WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.990
Volume 4, Issue 9, 565-575. Review Article ISSN 2277– 7105

REVIEW ON MANAGEMENT OF PHARMACEUTICAL WASTE WATER

Kalyan Kr Sarkar[2] and Tamal Mandal[1*]

[2]Research Scholar, Department of Chemical Engg, National Institute of Technology, Durgapur, West Bengal, 713209 –India.

[1]Professor, Department of Chemical Engg, National Institute of Technology, Durgapur, West Bengal, 713209 -India.

Article Received on
26 June 2015,

Revised on 16 July 2015,
Accepted on 10 Aug 2015

***Correspondence**
For Author
Tamal Mandal
Professor, Department of Chemical Engg, National Institute of Technology, Durgapur, West Bengal, 713209 -India.

ABSTRACT

Pharmaceutical (drugs) is a chemical used for prevention and treatment of human health and vet animal health. Pharmaceutical formulation is the preparation of various dosage forms such as tablets, capsules, liquids, parenteral, and creams and ointments etc. The pharmaceutical industry in India is the world's third-largest in terms of volume. The Indian pharmaceutical industry holds a market share of $14 billion in the United States. But the environmental impact of pharmaceuticals is largely speculative. Most pharmaceutical industry are manufacturing highly potent drug like cephalosporin, beta blocker agent, proton pump inhibitors, antibiotics, antidotes, contraceptive etc. which are the essentials medicine for human beings but may impact the aquatic environment that means the aquatic living beings. Waste discharged through pharmaceutical industries can contaminate water resources in the surrounding environment. As beside pharmaceutical chemicals in waterways have potentiality for effects on wildlife (Palace et al., 2002).Some pharmaceutical chemicals pass through the treatment plant in the drug manufacturing industry which are altered or unaltered and can enter rivers, lakes, living organisms, and groundwater. Pharmaceutical chemicals remain in the treatment plant's sludge, which is also having chance to enter in agricultural land as a fertilizer (Daughton and Ternes et al., 1999). This review outlines not only some of the problems encountered in assessing the risk from pharmaceutical which might enter the water cycle from human metabolic routes and industrial sources ,also the developed advance oxidation process which can be a alternate process of treatment beside to traditional.

KEYWORDS: Pharmaceuticals in environment; Waste water treatment; Advance oxidation process.

INTRODUCTION

The Pharmaceutical industry in India is the world's third-largest and second lead drug supplier to the USA market having market share of $14 billion. Most pharmaceutical companies operating in India, even the multinationals, employ Indians almost exclusively from the lowest ranks to high level management. Homegrown pharmaceuticals, like many other businesses in India, are often a mix of public and private enterprise. Indian companies are also starting to adapt their product development processes to the new environment. In the pharmaceutical industry various types of processes are involved to manufacture of pharmaceutical products. Due to the diversity of these processes, it provides a general set of waste minimization guidelines that would apply to all drugs manufacturing process (Y Askin et al., 2007). But the pharmaceuticals still are observed in the environment (Bendz et al., 2005) (Rechard et., 2007) alwhich may be the lead source from industries.Along with research and development, five methods are being used in the manufacturing of pharmaceuticals are considered:

1) Research and development.
2) Chemical synthesis.
3) Natural product extraction.
4) Formulation.
5) Quality testing and release.

Role and impact of Indian pharmaceutical industry on the environment and treatment strategy

The problem behind environmental impact from industry is loose of controls on Effluent Treatment Plant (ETP), and also casual approach towards ETP maintenance and Break downs, emissions, leakages, which leads water pollution. In the many of the factories storm water and drain water having their common outlets. The industry leaders are also intimating that the probable root cause is unskilled contract workers. And moreover the lack of training to these peoples. Another probable root cause is over capacity utilization of production schedules – system failure, leading to water pollution. Non standard use ETP material – in filtration, aeration is also a probable root cause of water contamination.

But today the pharmaceutical manufacturer association has taken initiative to make the ETP program more environments friendly. An interaction between plants, dialogues with local industrial for their problem has been initiated. They are also arranging workshops / seminars through associations to diffuse the gravity situations and joint forums to mitigate issues of hazardous waste processing to prevent mother nature. Association also helping to small scale industries through training and awareness for acquainting to Pollution /Environment controls. The main role by this group is expected through campaigning for hazardous waste generation by industry and their role as treatment.

