX was taken as 10mg/l in OFAT approach while in BBD, concentration AMX was varied from 10-50mg/l to evaluate the effect of AMX at higher concentration. At lower concentration (10mg/l), complete degradation of AMX was observed while at higher concentration of 30mg/l and 50mg/l, there was decrease in degradation of AMX. Higher concentration of AMX requires higher doses of oxidant *i.e.* H_2O_2 which act as a limiting factor. Similar study reported by (Ay & Kargi , 2010) which revealed that at lower concentration of 10mg/l complete degradation was achieved while higher AMX concentration required higher concentration of H_2O_2 for removal.

4.4.2 Effect of $FeSO_4$ concentration

The concentration of $FeSO_4$ was varied from 10 to 40 mg/l in OFAT approach as well as BBD design and concentration of AMX, H_2O_2 and pH was kept as 10 mg/l, 150 mg/l, and 3.0, respectively in OFAT approach, during the experiment. It was observed that with an increase in the concentration of $FeSO_4$, degradation of AMX increases. At 30 mg/l of $FeSO_4$ complete degradation of AMX was achieved at a reaction time of 25 minutes while at the same time degradation AMX was 51.75%, 80.25% and 97.17% for the $FeSO_4$ dose of 10, 20 and 40 mg/l, respectively, as shown in **Fig. 4.13**.

At Fe^{2+} concentration of 40 mg/l, slight decrease rate of degradation of AMX was observed. This may be due to the fact that at higher concentration of $FeSO_4$ there will be scavenging effect of hydroxyl radicals. Fe^{2+} ions act as a catalyst in the Fenton process for generation of Hydroxyl radicals by carrying out H_2O_2 degradation/decomposition. At higher doses, Fe^{2+} ions are responsible for producing scavenging effect on hydroxyl radicals. In a similar study, Kargi et al., (2010) obtained the similar pattern of degradation for AMX by varying the iron concentration from 0-50 mg/l. The maximum degradation for AMX was achieved at 25 mg/l in their study. In a similar

study Rozas et al., 2010 optimum degradation of ampicillin was observed at an optimum concentration of 87 µmol/l (13.2 mg/l) Fe^{2+} ion concentration and 400 µmol/l H_2O_2 concentration at initial ampicillin concentration of 20 mg/l using Fenton's process. The concentration of Fe^{2+} ions in the present study is of the similar order with the concentration reported in literature.

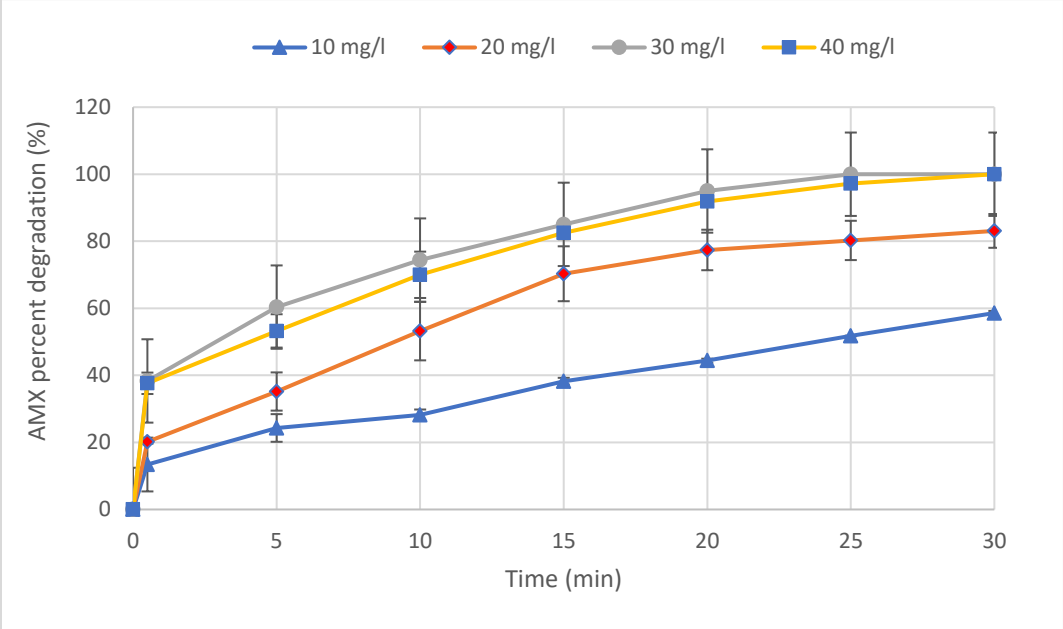

Figure 4.13. Effect of $FeSO_4$ concentration on degradation of AMX (AMX – 10 mg/l; H_2O_2 – 150 mg/l; and pH 3.0)

4.4.3 Effect of H_2O_2 concentration

The effect of H_2O_2 concentration was observed by varying the concentration from 150 to 600 mg/l (150, 225, 300, 375, 450 and 600 mg/l), at $FeSO_4$ concentration of 30 mg/l and pH 3.0. The same H_2O_2 concentration was varied for BBD design and obtained the optimum concentration of 375mg/l for complete degradation of AMX. It was observed that increase in concentration H_2O_2 from 150 mg/l to 375 mg/l resulted in enhance rate of degradation of AMX **(Fig. 4.14)**.

Under optimized concentration–of H_2O_2 (375 mg/l) during the Fenton's degradation of AMX, the residual concentration of H_2O_2 was read at regular intervals of 2.0 minutes. It was observed that the residual concentration was 34 mg/l H_2O_2 indicating that about 340 mg/l of H_2O_2 was consumed during the complete oxidation of AMX in a period of about 12 minutes **(Fig. 4.15)**. Further increase in H_2O_2 concentration (450 and 600 mg/l) resulted in decreased rate of

degradation which may be attributed to scavenging of hydroxyl radicals, and generation of $HO^{\cdot}_2$ radical at higher/excessive concentration of H_2O_2 as reported in literature (Nidheesh & Rajan, 2016).

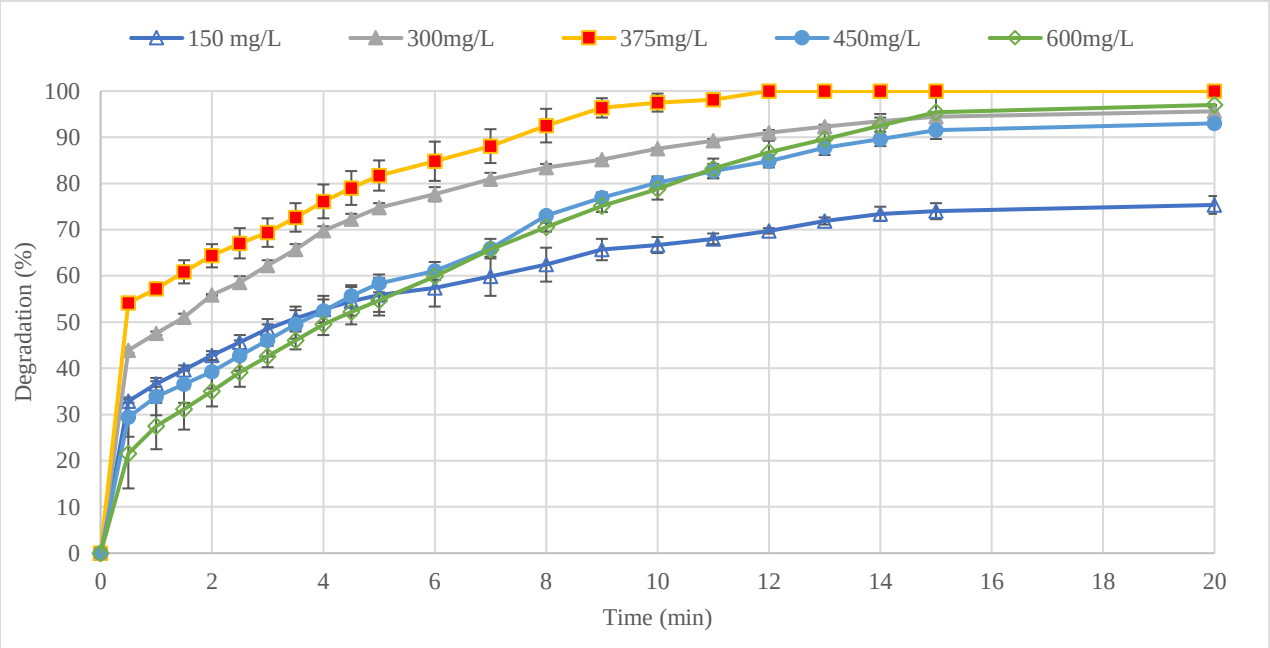

Figure 4.14. Effect of H_2O_2 concentration on degradation of AMX

$$HO^{\cdot} + H_2O_2 \rightarrow HO^{\cdot}_2 + H_2O \quad \text{.....4.5}$$

The degradation of AMX studied by Homem et al. (2010) also found that degradation increases with increase in concentration from 3.50-4.28 mg/l but at higher concentration H_2O_2 shows the scavenging effect. Relatively higher concentration of peroxide is required if the initial concentration of the substrate to be degraded (AMX) is high (Ay & Kargi, 2010).

4.4.4 Effect of pH

The degradation of organic impurities by Fenton's process is dominantly regulated by pH. It is effective in a pH range of 2-4 generating optimum amount of hydroxyl radicals required for degradation. Low value of pH (less than 2.0), results in formation of complex iron species, formation of oxonium ions ($H_3O_2^+$), and scavenging of hydroxyl radicals by H^+ ions (Kwon et al., 1995).

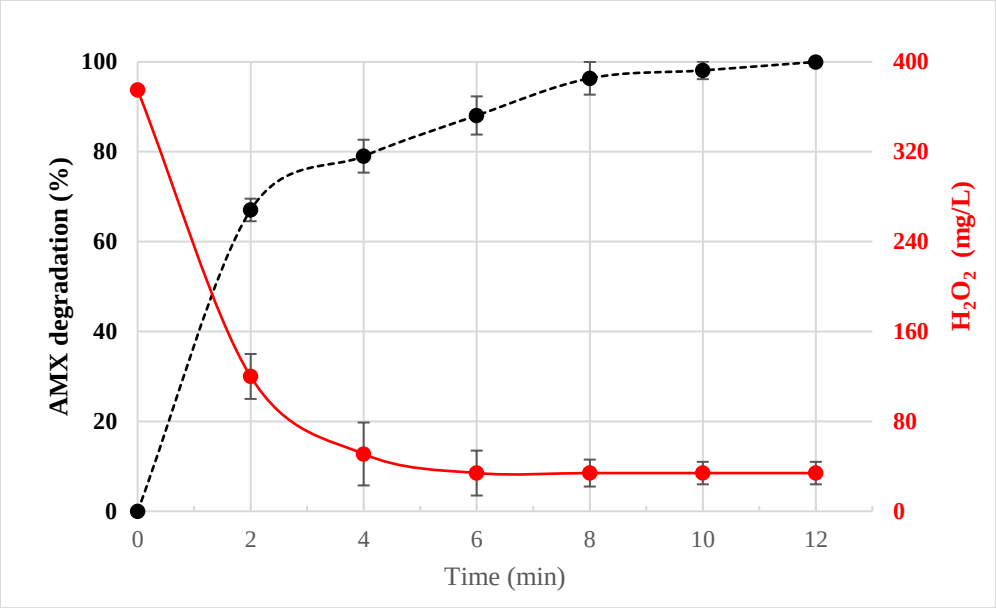

Figure 4.15. Consumption of H_2O_2 (mg/l) for complete oxidation of AMX (10 mg/l) during Fenton's process ($FeSO_4$ 3.0 mg/l; and H_2O_2 -375 mg/l; pH 3.0)

In the present study, effect of pH was studied in the range of 2.5 – 4.0. It was observed that pH 3.0 is the optimum pH for fast and complete degradation of AMX within 12 minutes of reaction time **(Fig. 4.16)**. Degradation of AMX was observed to be minimum at pH 2.5 with maximum degradation of the order of about 70%. Although pH 3.0 and 3.5 lead to complete degradation but in approximately 75 minutes which was significantly more (≈ 6times) time compared to pH 3.0. It has been reported that the pH of 3.0 is most effective for degradation of organic matter (Kochany et al., 2009). Apart from it the H_2O_2 and Fe^{2+} ions are more stable at lower pH. Optimum degradation of AMX and other organic pollutants by Fenton's process at pH 3.0 has been reported in several other studies as well (Kavitha & Palanivelu, 2005; Alalm et al., 2014).