Drug manufacturing plants having its own validated process flows like the chemical laboratory, microbiological laboratory, manufacturing laboratory, In the case of oral solid preparation which consist granulator for granulation vessel, fluidized bed dryer for drying process, Neo octagonal coater coating stage, Compression machine and in case of injectables preparation the process flow consist of solution preparation, filling, capping, sterilization etc. This all process stage having their own cleaning procedural technology and cleaning area. From all the area the waste water collecting pipe is connected with the centralized waste water treatment systems which will deliver the waste water into main collection tank. After treatment also there is a chance to impact or contaminate the surroundings environment and aquatic livings if any compounds among all pharmaceuticals passes in the environment. Mostly in the pharmaceutical manufacturing facility biological growth procedure is being followed as traditionally as waste water treatment. Where in equalization tank 24 hours is needed to be aerated and again another 24 hours is needed in aerobic zone for biological degradation of effluent to reducing the pollutant load. Nutrient is dosed in aerobic zone by adding the solution of Urea (2 kg Urea + 100 liters of water) and DAP (2 kg DAP+100 Liters) for growth of bacteria. And finally effluent is pass through activated carbon filter.

Estrogens in forms of pharmaceutical compounds are a group of steroid compounds that function as the primary female sex hormone. The pharmaceuticals like estrogen having robust favor effect on human life. Estrogen mainly responsible for adult changes in young ladies and secondary sexual characteristics. This is responsible for development of the vagina, uterus, and fallopian tubes and breast enlargement. This is available for oral, parenteral, transdermal, or topical administration. Two major uses of estrogens are as components of combination oral contraceptives and for menopausal hormone therapy. Even at low levels, estrogens can have a

feminization effect on male fish (Nash et al. 2004), and therefore may decrease the reproductive capacity of affected species.

On other hand antidepressants are designed to control or alter behaviors by inhibiting the uptake of key neurotransmitters such as serotonin, nor epinephrine, and dopamine. Once released into the environment. Most antidepressants are rapidly absorbed by oral administration. In order to their use in adult major depression syndrome other disorders that may or may not be related psychobiologically to the mood disorders are also been treated. Antidepressants have a growing role in other hyperactivity disorder in children and adults, Antidepressants tend to provide a more sustained and continuous improvement of the symptoms of hyperactivity disorder. Antidepressants also are leading choices in the treatment of severe anxiety disorders, including panic disorder with agoraphobia, generalized anxiety disorder, social phobia, and obsessive-compulsive disorder as well as for the common comorbidity of anxiety in depressive illness. Peptic ulcer and irritable bowel syndrome is a result sometimes of mental tension or depression, and antidepressant also prescribed to this type of patients.They can have similar or unforeseen effects on aquatic species and have been demonstrated to affect the spawning behavior of shellfish and delay fish and frog development (Holmes et al., 2003). They also have been observed to result in slower heart rates for the water flea Daphnia, which could indicate broader physiological effects.

Some pharmaceutical like anti-epileptics persist in the environment others are “pseudo-persistent”—they break down but are continually replaced because of widespread use. Propranolol, a non-specific beta adrenoreceptor blocker (β-blocker) is used to treat high blood pressure and heart disease (Angina pectoris) in human life. β -adrenoreceptor antagonists or β blockers are also frequently used drugs for the treatment of hypertension, glaucoma, angina pectoris, migraine and other disorders. Propranolol is lipophilic and readily cross the blood-brain barrier. Propranolol is the prototypical β -blocking drug. It has low and dose-dependent bioavailability. A long-acting form of propranolol is available that means prolonged absorption of the drug may occur over a 24-hour period. Propranolol, a non-selective β-blocker present in sewage effluents, affects heart rate in rainbow trout. Several β blockers including propranolol, metoprolol and atenolol have been found in the aquatic environment (Larsson et al., 2006). And its toxicity to the environment is also established (Huggett et al., 2002).

Some of researchers have found that chronic effect to low levels of pharmaceuticals within the same range of concentrations as has been observed in some cases and can have significant effects on aquatic animals including fish (Nash et al., 2004) . Some of researchers believes that small amount or little amount pharmaceuticals present in environment can also effect significantly to the living beings, Now in current days, the greatest concern regarding pharmaceutical compounds in the environment is their potential effects on small aquatic organisms as these organisms have short lifecycles, which can be a potential effect on their population generation. Several drugs with lower than the concentrations known to exert effects on humans. This makes direct human toxicity seem unlikely but having the greater chances of long-term effects.

PHARMACOENVIRONMENTOLOGY

According to World Health Organization and United States Food and Drugs Administration, Pharmacovigilance activities are done to monitor detection, assessment, understanding and prevention of any obnoxious adverse reactions to drugs at therapeutic concentration on animal and human beings. However, there is also a growing focus among researcher about the impact of drugs on environment and surroundings. As drugs having potentiality to impact aquatic living being if they are being entered in small amount The existing term 'Ecopharmacology' is too broad and which is dealing with the drugs impact on eco system (Kummerer et al., 2006) not even defined in a clear manner. The term 'Pharmacoenvironmentology' seeks to deal with the environmental impact of drugs given to humans and animals at therapeutic doses. Literature review reveals that, there is lot of example like anticancer, Beta blocker found. We found also example that a animal pharmaceuticals diaclofenac sodium cause death of aquatic living organisms.

ECOPHARMACOVIGILANCE

This is the science and activities associated with the detection, evaluation, understanding and prevention of adverse effects of pharmaceuticals in the environment. This is close to the WHO definition of pharmacovigilance, the science aiming to capture any adverse effects of pharmaceuticals in humans after use.

From the above discussion it is proved that after the several traditional treatments by industry the drugs are available in the aquatic environment and pharmaceuticals which are excoriated from human body may also cause the pharmaceutical toxic substance presence in environment and this all are well established with many of researchers (Rechard et al.,2007)

(Okas et al.2004) (Andreozzi et al., 2003) . Here we are on process to develop coupled methodology to enhance technology for treatment of pharmaceutical waste water which may be also profitable for drug makers.The drugs which is disturbing the eco system balance is now mandatory to get pass the screening in clinical trail before its commercialization. Today FDA is too concern about the side effect to the environment from the pharmaceuticals. And this test is mandatory and FDA having a cutoff limit already. And FDA expected that the pharma company should expect and have some risk assessment of their product which is having chance to impact the nature.

ADVANCE OXIDATION PROCESS (AOP) APPLICATIONS IN PHARMACEUTICAL WASTE MANAGEMENT

Various studies have confirmed the potential of AOPs for removing pharmaceuticals (Huber et al., 2003). It has been proven that oxidation reactions have initially been used to additive rather than suppliment conventional systems and to enhance the treatment of refractory organic pollutants. (Khetan and Collins, 2007) demonstrated that AOP technology was also being implemented the management of pharmaceuticals waste water. It is stated that AOPs are mainly production of free radicals, in particular the hydroxyl radical and initiate the conversion of pollutants to less harmful and more degradable elements (Ikehata et al., 2006). Mainly fenton chemistry involves reactions of hydrogen peroxide in the presence of iron to generate hydroxyl radicals (Carey et al.; 1992). In the year 2002 (Ravina et al., 2002) it was invented and reported that ultraviolet light enhances this generation by the photo reduction of Fe (III) to Fe (II). Since iron is abundant and non-toxic, Photo-Fenton reactions have been used for the degradation. So that Fenton reactions and photo phenton reactions are a viable option for pharmaceutical wastewater treatment. Complete degradation of diclofenac via photo-Fenton reactions in a photo reactor took approximately 50 min (Ravina et al., 2002). In another study it has been reported that effect of fenton action is depend on perfect ration of H_2O_2 and Fe^{2+} (Dilek et al.,2006). So, AOP have proved effective for the treatment of industrial wastewater. In a study fenton and fenton-like reactions were compared for both dark and photo-assisted reactions (Arslan-Alaton and Dogruel, et.al. 2004). Penicillin was completely removed after 40 min of advanced oxidation with Fe^{2+}/H_2O_2 at pH 3. Higher COD and Total organic carbon (TOC) removals were obtained with dark Fe^{2+}/H_2O_2 at pH 3 compared with dark Fenton-like Fe^{3+}/H_2O_2 (Arslan-Alaton and Dogruel et.al., 2004). On the other hand, the strong dependence on the aqueous solution pH and on the concentrations of hydrogen peroxide and ferric / ferrous ions and the disposal of the iron sludge are factors