4.4.5 Statistical analysis: optimization and validation of model

The parameters which mainly influence the AMX degradation are initial AMX concentration (X_1), H_2O_2 concentration (X_2), $FeSO_4$ concentration (X_3) and pH (X_4). The parameters X_1, X_2, X_3 and X_4 are varied within the range 10-50mg/l, 10-40mg/l, 150-600mg/l and 2.5-3.5, respectively.

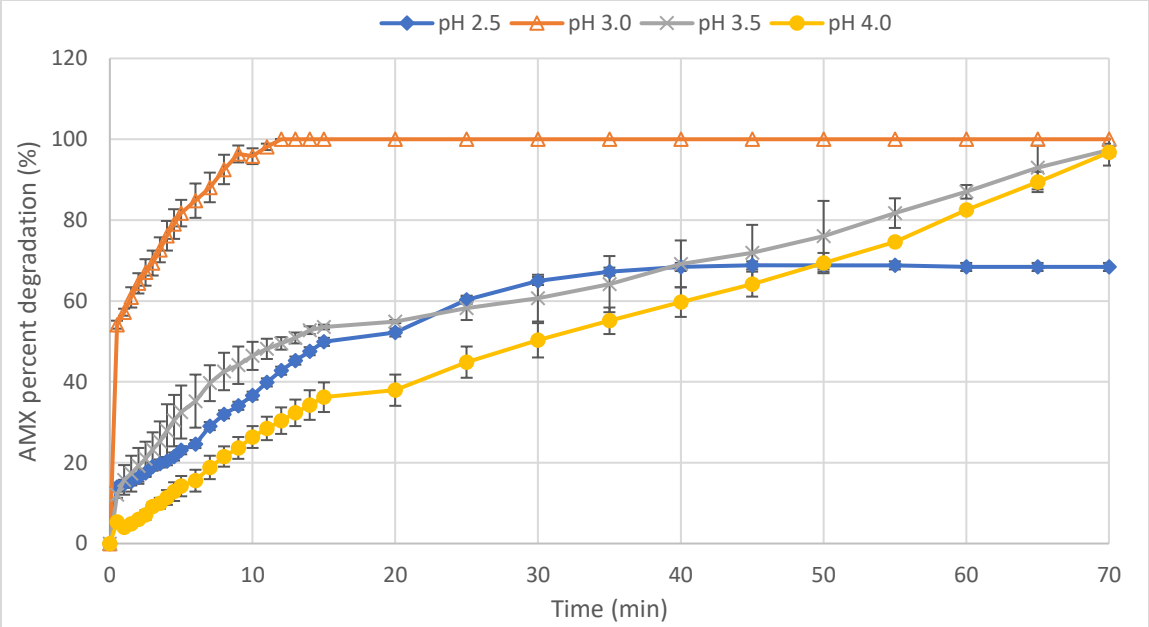

Figure 4.16. Degradation of AMX at pH 2.5, 3.0, 3.5 and 4.0 (AMX – 10 mg/l; $FeSO_4$ 3.0 mg/l; and H_2O_2 -375 mg/l)

The experiments were designed using BBD and obtained 27 number of runs for AMX degradation. In order to determine the impact of independent variables (Y) on percent degradation, the following regression equation (reaction 4.6) was achieved:

$$Y= -27.5894 + 0.8460X_1 - 4.8282X_2 + 0.0402X3 + 82.2150X_4 + 0.0161X1X1 + 0.0351X_2X_2 + 0.0001X_3X_3 - 11.7300X4X4 - 0.0036X1X2 + 0.0001X1X3 - 0.8955\ X_1X_4 - 0.0003X2X3 + 1.0675X_2X_4 - 0.0086X3X4 \quad \ldots 4.6$$

Where, Y is percent degradation, X_1 is AMX concentration, X_2 is $FeSO_4$ concentration, X_3 is H_2O_2 concentration and X_4 is pH. The observed and predicted values were compared as given in **Fig. 4.17** and **Table 4.7**. Response predicted values obtained from model and observed values from experiments are in good agreement with each other. The analysis of variance (ANOVA) further determined the model adequacy. The significance of the model was indicated by F value and P value. The higher F-value of 15.44 for the model indicates that the model is efficient ($P<0.05$ for 95% confidence level). The regression coefficient (R^2) of 94% indicates the good fit of model. Positive and negative effect on percent degradation of AMX was illustrated by quadratic terms X_1, X_2, X_3, X_4, X_1^2, X_2^2, X_3^2, X_4^2 as presented in **Table 4.8**. The interaction between each parameter was determined by using Response surface plots as shown in **Fig 4.18**. Optimized value for

complete degradation of AMX was achieved at AMX 10 mg/l, $FeSO_4$ 40 mg/l, H_2O_2 375 mg/l and pH 3 within 30min of reaction time.

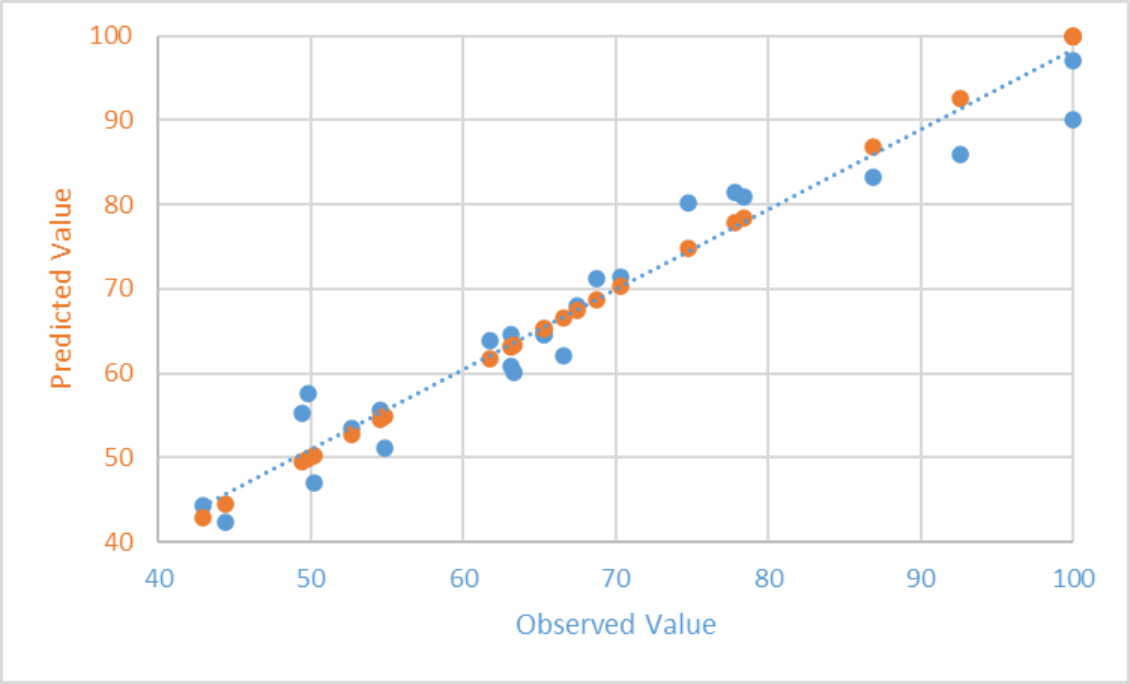

Figure 4.17. Relationship of predicted values and observed values for percent degradation of AMX (Fenton) indicating fit of the model

4.4.6 Fenton integrated with light (solar/UV) and Ultrasound

The optimized conditions for complete degradation of AMX were obtained as Fe^{2+} concentration 30 mg/l, H_2O_2 375 mg/l and pH 3.0. Further, using the same optimized conditions, degradation was studied using photo-Fenton, solar photo-Fenton, sono-Fenton, and sono-photo-Fenton. When Fenton process was coupled with UV light, complete degradation of AMX was observed within 3.5 minutes, whereas, in the case of solar- photo-Fenton complete degradation was achieved in 9.0 minutes as shown in **Fig. 4.19**. During photo-Fenton, when UV light was irradiated, the reduction of ferric ions to ferrous ions occurs which leads to the generation of more hydroxyl radicals and ultimately fasten the rate of degradation of AMX in comparison to Fenton process.

Table 4.7. Box-Behnken Design matrix and response factor results for degradation of AMX using Fenton treatment

	X1	X2	X3	X4	Degradation (%)	
Run	**AMX (mg/l)**	**$FeSO_4$(mg/l)**	**H_2O_2(mg/l)**	**pH**	**Predicted**	**Observed**
1	50	30	600	3	68	68
2	10	30	600	3	105	100
3	30	40	150	3	62	67
4	10	20	375	3	90	100
5	30	20	600	3	81	78
6	30	30	150	3.5	60	63
7	50	20	375	3	53	53
8	30	40	375	3.5	80	75
9	30	20	375	2.5	61	63
10	10	30	375	3.5	103	100
11	30	30	150	2.5	44	43
12	**10**	**40**	**375**	**3**	97	100
13	50	30	150	3	42	44

14	30	30	600	3.5	83	87
15	30	20	150	3	55	49
16	10	30	150	3	81	78
17	50	40	375	3	58	50
18	30	30	375	3	65	63
19	50	30	375	2.5	51	55
20	30	30	600	2.5	71	70
21	30	30	375	3	65	65
22	30	40	375	2.5	56	55
23	30	20	375	3.5	64	62
24	30	30	375	3	65	65
25	30	40	600	3	86	93
26	10	30	375	2.5	71	69
27	50	30	375	3.5	47	50

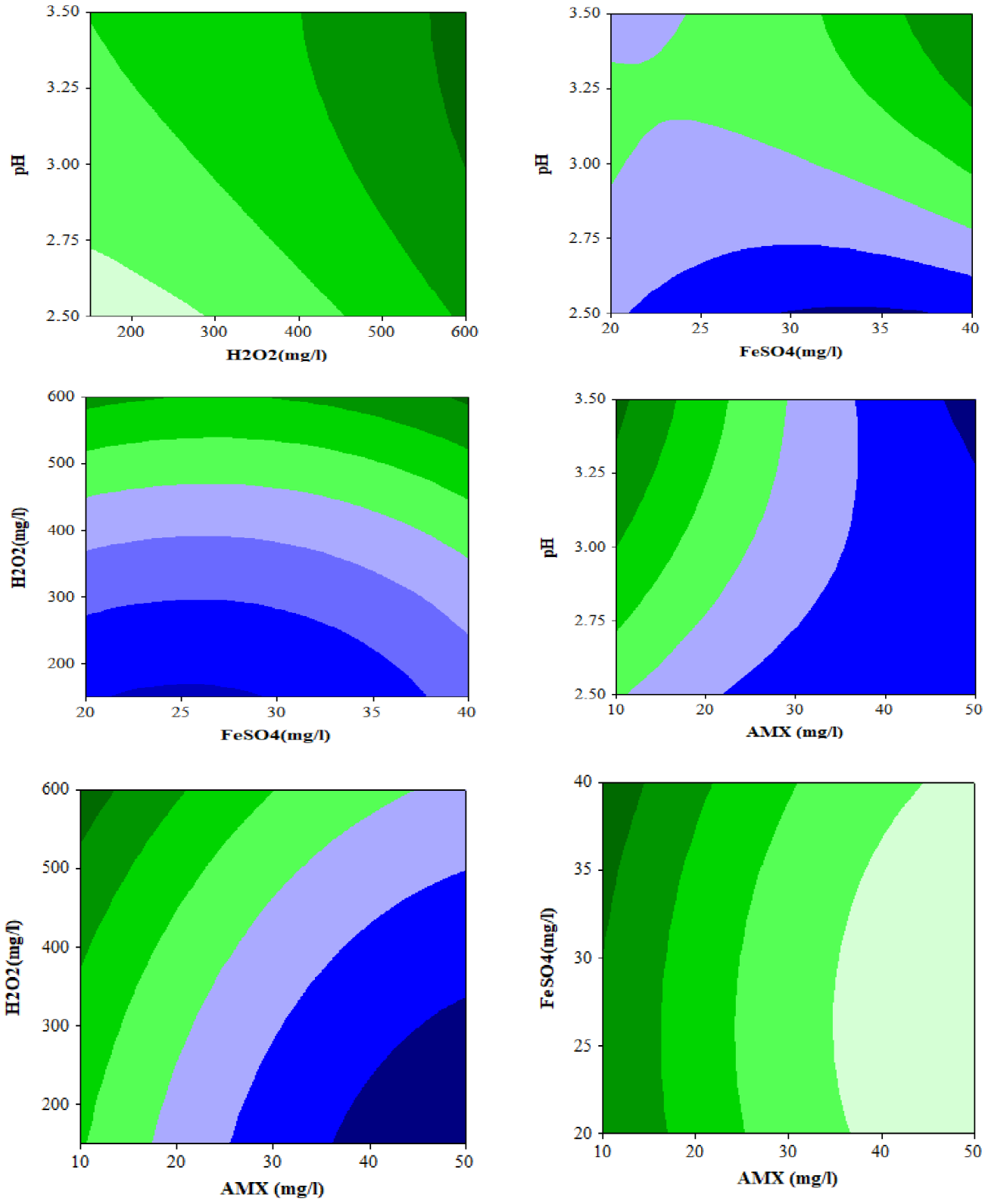

Figure 4.18. Response surface plots of percent degradation of amoxicillin under different sets of conditions (Fenton treatment)

Table 4.8. Results of ANOVA-test for response percent degradation of AMX (Fenton treatment)

Source	Coefficient	Degrees of freedom	F-ratio	P-value
Model	-27.5894	14	-0.216	0.833
X_1 (AMX)	0.8460	1	0.764	0.460
X_2 ($FeSO_4$)	-4.8282	1	-1.952	0.075
X_3 (H_2O_2)	0.0402	1	0.404	0.693
X_4 (pH)	82.2150	1	1.243	0.238
X_1 X_1	0.0161	1	2.489	0.028
X_2 X_2	0.0351	1	1.356	0.200
X_3 X_3	0.0001	1	1.205	0.251
X_4 X_4	-11.7300	1	-1.132	0.280
X_1 X_2	-0.0036	1	-0.237	0.816
X_1 X_3	0.0001	1	0.127	0.901
X_1 X_4	-0.8955	1	-2.994	0.011
X_2 X_3	-0.0003	1	-0.194	0.894
X_2 X_4	1.0675	1	1.785	0.100
X_3 X_4	-0.0086	1	-0.323	0.753

The efficiency of solar light towards production of $OH^{\cdot}$ radicals is relatively less due to lower energy of solar light compared to UV-irradiation. Although its energy is less than UV, it had a positive effect on degradation since the extra energy compared to Fenton alone, enhanced the production of oxidizing $OH^{\cdot}$ radicals. When the ultrasonic waves were irradiated to Fenton process, the rate of degradation becomes slow and the complete degradation of AMX was obtained in 20 minutes. This is attributed to the fact that during sono-Fenton, both the sources for generation of hydroxyl radicals *i.e.* ultrasound as well as Fenton act as a competitor for H_2O_2 which ultimately decreases Fenton reagent in the process, resulting in reduced rate of degradation of AMX. Similar effect has been reported when sono-Fenton was applied for degradation of phenols. It took 3 hours' time for complete degradation with sono-photo-Fenton, while in photo-Fenton complete degradation was achieved in 90 minutes of reaction time (Segura et al., 2009).

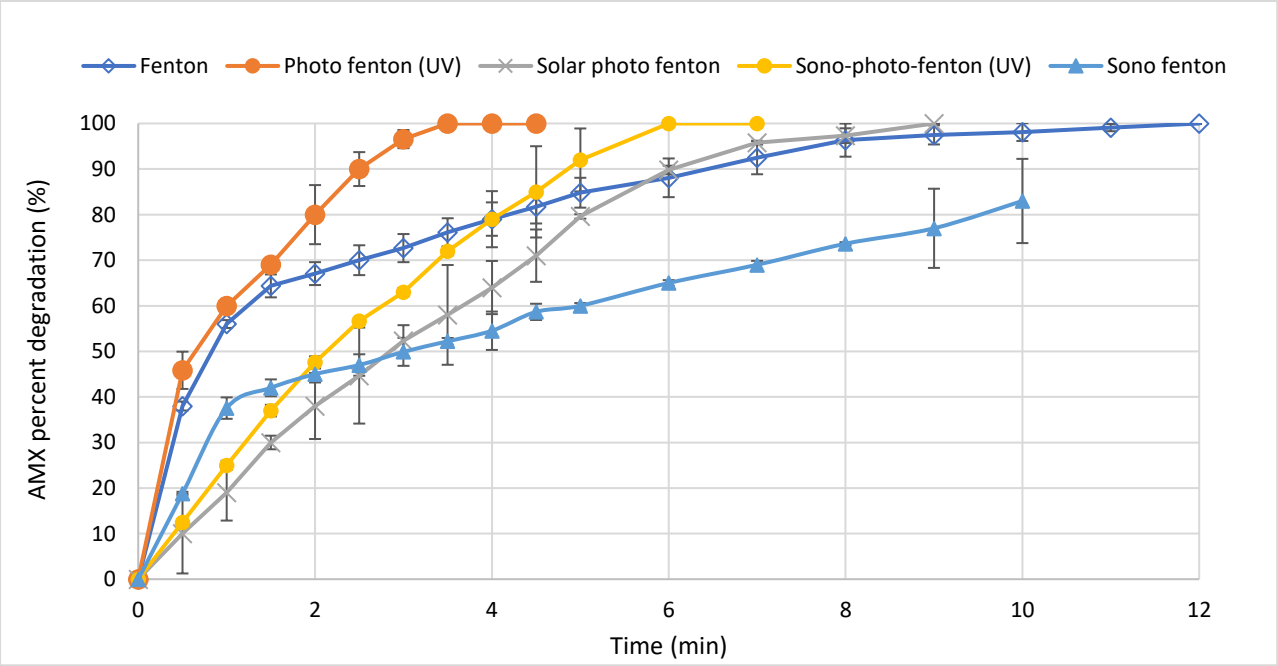

Fig 4.19. Comparison of Fenton, photo-Fenton, solar photo-Fenton, sono-Fenton and sono-photo-Fenton for complete degradation AMX.

Complete degradation of AMX was achieved within 6 minutes of reaction time in case of sono-photo-Fenton process **(Table 4.9)**. In comparison to Fenton and sono- Fenton, the rate of degradation was rapid in sono-photo-Fenton process. The size of particles of the catalyst becomes smaller when the ultrasound and UV light was applied during the sono-photo-Fenton process. This leads to an increase in active sites of iron in solution and ultimately the rate of

reaction becomes faster. Although sono-photo-Fenton resulted in rapid degradation of AMX, the rate was still less than photo-Fenton (UV). This may be due to the inter-specific competition of Fenton and ultrasound despite an increase in active sites of iron. Therefore, it was summarized that combination of Fenton process with other process is more effective in the degradation of AMX than the individual Fenton's process, but integration with ultrasonic treatment may act as a competitor to reduce the rate degradation of AMX.

Table 4.9. Comparison of Fenton and Fenton integrated processes (AMX)

Processes	Conditions	Time (min)	Degradation (%)
Fenton	AMX:10mg/L Fe^{2+} - 30 mg/l H_2O_2 – 375 mg/l pH – 3.0	12	100
Photo-Fenton	UV (365nm) Fe^{2+} - 30 mg/l H_2O_2 – 375 mg/l pH – 3.0	3.5	100
Solar photo-Fenton	UV (Sunlight) Fe^{2+} - 30 mg/l H_2O_2 – 375 mg/l pH – 3.0	9	100
Sono-Fenton	Ultrasound: 40kHz Fe^{2+} - 30 mg/l H_2O_2 – 375 mg/l pH – 3.0	20	100
Sono-photo-Fenton	UV (365nm) Ultrasound: 40kHz Fe^{2+} - 30 mg/l H_2O_2 – 375 mg/l pH – 3.0	6	100

4.5 Degradation of AMX in Pharmaceutical wastewater using Fenton

In order to degrade the AMX in pharmaceutical wastewater the experiments were performed to optimize the concentration of $FeSO_4$ and H_2O_2 at initial AMX concentration of 10mg/l and pH 3. Further increase in degradation was also observed using integrated processes such as photo-Fenton, solar photo-Fenton, sono-Fenton, sono-photo-Fenton and solar sono-photo-Fenton.

4.5.1 Effect of H_2O_2

The concentration of H_2O_2 was varied from 150-360mg/l (150, 210, 240, 270, 300, 330 and 360mg/l) at FeSO4 concentration of 10mg/l and pH 3.0. The degradation of wastewater was enhanced with increase in concentration of H_2O_2 from 150mg/l to 270mg/l and complete degradation of AMX in wastewater was achieved at 270mg/l within 35min of reaction time as shown in **Fig. 4.20**. There was gradual decrease in degradation of wastewater with increase in H_2O_2 concentration at 300, 330 and 360mg/l. It was also discussed earlier that higher concentration of H_2O_2 may lead to production of additional radical *i.e.* $HO_2^{\bullet}$ having oxidation potential lower than $HO^{\bullet}$ radical also stimulate the scavenging of hydroxyl radicals ($HO^{\bullet}$).

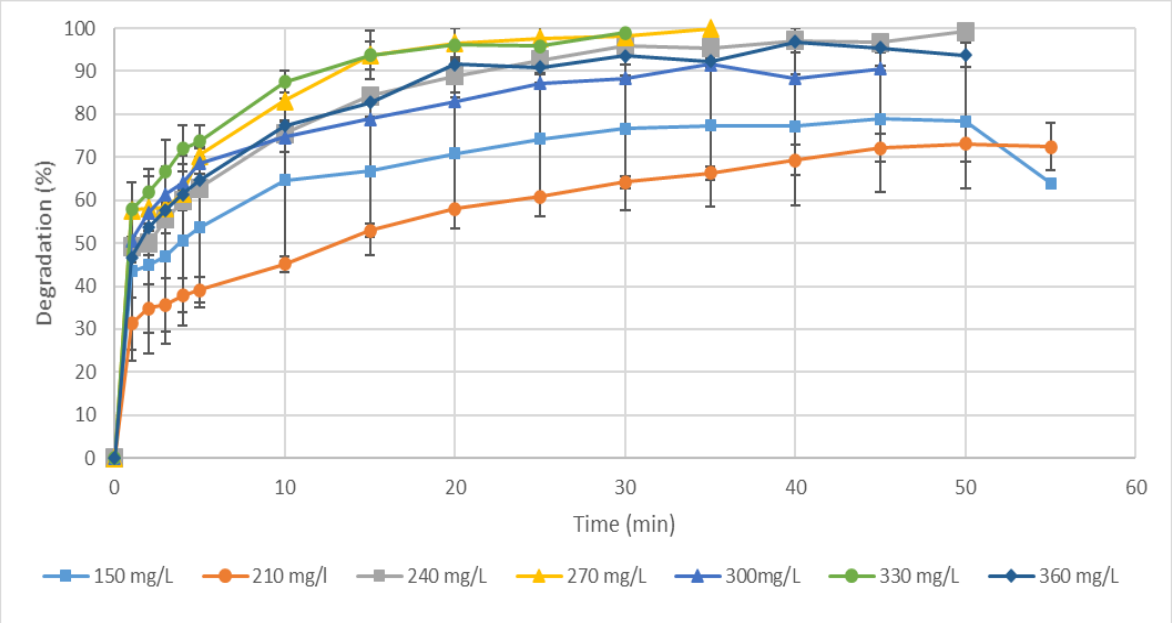

Figure 4.20. Effect of H_2O_2 concentration on degradation of pharmaceutical wastewater

4.5.2 Effect of $FeSO_4$

The concentration of $FeSO_4$ is another parameter which influences the degradation of wastewater. Fe^{2+} act as catalyst in the reaction and involves in decomposition of H_2O_2. The concentration of $FeSO_4$ was varied from 10-40mg/l (10, 20, 30 and 40mg/l) at H_2O_2 270mg/l and pH 3. It was demonstrated that at 10mg/l of $FeSO_4$ concentration, complete degradation of wastewater was observed within 35min of reaction time as shown in **Fig.4.21** while further increase in concentration of $FeSO_4$ leads to decrease in degradation. This may be due to reason that at higher concentration, scavenging effect of hydroxyl radicals occurs.