which need to be taken into consideration (Shemer et al., 2006). One possibility is the partial use of Fenton reactions to produce a non-toxic and biodegradable intermediate which could then be treated in an inexpensive biological step to achieve complete degradation with less sludge (Munoz et al., 2006). Advance oxidation treatment also works with combination of biotreatment effectively on combined industrial wastewater treatment (Mandal et al., 2009). It is also been demonstrated that in the treatment of leather industry wastewater by aerobic biological and fenton oxidation process there is more biodegrability of pollutant load and having less sludge.(Mandal et al., 2010). The UV Fenton treatment was firstly observed by its H.J.H.Fenton in 1894. It is another type of advanced oxidation processes (AOPs) that nowadays it is having more importance in wastewater treatments across the industries. It is consist of hydrogen peroxide and a ferric salt which is adding in wastewater. The waste water sample should be at acidic pH. To produce hydroxyl radicals that degrades the organic substances (Barbeni et al., 1987). UV light in photo-Fenton treatment is producing more irradiation to make that faster to produce more radicals (Bozzi et al., 2003;). Ozonation treatment is a another popular way for treating waste water. Ozone is a very strong oxidizing agent and having highest thermodynamic oxidation potential (Glaze et al., 1987; Hoigne et.al., 1988) in the ozonation treatment the sample is need to be applied with ozone stream in order to minimizing pollutants or degrades the organic substances present there.

For pharmaceutical industrial waste, this path way can be used for better economic ,less sludge generation and environmentally safe process.

Table: 1

Author	Year	Type of pharmaceutical waste	% COD removal	Remarks
Huseyin Tekin et al	2006	Antiseptic gargle and an antiseptic liquid soap formulated	98	Very good in COD reduction
Merih € O Otker et al	2002	Antibiotics	74	Average in COD reduction
T.Mandal et al	2014	Betablocker	95	Very good in COD reduction
M S Mukhopadhyay	2013	Bulk Drug	98.2	Very good in COD reduction
Sayyed Hussain et al	2011	Atenolol	66	Not good in COD reduction
Irina Epold et al	2012	Diclofenac	60	Not so good in COD reduction
Antoni S Ferrer et al	2003	Mixed pharmaceuticals	90	Good in COD reduction

CONCLUSION

Pharmacologists and envioronmentologist having the particular expertise may be made a compulsory component of impact assessment and effectiveness checks of drug safety. We need to monitor the effects of drugs not only as a good health practice, but also to safeguard our environment. And will establish a robust management technology for treatment of pharmaceuticals wastewater which will be industries / business friendly by using AOP and its moderated hybrid revolution.

REFERENCES

1. D.G. Joakim Larsson et.al, Is heart rate in fish a sensitive indicator to evaluate acute effects of β-blockers in surface water? Environmental Toxicology and Pharmacology., 2006; xxx: xxx–xxx.
2. Yalcin Askin Oktem, Orhan Ince, Paul Sallis, Tom Donnelly, Bahar Kasapgil Ince "Anaerobic treatment of a chemical synthesis-based pharmaceutical wastewater in a hybrid upflow anaerobic sludge blanket reactor" Bioresource Technology., 2007; 99: 1089–1096.
3. Barbara Bianco, Ida De Michelis, Francesco Vegliò ,Fenton treatment of complex industrial wastewater: Optimization of process conditions by surface response method,Journal of Hazardous Materials., 2011; 186: 1733–1738.
4. Bendz, D., Paxeus, N., Ginn, T.R., Loge, F.J. Occurrence and fate of pharmaceutically active compounds in the environment, a case study: H¨oje River in Sweden. J. Hazard. Mater., 2005; 122: 195– 204.
5. D.B.Huggett, Toxicity of select beta adrenergic receptor-blocking pharmaceuticals (β-Blockers) on aquatic organisms, Arch. Environ. Contam. Toxicol, 2002; 43: 229-235.
6. Richard Williams T, Cook Jon C: Exposure to Pharmaceuticals Present in the Environment. Drug Information Journal., 2007; 41(2): 133-141.
7. Rahman SZ, Khan RA: Environmental Pharmacology – A New Discipline (Editorial). Indian J Pharmacol., 2006; 34(4): 1-2.
8. Kummerer Klaus, Velo Giampaolo: Ecopharmacology: A New Topic of Importance in Pharmacovigilance. Drug Safety., 2006: 29(5): 371-373.
9. Oaks JL, Gilbert M, Virani MZ, Watson RT, Meteyer CU, Rideout B, Shivaprasad HL, Ahmed S, Chaudhry MJI, Arshad M, Mahmood S, Ali A, Khan AA: Diclofenac residues as a cause of population decline of White-backed Vultures in Pakistan. Nature., 2004; 427: 630-633.