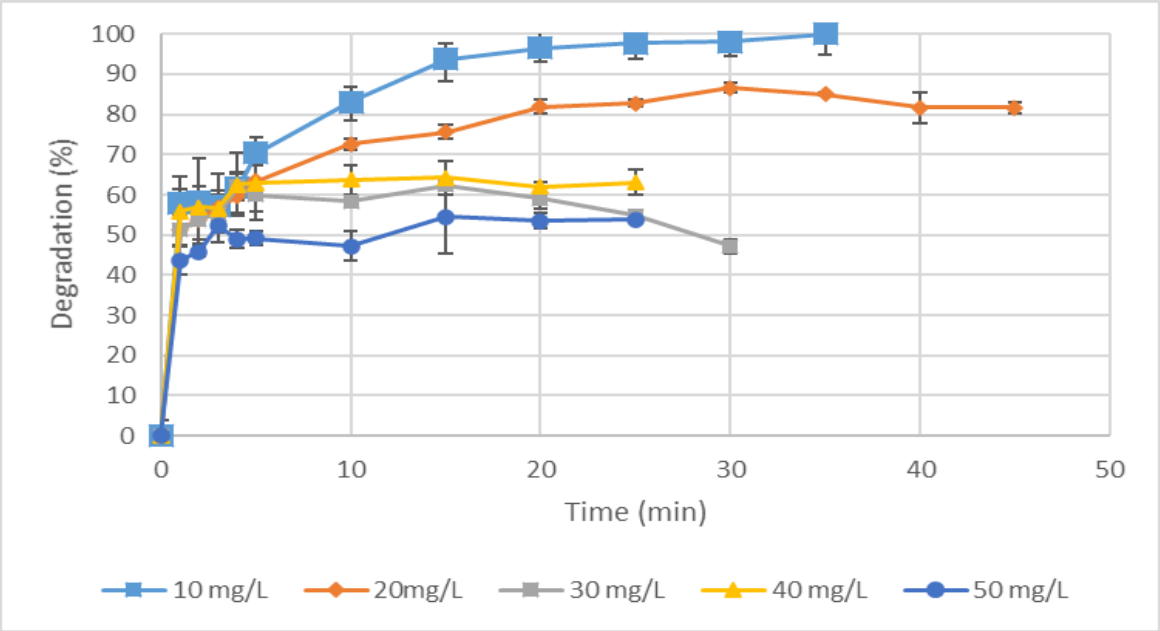

Figure 4.21. Effect of $FeSO_4$ concentration on degradation of pharmaceutical wastewater

4.5.3 Comparison of Fenton and integrated processes using solar and UV light for degradation of pharmaceutical wastewater

The optimized conditions for degradation of pharmaceutical wastewater using Fenton were achieved at wastewater AMX concentration - 10mg/l, H_2O_2-270mg/l, $FeSO_4$ – 10mg/l and pH-3. The same optimized conditions were further utilized to observe the degradation of wastewater using photo-Fenton, solar photo-Fenton, sono-Fenton, sono-photo-Fenton and solar sono-photo-Fenton. Results shown in **Fig 4.22**. revealed that solar sono-photo-Fenton completely degrade the wastewater within 3min of reaction time while Solar photo-Fenton,

Sono photo-Fenton, Photo-Fenton, Fenton completely degrade the wastewater within 8min, 15min, 20min and 30min of reaction time, respectively **(Table 4.10)**. On the other hand, maximum degradation achieved during sono-Fenton was 37% within 30 min of reaction time. This is because throughout the sono-fenton reaction, Fenton reagent and ultrasonic waves behave as competitor for H_2O_2 due to which production of hydroxyl radicals is affected. The efficiency of degradation was higher in combined processes due to synergistic effect. HPLC chromatogram as shown in **Fig. 4.23** revealed the degradation of wastewater without formation of secondary metabolites.

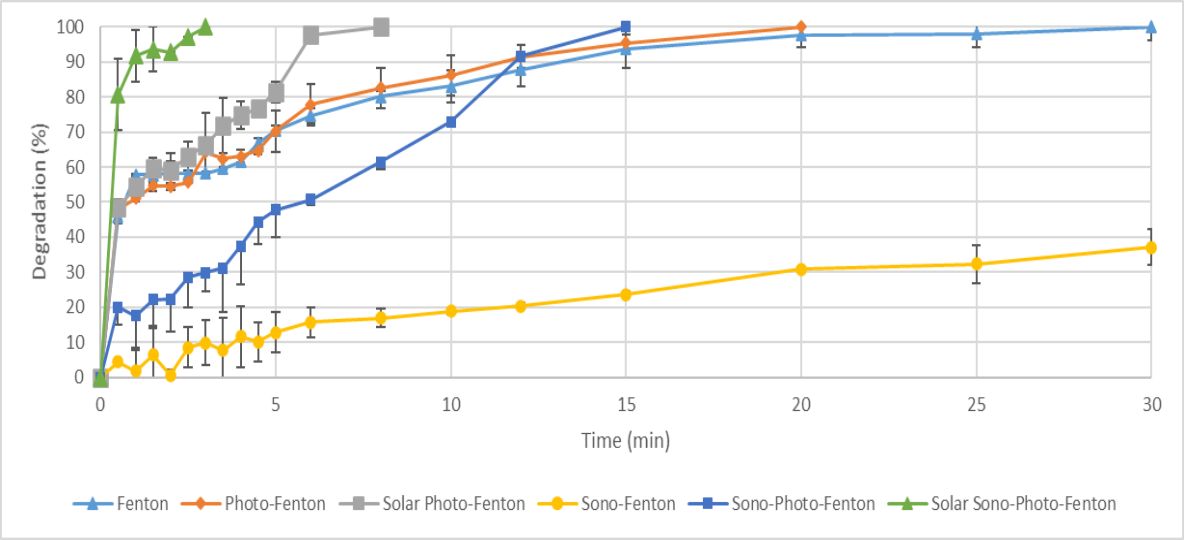

Figure 4.22. Comparison of Fenton, photo-Fenton, solar photo-Fenton, sono-Fenton, sono-photo-Fenton and solar sono-photo-Fenton for degradation wastewater

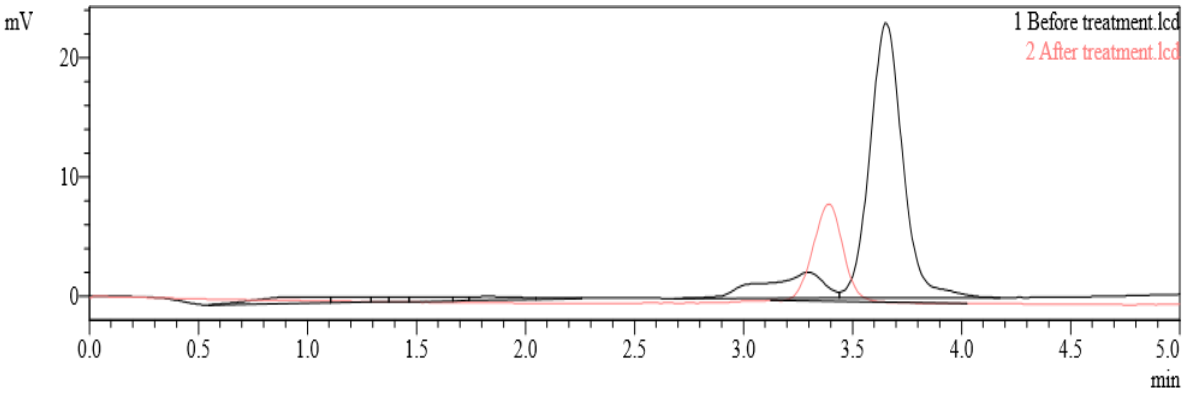

Figure 4.23. HPLC spectra for Fenton's treatment of AMX in pharmaceutical wastewater

Table 4.10. Comparison of Fenton and Fenton integrated processes for real pharmaceutical wastewater

Processes	Conditions	Time (min)	Degradation (%)
Fenton	AMX:10mg/L Fe^{2+} - 10 mg/l H_2O_2 – 270 mg/l pH – 3.0	30	100
Photo-Fenton	UV (365nm) Fe^{2+} - 10 mg/l H_2O_2 – 270 mg/l pH – 3.0	20	100
Solar photo-Fenton	UV (Sunlight) Fe^{2+} - 10 mg/l H_2O_2 – 270mg/l pH – 3.0	8	100
Sono-Fenton	Ultrasound: 40kHz Fe^{2+} - 10 mg/l H_2O_2 – 270 mg/l pH – 3.0	30	37
Sono-photo-Fenton	UV (365nm) Ultrasound: 40kHz Fe^{2+} - 10 mg/l H_2O_2 – 270mg/l pH – 3.0	15	100
Solar Sono-photo-Fenton	UV (Sunlight) Ultrasound: 40kHz Fe^{2+} - 10 mg/l H_2O_2 – 270mg/l pH – 3.0	3	100

4.6 Degradation of Atenolol

4.6.1 Photocatalysis of Atenolol (ATL)

Experiments were performed using photocatalysis, solar photocatalysis, sono photocatalysis, solar sono photocatalysis and photocatalysis with H_2O_2 to evaluate the degradation of ATL. The efficacy of photocatalysis and its combination with sonication was observed by varying ATL concentration, TiO_2 dosage and pH. The effect of each parameter on ATL degradation is described below:

4.6.1.1 Effect of initial ATL concentration

The degradation of ATL was conducted by varying its initial concentration from 10mg/l to 40mg/l. At lower concentration of 10mg/L (TiO_2 450mg/l; pH 3), complete degradation of ATL was observed within 120 min of reaction time. At higher concentration of 40mg/L (TiO_2 450mg/l; pH 3), there has been slight decrease in degradation of ATL and the maximum degradation of 96.21% was achieved within 210 min of reaction time. This could be illustrated by the fact that at higher concentration of ATL, adsorption of ATL molecules on the surface of TiO_2 has increased which leads to decrease in generation of attacking molecules i.e. $^{\bullet}OH$ and $O_2^{\cdot-}$ radicals and ultimately results in decrease in photocatalytic degradation of ATL. Similar pattern of degradation was observed by (Hapeshi, et al., 2010) when the concentration of ATL was varied from 5-20mg/l and the maximum degradation of 85% was observed at initial concentration of 5mg/l of ATL. Tammaro et al., (2017) also observed that increase in ATL concentration results in decrease in degradation of ATL when the initial concentration of ATL was varied from 4.5-30mg/l.

4.6.1.2 Effect of catalyst (TiO_2) dose

The degradation of ATL was carried out using TiO_2 P 25 as it is more effective than other catalysts. The catalyst dose was varied from 300mg/l-600mg/l and degradation of ATL was increased with increase in catalyst dose but upto a certain level and further increase in dose resulted in decrease in degradation. Degradation of ATL was increased when the dose of TiO_2 was increased to 450mg/l while at 300mg/l (lower dose) and 600mg/l (higher dose), rate of degradation was quite slower. This could be justified by examining the fact that increase in catalyst dose would lead to increase in active sites on the surface of catalyst for photocatalytic reactions but this happens upto a certain point where all the particles of catalyst are fully irradiated. At higher catalyst dose, light penetration gets retarded or reflected as screening

effect of residual particles appears that results in shielding of section of photosensitive area. This would ultimately lead to fall of photons resulting in modification to decrease or to plateau (Hapeshi et al., 2010).

4.6.1.3 Effect of pH

The pH of the aqueous solution is one of the important parameter which can influence the efficacy of photocatalytic degradation of ATL. The initial pH of ATL solution was 6.9, and to investigate the effect of pH on photocatalytic degradation, it was varied at 3,7 and 11. It is very contrary to describe the impact of pH as it is delineated with radical formation and presence of reactive substances in mixture and also state of ionization of surface, substrate and catalyst (Tammaro et al., 2017). When the pH of the catalyst is less than 6, the surface of TiO_2 is positively charged while at pH greater than 6, the surface of TiO_2 is charged negatively as shown in eq. 4.7 and 4.8

$$TiOH + H^+ \leftrightarrow TiOH^+_2 \quad (4.7)$$

$$TiOH + OH^+ \leftrightarrow TiO^- + H_2O \quad (4.8)$$

At pH 3, complete degradation of ATL was achieved (ATL 10mg/l, TiO_2 450mg/l). At neutral pH 7, around 80% degradation was achieved while in alkaline conditions of pH 11, approximately 70-50% ATL degradation was achieved. An aromatic ring and a secondary amine -moiety are the reactive site which are accommodated by ATL. Among these, pH of the solution influence amine-moiety but aromatic ring reaction remains unaffected. Therefore, ATL reaction depends on pH of solution and pKa of amines (*i.e.* 9.6). The surface of TiO_2 is negatively charged because at 9.6 > pH > 6, amino group may be protonated. Consequently, the electrostatic attraction between ATL and TiO_2 surface has increased due to which higher conversion is reported around neutral conditions (Bhatia et al., 2017). It was also investigated from the previous studies that at lower pH, major oxidative species are positive holes while major species are hydroxyl radicals at high or neutral pH. So, it may be considered that in this case conversion mainly occur due to valance band more than radicals (Hapeshi et al., 2010).

4.6.1.4 Effect of H_2O_2 concentration

Addition of H_2O_2 in the photocatalysis process plays dual function for degradation. Firstly, it encouraged separation of charge by accepting a photo-generated electron from conduction band of semiconductor (TiO_2) so as to increase the production of $^{\bullet}OH$ radicals (eq. 4.9). Furthermore, it also involves in production of radicals through superoxide as per eq (4.10).

$$H_2O_2 + e^- \rightarrow {}^{\bullet}OH + OH^- \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots 4.9$$

$$H_2O_2 + O_2^{\bullet-} \rightarrow {}^{\bullet}OH + OH^- + O_2 \quad \ldots\ldots\ldots\ldots\ldots 4.10$$

At optimum ATL concentration of 10mg/L, TiO_2 dosage 450mg/l and pH 3, concentration of H_2O_2 was varied from 0.5mM to 1.5mM. When the varying concentration of H_2O_2 was added to aqueous solution of ATL, maximum degradation of around 96% was achieved within 150min of reaction time at 0.5mM. There has been slight decrease in degradation of ATL reported on further addition of H_2O_2. At H_2O_2 concentration of 1.0mM and 1.5mM, around 95% and 93% degradation were attained respectively, while the rate of degradation was quite higher at 1.5mM as seen in **Fig.4.24**. Overall, none of H_2O_2 concentration results in enhanced degradation efficiency of ATL as compared to TiO_2 photocatalyst. When the H_2O_2 is present in excess, it may behave as radical ($^{\bullet}OH$) scavenger or may also form peroxo compounds by reacting with TiO_2 photocatalyst. This behaviour of H_2O_2 shows damaging effect to photocatalytic process (Poulios et al., 2003). Here this could be the reason for decreased ATL degradation with increase in H_2O_2 concentration. Similar results were also reported by Ponkshe et al. (2019) by varying the concentration of H_2O_2 from 0.2mM-1.2mM for degradation of ATL and propranolol. It was revealed from the study that addition of H_2O_2 does not show increase in degradation efficiency in photocatalytic process.

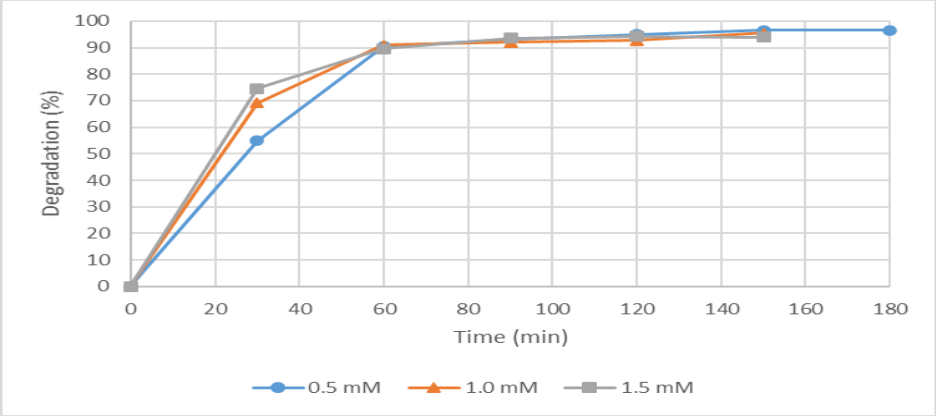

Figure 4.24. Effect of H_2O_2 concentration on degradation of ATL using photocatalysis

4.6.1.5 Statistical analysis: Optimization and validation of model

The initial concentration of ATL (X_1), TiO_2 (X_2) and pH (X_3) were varied as independent variables for photocatalytic degradation of AMX using BBD. The concentration of ATL, TiO_2 and pH at minimum and maximum level was taken as 10-40mg/L, 300-600mg/L and 3.0-11 respectively. The effect of independent variable on percent degradation (Y) of ATL was computed with the following polynomial equation (eq. 4.11):

$$Y = -83.4700 – 1.6713X_1 + 0.3850\ X_2 – 15.5213X_3 – 2.3325X_1X_1 – 2.5350\ X_2X_2 – 2.3575X_3X_3 – 1.6025X_1X_2 – 3.6350X_1X_3 – 0.5375X_2X_3 \quad \text{4.11}$$

The reliability of the model was exhibited from higher value of R^2 i.e. 89%. The significant positive and negative effect on Y was represented by the quadratic terms X_1, X_2, X_3, X_4, and X_1^2, X_2^2, X_3^2, $X_4^{2.}$ The F-value 4.79 and low probability value $P<0.05$ elucidated that the model is highly significant. The model adequacy was further summarized through analysis of variance (ANOVA) as indicated in **Table 4.12**. The predicted values of ATL degradation obtained from model were analogized with actual values of ATL degradation attained from the model as shown in **Fig. 4.25** and **Table 4.11**. Response surface plots as shown in **Fig. 4.26** illustrated the maximum ATL degradation which can be demonstrated by confining the surface to the smaller curve of surface plot considering two factors at a time and holding the others factors at a level of zero as per eq. Complete degradation of ATL was achieved at ATL conc. 10mg/L, TiO_2 450mg/L and pH 3.0 within 120min of reaction time while at higher concentration of ATL 40mg/L, TiO_2 600mg/L and pH 11 minimum degradation of around 50% was achieved.

4.6.1.6 Comparison of photocatalysis, solar photocatalysis, sono photocatalysis and solar sono photocatalysis

The optimum concentration for complete degradation of ATL was obtained as ATL 10mg/L, TiO_2 450mg/L and pH 3.0 within 120min of reaction time. Furthermore, the effect of integrated processes were studied by combining the photocatalysis with sonication under solar and UV irradiation. The optimized conditions from photocatalysis were employed to study the degradation ATL using solar photocatalysis, sono photocatalysis and solar sono photocatalysis. From the study, it was revealed that solar photocatalysis degrade the ATL around 98% within 90min of reaction time and the same time 99% degradation was achieved in photocatalysis process as shown in **Fig. 4.27**.

Table 4.11. Box-Behnken Design matrix and response factor results for degradation of ATL by photocatalysis

	X1	X2	X3	Degradation (%)	
Run	ATL (mg/L)	TiO_2(mg/L)	pH	Predicted	Observed
1	25	600	3	100	95
2	40	450	11	58	50
3	10	300	7	83	79
4	10	450	11	69	69
5	40	600	7	80	86
6	10	600	7	87	84
7	40	450	3	96	96
8	25	300	11	68	73
9	10	450	3	92	100
10	25	450	7	83	83
11	25	300	3	98	95
12	25	450	7	83	83
13	40	300	7	83	86
14	25	450	7	83	83
15	25	600	11	68	71

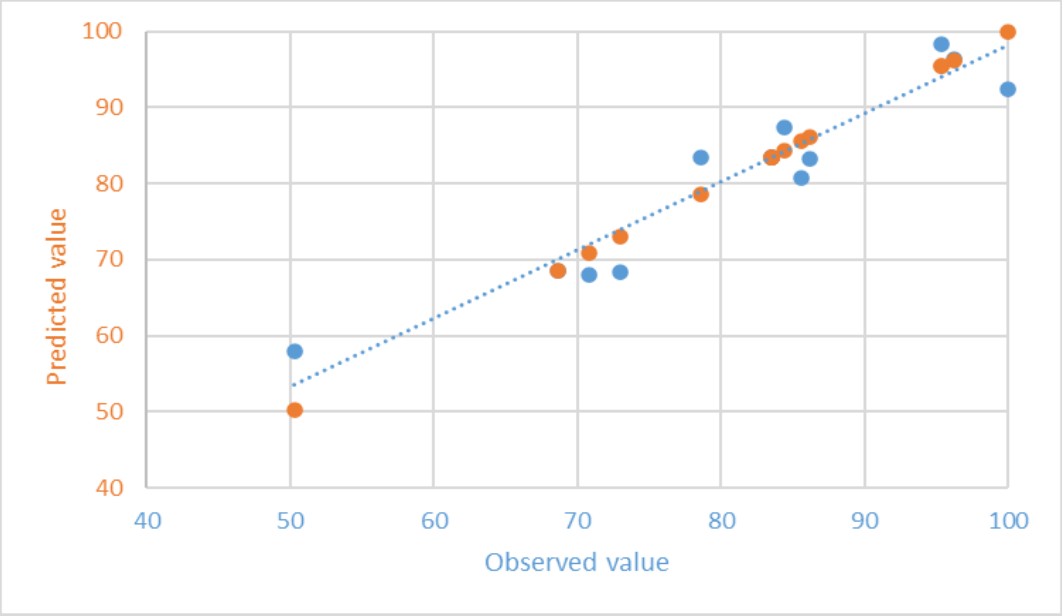

Figure 4.25. Relationship of predicted and observed values for percent degradation of ATL by photocatalysis

Table 4.12. Results of ANOVA-test for response percent degradation of ATL

Source	Coefficient	P-value
Model	-83.4700	0.050
X_1 (ATL)	-1.6713	0.527
X_2 (TiO_2)	0.3850	0.882
X_3 (pH)	-15.5213	0.001
X_1 X_1	-2.3325	0.548
X_2 X_2	2.5350	0.515
X_3 X_3	-2.3575	0.543
X_1 X_2	-1.6025	0.664
X_1 X_3	-3.6350	0.344
X_2 X_3	-0.5375	0.883

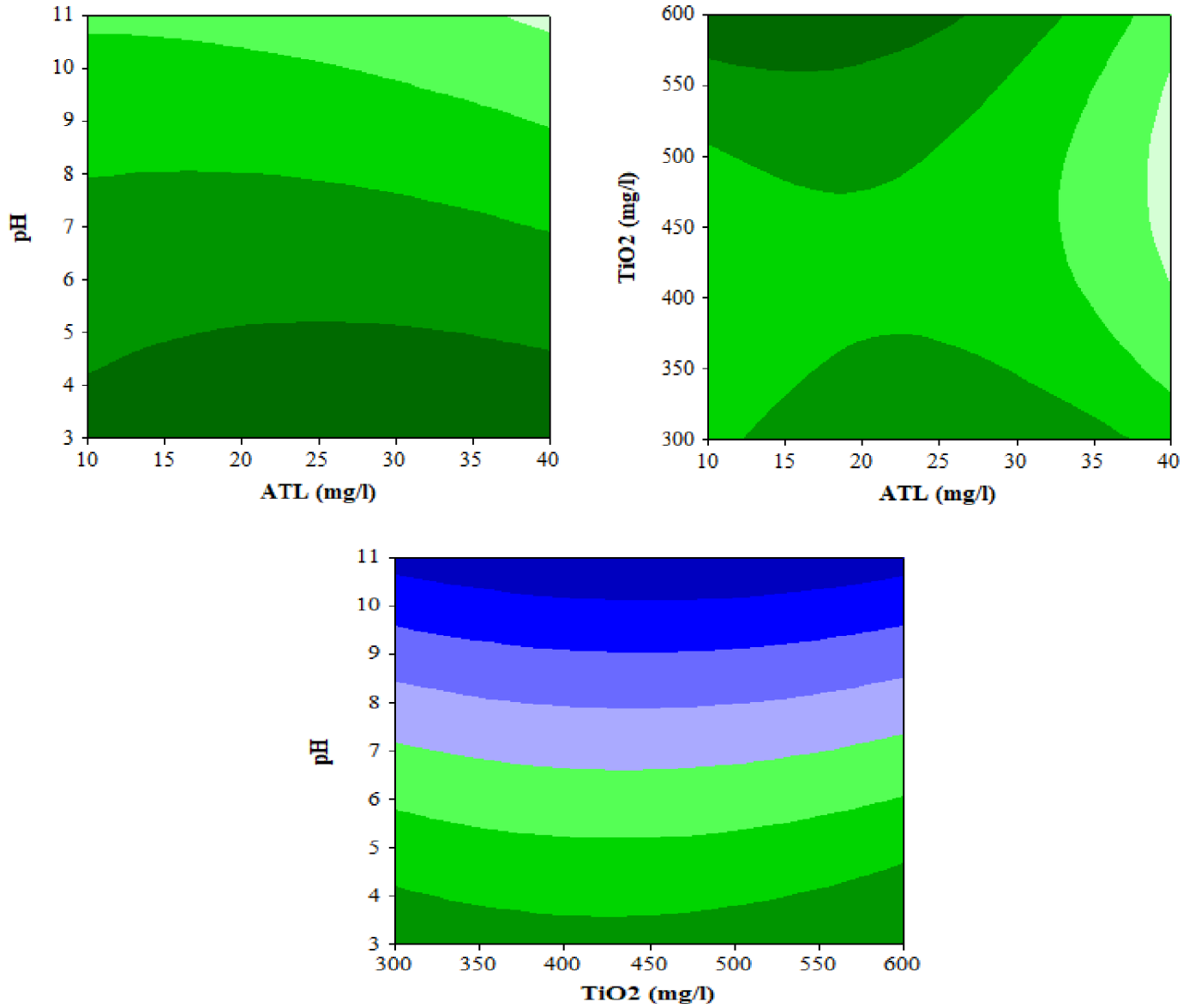

Figure 4.26. Response surface plots of percent degradation of Atenolol under different sets of conditions

Rate of degradation was almost similar in both photocatalysis as well as solar photocatalysis process. The degradation of ATL in sono photocatalysis and solar sono photocatalysis was obtained as 98% and 92% within 180min and 150min, respectively **(Table 4.13)**. HPLC analysis of ATL revealed the degradation of ATL around 90% at optimized conditions of photocatalysis without formation of any major intermediates **(Fig. 4.28)**.

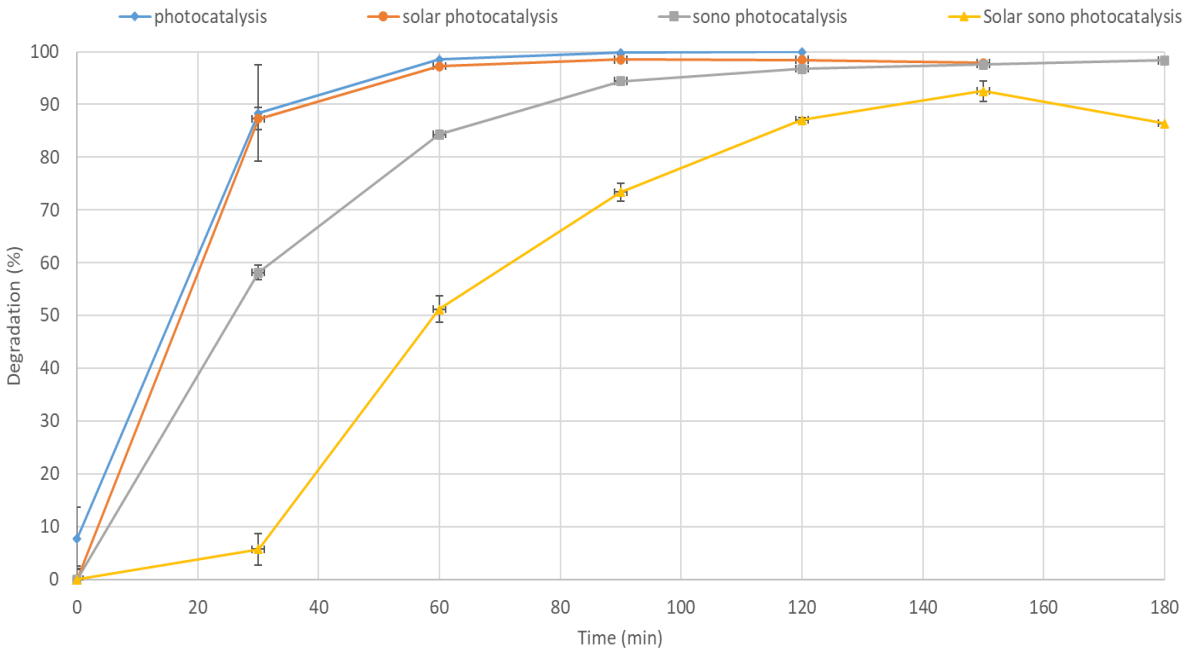

Figure 4.27. Comparison of Photocatalysis, Solar Photocatalysis, Sono-photocatalysis and Solar Sono photocatalysis for degradation of ATL

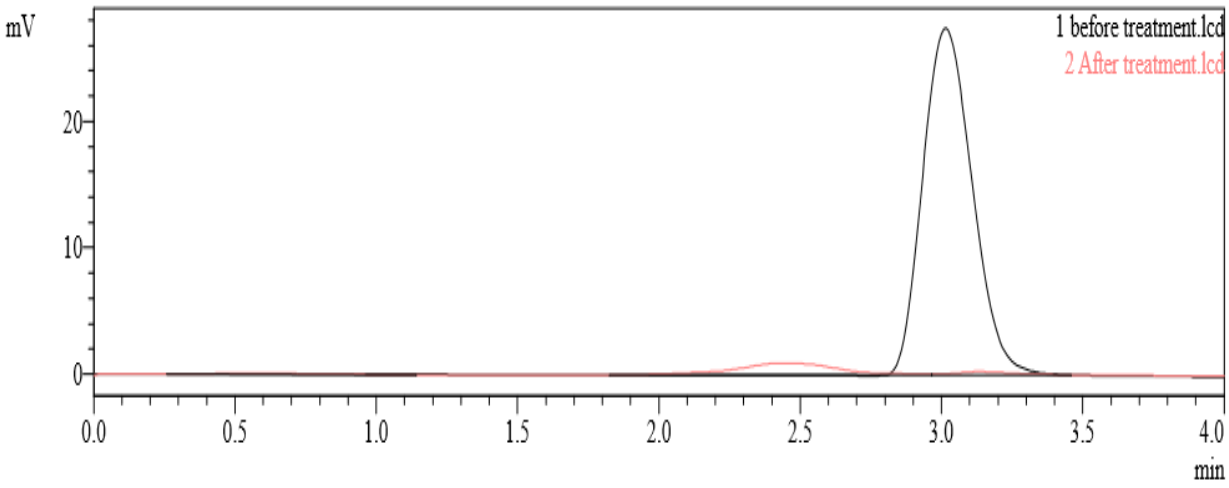

Figure 4.28. HPLC spectra for degradation of ATL by photocatalysis

Table 4.13. Comparison of photocatalysis and photocatalysis integrated processes for degradation of ATL

Process	Conditions	Time (min)	Degradation (%)
Photocatalysis	UV (365nm) ATL:25mg/L TiO_2: 600mg/L; pH: 3.0	120	100
Solar Photocatalysis	UV (Sunlight) ATL:25mg/L TiO_2: 600mg/L; pH: 3.0	90	98
Sono-photocatalysis	UV (365nm) Ultrasound: 40kHz ATL:25mg/L TiO_2: 600mg/L pH: 3.0	180	98
Solar Sono-photocatalysis	UV (Sunlight) Ultrasound: 40kHz ATL:25mg/L TiO_2: 600mg/L; pH: 3.0	150	92

4.6.2 Degradation of ATL using Fenton treatment

Fenton, photo-Fenton, Sono-Fenton, and Sono-photo-Fenton technologies were adopted in order to estimate the degradation of ATL and effects of various parameters on degradation. The concentration of various parameters such as initial ATL concentration, $FeSO_4$, and H_2O_2 was varied at pH 3 to study the variations in ATL degradation.

4.6.2.1 Effect of initial ATL concentration

The effect of initial ATL concentration on percent degradation of ATL was investigated by varying the concentration from 10 to 40mg/l. With increase in concentration of ATL, decrease in degradation was observed. Complete degradation of ATL was observed at 10mg/l of ATL concentration within 10min and 25min of reaction time while at higher concentration (40mg/l), minimum degradation of around 13% was observed.

4.6.2.2 Effect of $FeSO_4$

The concentration of $FeSO_4$ is the most significant parameter which primarily affects the degradation of ATL. To achieve the maximum degradation of ATL, concentration of $FeSO_4$ was varied from 5-50mg/l. Results from the study revealed that at lower concentration of 5mg/l, rate of degradation was lesser and around 45% degradation was achieved at 10mg/l and 300mg/l of ATL and H_2O_2 concentration, respectively. Complete degradation of ATL was observed at 27.5mg/l and 50mg/l of $FeSO_4$ concentration within 7min and 25min of reaction time, respectively. At lower concentration of $FeSO_4$ lesser $^{\bullet}OH$ radicals were generated for oxidation which leads to lower rate of degradation of ATL. At higher concentration of $FeSO_4$, rate of degradation was relatively decreased as Fe^{2+} ions generate scavenging effect of $^{\bullet}OH$ radicals. Romero et al., (2016) studied the degradation of β-blocker metoprolol using Fenton and Photo-Fenton by varying the concentration of Fe^{2+} from 1-10mg/l. At initial concentration of 50mg/l metoprolol, around 90% degradation was achieved.

4.6.2.3 Effect of H_2O_2 concentration

The effect of H_2O_2 concentration on degradation of ATL was studied by varying the concentration from 100-300mg/l. At H_2O_2 concentration of 100 and 300mg/l, degradation rate was quite higher and complete degradation was achieved at ATL concentration of 10mg/l, while at higher concentration of 500mg/l of H_2O_2, rate of degradation gets slower. This may be due to the fact that at higher concentration $HO^{\cdot}_2$ radicals were produced and scavenging effect of hydroxyl radicals occurs as shown in equation (4.12, 4.13,4.14)

$$H_2O_2 + {}^{\bullet}OH \rightarrow H_2O + HO_2{}^{\bullet} \quad \ldots\ldots 4.12$$

$$HO_2{}^{\bullet} + {}^{\bullet}OH \rightarrow H_2O + O_2 \quad \ldots\ldots 4.13$$

$$^{\bullet}OH + {}^{\bullet}OH \rightarrow H_2O_2 \quad \ldots\ldots 4.14$$

In a similar study, Veloutsou et al. (2014) varied H_2O_2 concentration at 52.5,100 and 5.0mg/l for ATL degradation using photo-Fenton and found 100mg/l as optimum concentration for degradation and mineralization of ATL.

The optimum condition for ATL degradation using BBD was achieved as initial ATL concentration 10mg/l, $FeSO_4$ 27.5mg/l and H_2O_2 100mg/l and the complete degradation was achieved at these concentrations within 7minutes of reaction time.

4.6.2.4 Statistical analysis: Validation of model

The percent degradation of ATL was considered as response in BBD and the independent variables were initial concentration of ATL (X_1), $FeSO_4$ (X_2) and H_2O_2 (X_3) with maximum and minimum levels as 10-40mg/l, 5-50mg/l and 100-500mg/l, respectively, as shown in Table 4.14. The effect of each variable on ATL degradation was represented in surface and contour plots as shown in Fig. 4.30. Fifteen (15) experimental runs were employed for BBD matrix and the results obtained from each factor are represented in **Table 4.14**. Actual values and the predicted values obtained from model for degradation of ATL are also depicted in **Table 4.14** and **Fig. 4.29**. In order to compute the effect of independent variable on percent degradation (Y) of ATL, the following polynomial equation (4.15) was obtained:

$$Y = -60.340 - 9.336X_1 + 33.653X_2 - 3.776X_3 + 12.630X_1X_1 - 12.102X_2X_2 + 6.005X_3X_3 + 4.297X_1X_2 - 4.780X_1X_3 + 3.617X_2X_3 \quad \ldots\ldots 4.15$$

The negative and positive sign marked before each term implies the synergistic and antagonistic effect of each parameter on degradation of ATL (Moosavi & Tavakoli, 2016). Analysis of variance (ANOVA) and several other factors such as correlation coefficient (R^2), F- value and adequate precision etc. were further explained the adequacy of the model (Khuri & Cornell, 1987). The higher F value 2.16 and the low probability value $P<0.05$ (95% confidence level) illustrated that the model is highly significant. The R^2 value indicates the suitability of the model in terms of predicting the values of response which can be explained by the experimental values and their interactions. The larger value of R^2 (97%) shows that the model is highly reliable. Furthermore, the quadratic terms X_1, X_2, X_3, X_4, and X_1^2, X_2^2, X_3^2, X_4^2 represents the significant positive and negative effect on Y respectively as indicated in **Table 4.15**.

Table 4.14. Box-Behnken Design matrix and response factor results for degradation of ATL

	X1	X2	X3	Degradation (%)	
Run	**ATL (mg/L)**	**$FeSO_4$(mg/L)**	**H_2O_2(mg/L)**	**Observed**	**Predicted**
1	40	27.5	100	79.34	68.63
2	10	50.0	300	100	99.55
3	10	27.5	100	100	96.86
4	40	27.5	500	67.51	70.64
5	25	50	500	98	87.73
6	25	27.5	300	60.51	60.34
7	25	50	100	84.48	88.05
8	10	5.0	300	47.98	40.84
9	25	27.5	300	60.51	60.34
10	10	27.5	500	69.05	79.75
11	25	5.0	500	16.77	13.19
12	40	50	300	82.35	89.48
13	25	27.5	300	60.51	60.34
14	25	5.0	100	17.72	27.98
15	40	5.0	300	13.14	13.58

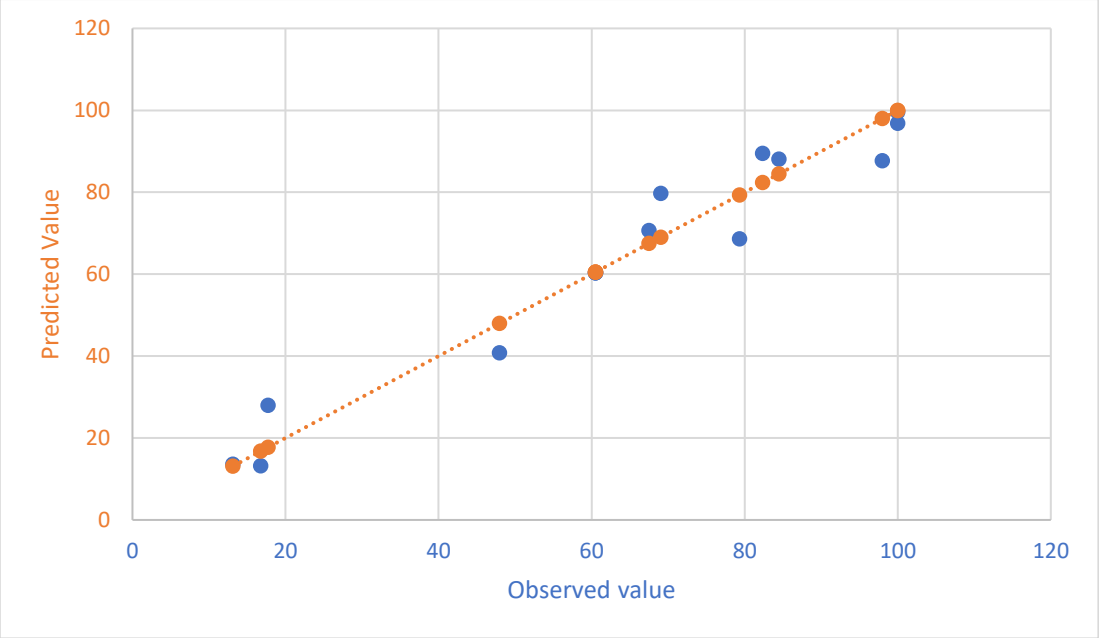

Figure 4.29. Relationship of predicted values and observed values for percent degradation of ATL

Table 4.15. Results of ANOVA-test for response percent degradation

Source	Coefficient	Degrees of freedom	F-ratio	P-value
Model	-60.340	9	2.16	0.205
X_1 (ATL)	-9.336	1	1.18	0.326
X_2 ($FeSO_4$)	33.653	1	15.37	0.011
X_3 (H_2O_2)	-3.776	1	0.19	0.678
X_1 X_1	12.630	1	1.00	0.363
X_2 X_2	-12.102	1	0.92	0.382
X_3 X_3	6.005	1	0.23	0.655
X_1 X_2	4.297	1	0.13	0.738
X_1 X_3	4.780	1	0.16	0.710
X_2 X_3	3.617	1	0.09	0.778

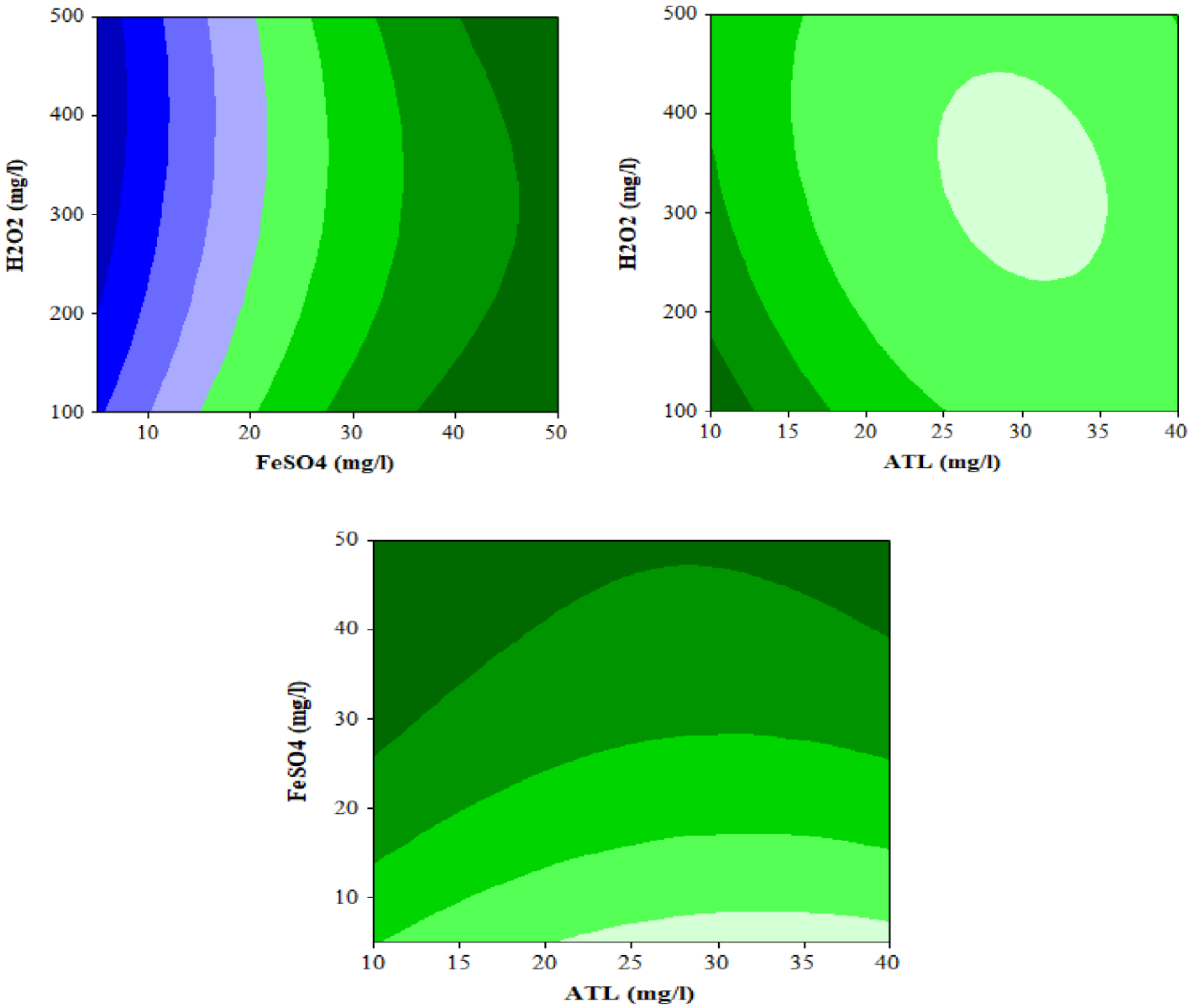

Figure 4.30. Response surface plots of percent degradation of Atenolol under different sets of conditions

4.6.2.5 Comparison of Fenton with integrated processes

Fenton reaction was compared with photo-Fenton, solar photo-Fenton, Sono-Fenton, Solar Sono-Fenton, Sono-photo-Fenton and Solar Sono-photo-Fenton at initial concentration of ATL 10mg/l, Fe^{2+} concentration 27.5 mg/l, H_2O_2 100 mg/l and pH 3.0. It was observed that at the same conditions, solar photo-Fenton and solar sono-photo-Fenton completely degrade the ATL within 3 minutes of reaction time while photo- Fenton and sono-photo-Fenton under artificial UV irradiation degrade the ATL in 3.5 minutes and 20 minutes, respectively, as shown

in **Fig. 4.31**. When the light was irradiated (solar or UV) during photo-Fenton reaction, reaction rate was faster as compared to Fenton reaction as more hydroxyl radicals were produced due to conversion of ferric ions to ferrous ions and ultimately reduced the degradation time of ATL degradation. The rate of degradation was also faster in sono-photo-Fenton combined with ultrasound, and UV light with Fenton decreases the particle size of catalyst *i.e.* Fe^{2+} due to which active sites for iron increases and leads to rapid rate of degradation. On the other hand, in case of solar sono-Fenton, complete degradation was achieved while in sono-Fenton around 90% degradation was achieved within 20 minutes **(Table 4.16)**. In sono-Fenton, ultrasonication and Fenton are coupled, so these two are responsible for generating $^{\bullet}OH$ radicals but both of these start competing for H_2O_2 which ultimately decreases the rate of reaction. It was investigated from HPLC results that during the reaction the formation of intermediates was negligible and degradation of ATL was around 90% **(Fig. 4.32)**.

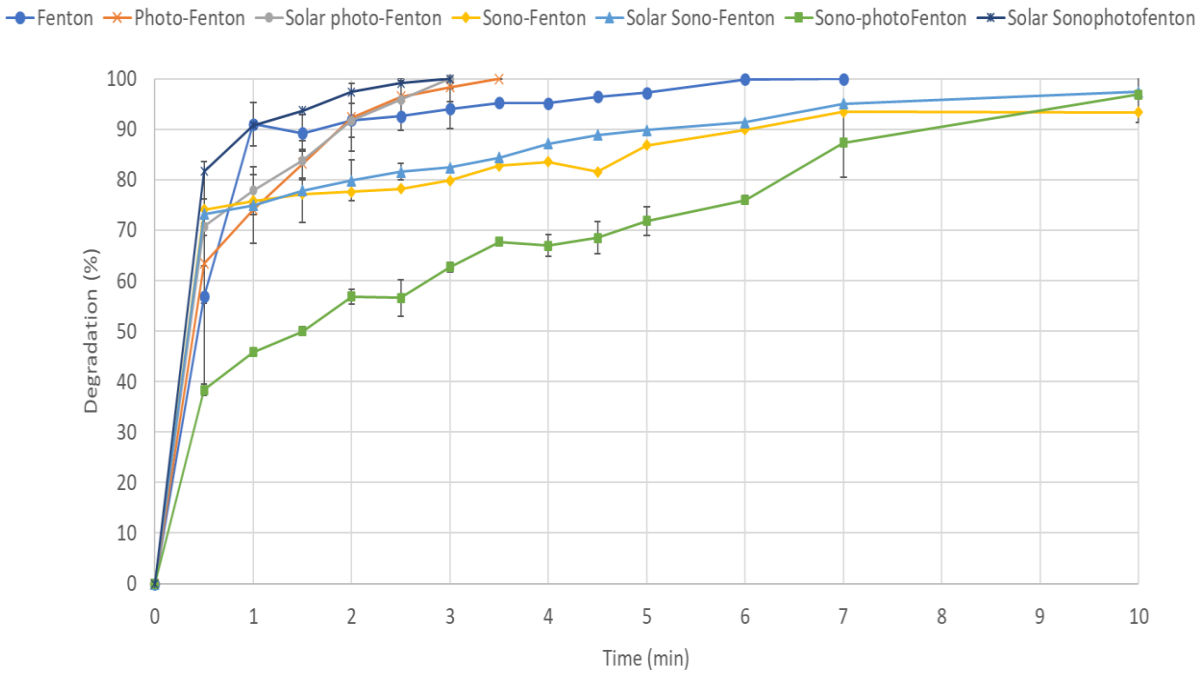

Figure 4.31. Comparison of Fenton, photo-Fenton, solar photo-Fenton, sono-Fenton, solar sono-Fenton and sono-photo-Fenton for complete degradation ATL

Table 4.16. Comparison of Fenton and Fenton integrated processes (ATL)

Processes	Conditions	Time (min)	Degradation (%)
Fenton	ATL:10mg/L Fe^{2+} - 27.5 mg/L H_2O_2 – 100 mg/L pH – 3.0	7	100
Photo-Fenton	UV (365nm) ATL:10mg/L Fe^{2+} - 27.5 mg/L H_2O_2 – 100 mg/L pH – 3.0	3.5	100
Solar photo-Fenton	UV (Sunlight) ATL:10mg/L Fe^{2+} - 27.5 mg/L H_2O_2 – 100mg/L pH – 3.0	3	100
Sono-Fenton	Ultrasound: 40kHz ATL: 10mg/L Fe^{2+} - 27.5 mg/L H_2O_2 – 100 mg/L pH – 3.0	7	93
Solar Sono-Fenton	Ultrasound: 40kHz ATL: 10mg/L Fe^{2+} - 27.5 mg/L H_2O_2 – 100 mg/L pH – 3.0	20	100
Sono-photo-Fenton	UV (365nm) Ultrasound: 40kHz ATL: 10mg/L Fe^{2+} - 27.5mg/L H_2O_2 – 100mg/L pH – 3.0	15	100
Solar Sono-photo-Fenton	UV (Sunlight) Ultrasound: 40kHz Fe^{2+} - 27.5mg/l H_2O_2 – 100mg/l pH – 3.0	3	100

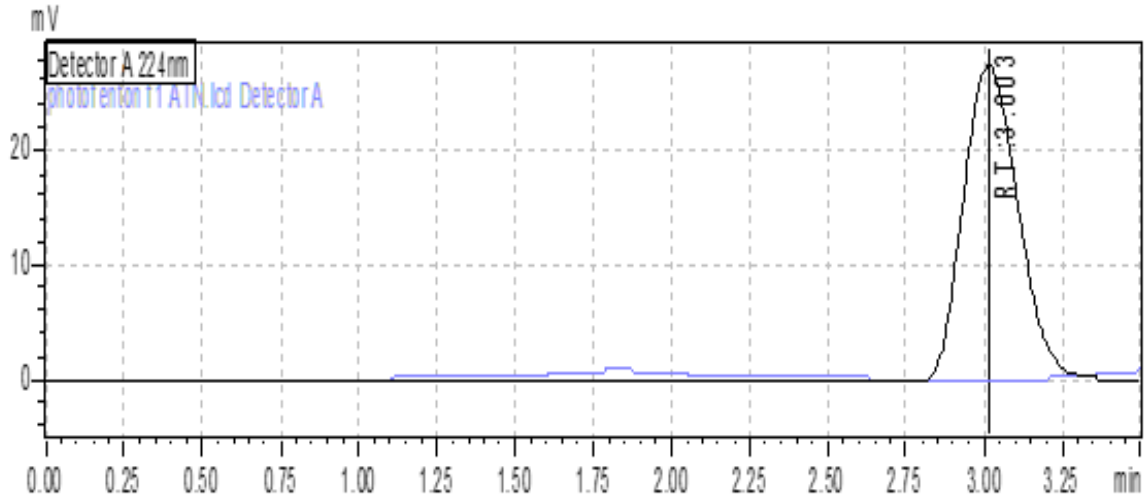

Figure 4.32. HPLC spectra for degradation of ATL with formation of no intermediates

4.7 Feasibility Analysis of different AOPs for treatment of pharmaceutical drugs

The efficiency of the processes used for the degradation amoxicillin and atenolol were compared with each other and it was concluded that sono-Fenton and Sono-photocatalysis are less efficient than other processes.

Table 4.17. Feasibility study of different AOPs

Process	Percent Degradation (%)	
	Amoxicillin	Atenolol
Fenton	100	100
Photo-Fenton	100	100
Solar photo-Fenton	100	100
Sono-Fenton	37	93
Sono-photo-Fenton	100	100
Solar Sono-photo-Fenton	100	100
Photocatalysis	95	100
Solar photocatalysis	90	98
Sono photocatalysis	90	98
Solar Sono-photocatalysis	95	92

Table 4.18. Advantages and Disadvantages of AOPs

Technologies	Advantages	Disadvantages
Photocatalysis	Cost-efficient, non-toxic, mass transfer limitation is absent, chemically stable and can be operated at ambient temperature	Separation of catalyst is required if it is present in form of slurry, requirement of UV light for surface activation
Fenton like processes	Fenton: Highly efficient, easy to operate and maintain, reaction time is less Photo-Fenton: leads to rapid mineralization, increase rate of reaction, reduce iron sludge production Electro-Fenton process: production of H_2O_2 is in-situ so risk of handling, storage and transportation can be avoided, continuously regenerate Fe^{2+} on cathode which decreases iron sludge production, Higher degradation efficiency	Fenton: generation of iron sludge, low pH is required Photo-Fenton: High operation cost, cost of UV-visible lamps Electro-Fenton process: low conductivity, low current density, H_2O_2 yield is low
Ultrasonication	Initiates reaction without external reagents, generates mass transfer effect at microscopic and macroscopic levels	Full scale application does not exist, oxidation is needed to improve the efficiency of the treatment which increases the cost

Considering the efficiency towards degradation Fenton treatment and its integrated methods were found to be more useful towards degradation of pharmaceutical drugs. On the other hand, the degradation rate and maximal degradation in photocatalysis is slightly less (95%) for AMX **(Fig. 4.17)**, but complete degradation of ATL was observed. A comparison of advantages and disadvantages **(Table 4.18)** of different treatment options may be made to finalize a treatment scheme for pharmaceutical drugs considering the availability of resources and other conditions. Finally, combination of two or more methods would also improve the rate kinetics, thereby helping in treatment of larger volumes of water lesser time.

CHAPTER 5
CONCLUSION AND RECOMMENDATION

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CONCLUSIONS AND RECOMMENDATION

5.1 CONCLUSIONS

Based on the results obtained in the present study, following conclusions are made.

I. Photocatalysis with TiO_2 (P 25) is a potential and effective method for degradation of AMX in pharmaceutical wastewater. Under the optimized set of conditions, photocatalysis amended with H_2O_2 and Ultrasonication (40kHz) can result in slightly enhanced rate of degradation, but the overall efficiency is reduced. Therefore, combination of photocatalysis process with H_2O_2 and Ultrasonication (40kHz) is not an effective method for degradation of AMX and ATL.

II. The rate of degradation for AMX and ATL is slightly enhanced when H_2O_2 and ultrasonication are used in combination with Fenton or photocatalysis, but the extra input of chemical and energy stands as added cost to treatment. So, addition of H_2O_2 and ultrasound may be avoided for degradation AMX and ATL, if the volume of wastewater to be treated is less.

III. Fenton's process is an effective tool for complete degradation of AMX and ATL. The integration of Fenton's process with light exposure *i.e.* solar (visible) and UV promotes enhanced rate of degradation. The integration of these methods may be taken up in pharmaceutical industries producing more volume of wastewater.

IV. Photo-Fenton (UV) process can be used as a sustainable option for degrading pharmaceutically active compounds, particularly AMX and ATL. Solar photocatalysis has also produced promising results, it may be regarded as sustainable, low-cost, viable, and efficient green technology for the treatment of residual antibiotics in wastewater.

V. Fenton's process is more effective than Photocatalytic treatment of Pharmaceutical wastewater because in Fenton process time for degradation of AMX and ATL is comparatively lesser than photocatalysis. Combining Fenton with ultrasound has an inhibitory effect since ultrasound and Fenton have inter-species competition for H_2O_2 which results in reduction of AMX and ATL degradation. Therefore, combination of Fenton with ultrasound for degradation of AMX and ATL may be avoided.

5.2 RECOMMENDATION

Based on the observations of the present study, following recommendations are made

I. Photocatalytic and Photo-Fenton treatment can be used for treatment of pharmaceutical wastewater, particularly for the degradation of AMX and ATL. These methods are recommended since no secondary metabolites are formed during treatment.

II. For complete removal of drugs, Photo-Fenton treatment is recommended. It is recommended for the industries producing larger volumes of wastewater since the rate treatment is high.

III. Industries producing more volume of wastewater should use combination of AOPs to reach higher rate of degradation/removal. The combination of techniques improves the rate of degradation it reduces the time of treatment.

IV. Combination of Ultrasonication with Fenton's treatment should be avoided, as these processes have inhibitory effect. Both the processes shows inter-species competition for H_2O_2 which ultimately results in reduction in process efficiency.

V. For smaller volumes of wastewater being produced, Solar Fenton's treatment may be used to save energy. Although the rate kinetics in solar Fenton is slow, but complete degradation ensures no formation of secondary metabolites and removal of ecological toxicity.

5.3 SCOPE FOR THE FUTURE WORK

The AOPs have been potentially effective for degradation of AMX and ATL, but their application for other pharmaceuticals drugs is a scope of further investigation. With advent of recent drug discovery and accelerated use of chemotherapeutic agents, antineoplastic drugs, and drugs with associated radioactivity (for treatment of thyroid related disorders), their environmental effects are yet to be explored. Degradation of such drugs may also be studied to further strengthen the comprehensive treatment of pharmaceutical waste. As per the present study, although ultrasound and Fenton's process exhibited inter-specific competition for production of $\cdot OH$ radicals, but application of higher frequencies (>40KHz) may result in improved degradation efficiency as observed for other persistent pollutants like dyes. A combination of conventional/biological and AOP treatment may be studied to design a sustainable treatment scheme for efficient removal of pharmaceutical from environment.

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LIST OF PUBLICATIONS

1. Verma M., Haritash A.K. (2020). **Photocatalytic degradation of Amoxicillin in pharmaceutical wastewater: A potential tool to manage residual antibiotics.** *Environmental Technology & Innovation (Elsevier)*-Accepted.

2. Verma M., Haritash A.K. (2020). **Review of advanced oxidation processes (AOPs) for treatment of pharmaceutical wastewater**. *Advances in Environmental Research.* 9(1),1-17.

3. Verma M., Haritash A.K. (2019) **Degradation of amoxicillin by Fenton and Fenton-integrated hybrid oxidation processes**. *Journal of Environmental Chemical Engineering.* 7, 102886.

4. Sharma A., Verma M., Haritash A.K. (2016) **Degradation of toxic azo dye (AO7) using Fenton's Process.** *Advances in Environmental Research*. 5(3), 189-200.

5. Deepika, Verma M., Shan V., Haritash A.K. (2016) **Degradation of acid yellow 36(AY36) dye using Fenton's Process**. *International Journal of Environmental Sciences.* 6(6), 1061-1067.

6. Sharma A., Verma M., Haritash A.K. (2015) **Photocatalytic degradation of Acid Orange 7 (AO7) dye using TiO_2.** *International Journal of Engineering Research & Technology*. 4 (3).

CURRICULUM VITAE

Name: Manisha Verma
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Education

S. No.	Exam/ Degree	Board/ University	Year	Percentage/ Division	Subject(s)
1	M.Tech.	Thapar University, Patiala, Punjab	2011	70	Environmental Science & Technology
2	M.Sc.	GJ University of Science & Technology, Hisar, Haryana	2009	82	Environmental Science
3	B.Sc.	MD University, Rohtak, Haryana	2007	60	Life Science (Botany, Zoology, Chemistry)

Teaching Experience: 03 Years

S. No.	Department/ Organization	Designation	Period	Class Taught
1	RIMT Institute of Engg. & Technology, Mandi Gobindgarh, Punjab	Assistant Professor	August 2011 To June 2014	B. Tech.

Research/Training Experience: 05 Years

S. No.	Department/ Organization	Designation	Period	Class Taught
1	Delhi Technological University, Delhi	Ph.D. scholar	July 2014 To June 2019 (05 Years)	B. Tech. (Environmental Studies)
2	NEERI, Nagpur	M. Tech. (Research Trainee)	January 2011 to June 2011 (06 months)	Research trainee

Seminars/ Conferences attended:

1. Verma M., Haritash A.K. (2019). Photo and Sono-photocatalytic degradation of Amoxicillin using Degussa P-25 TiO_2. *Sustainable technologies for environmental Management (STEM 2019)* was attended from March 25-26,2020 at Department of Environmental Engineering, Delhi Technological University, Delhi.

2. Two weeks' GIAN (Global Initiative of Academic Networks) (2018) Course on *Systems Thinking for Enhanced Water Security in Urban India* was attended from 3rd December to 15th December 2018 Department of Environmental Engineering, Delhi Technological University, Delhi.

3. Verma M., Haritash A.K. (2018). Degradation of Pharmaceutical Compounds using Advanced Oxidation Processes. *Go Green Summit 2018* was attended from March 23rd – 24th, 2018 at Manila, Philippines.

4. Verma M., Haritash A.K. (2017). Photocatalytic degradation of antibiotics in pharmaceutical wastewater. *Emerging Areas of Environmental Science & Engineering (EAESE-2017)* was attended from February 16-18, 2017 at Department of Environmental Science & Engineering, Guru Jambheshwar University of Science & Technology, Hisar, Haryana

5. Verma M., Sharma A., Deepika., Haritash A.K. (2016). Decolourisation of Acid Orange 7 by Fenton's process -optimisation and validation. *New Paradigm in Chemical Sciences: Synthetic and analytical Prespectives-2016*" was attended during 4th & 5th Feb., 2016 held at Punjabi University, Patiala, Punjab.

6. Two weeks' GIAN (Global Initiative of Academic Networks) (2016). Course on *Polluted Sites: Characterization and Remediation* was attended from 25th July to 5th August 2016 at IIT Bhubaneswar (Orissa).

7. Sharma A., Verma M., Haritash A.K. (2016). Enhanced Decolourisation of Acid Orange 7 using Fenton's process: validation by Response Surface Methodology. *Advanced Oxidation Processes, AOP 2016* was attended during 17-20th December, 2016 held at BITS Pilani Goa Campus, Goa.

8. Sharma A, Verma M, Haritash AK. (2015) Photocatalytic degradation of Acid Orange 7 dye using TiO_2. National seminar on Recent Advances in Civil and Environmental Engineering, Organised by BRCM College of Engineering & Technology, Bahl, Haryana (Nov. 28-29, 2015), pp 37-40.

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