10. Andreozzi, R., Marotta, R., Paxeus, N. Pharmaceuticals in STP effluents and their solarphotodegradation in aquatic environment. Chemosphere., 2003; 50: 1319–1330.
11. Jelena Radjenovic,1 Mira Petrovic,1,2 and Damiá Barceló1. Analysis of pharmaceuticals in wastewater and removal using a membrane bioreactor. Anal Bioanal Chem., 2007; 387(4): 1365–1377.
12. Akmehmet Balcioğlu I, Otker M. Treatment of pharmaceutical wastewater containing antibiotics by O3 and O3/H2O2 processes.., 2003; 50(1): 85-95.
13. Sayyed Hussain a, Shahid Shaikh a, Mazahar Farooqui b.COD reduction of waste water streams of active pharmaceutical ingredient – Atenolol manufacturing unit by advanced oxidation-Fenton process.Journal of Saudi Chemical Society., 2013; 17: 199–202.
14. Irina Epold, Niina Dulova, Marina Trapido. Degradation of diclofenac in aqueous solution by homogeneous and heterogeneous photolysis. Journal of Environmental Engineering & Ecological Science., 2012: 2050-1323.
15. H. Tekin, et al., Use of Fenton oxidation to improve the biodegradability of a pharmaceutical wastewater, J. Hazard. Mater., 2006; B136: 258–265.
16. Mriganka sekhar mukhopadhyay. Treatability study of effluent from bulk drug (calsium d-secharet) industry using aerobic biological treatment. Issue 3, Vol.1 , International journal of emerging trends in engineering and development, January 2013 Page 264.
17. Barbeni, M., C.Minero, E. Pelezzitti, E. Borgarrello, and N. Serpone, ‘‘Chemical Degradation of Chlorophenols with Fenton’s Reagent,’’ Chemosphere., 1987; 16: 2225–2237.
18. Bozzi, A., T. Yuranova, E. Mielczarski, J. Mielczarski, P. A. Buffat, P. Lais, and J. Kiwi, ‘‘Superior Biodegradability Mediated by Immobilized Fe-fabrics of Wastewaters. Compared to Fenton Homogeneous Reactions,’’ Appli.Catal. B: Environ., 2003; 42: 289–303.
19. Glaze, W. H., J.-W. Kang, and D. H. Chaplin, ‘‘The Chemistry of Water Treatment Processes Involving Ozone, Hydrogen Peroxide and Ultraviolet Radiation,’’ Ozone Sci. Eng., 1987; 9: 335–352.
20. Hoigne´ , J. ‘‘The Chemistry of Ozone in Water,’’ Process Technologies for Water Treatment. Plenum Publishing Corporation .1988.
21. Palace V, Evans R, Wautier K, Vandenbyllardt L, Vandersteen W, Kidd K. Induction of vitellogenin and histological effects in wild fathead minnows from a lake experimentally treated with the synthetic estrogen, ethynylestradiol. Water Qual Res J Can., 2002; 37: 637 – 50.

22. Ternes TA, Kreckel P, Mueller J. Behaviour and occurrence of estrogens in municipal sewage treatment plants — II. Aerobic batch experiments with activated sludge. Sci Total Environ., 1999; 225: 91 – 9.
23. Daughton CG; Ternes TA "Pharmaceuticals and Personal Care Products in the Environment: Agents of Subtle Change?" Environmental Health Perspectives., 1999; 107(suppl 6): 907-938.
24. Nash,J.P., kime, D.E., van der Ven, L.T.,M., Wester, P.W., Brion F., Maack,G., Stahlschmidt-Allner, P., Tyler, C.R. Long term exposure to environmental concentrations of the pharmaceutical ethynylestradiol causes reproductive failure in fish. Environmental Health Perspectives., 2004; 112 (17): 1725- 1733.
25. Huber JA, Butterfield DA & Baross JA. Bacterial diversity in a subseafloor habitat following a deep-sea volcanic eruption. FEMS Microbiol Ecol., 2003; 43: 393–409.
26. Khetan, S.K. & Collins, T.J., Human pharmaceuticals in the aquatic environment: A challenge to Green Chemistry. Chemical Reviews., 2007; 107: 2319 – 2364.
27. Ikehata, K.; Naghashkar, N. J.; El-Din, M. G. Degradation of aqueous pharmaceuticals by ozonation and advanced oxidation processes: A review. Ozone Sci. Eng., 2006; 2(6): 353-414.
28. Carey J.R., Liedo P., Orozdo D., Vaupel J. W. Slowing of mortality rates at older ages in large medfly cohorts., 1992; 258: 447-461 .
29. Arslan-Alaton I, Dogruel S. Pre-treatment of penicillin formulation effluent by advanced oxidation processes. J Hazard Mater., 2004: 9; 112(1-2): 105-13.
30. İ. Gulkaya, G.A. Surucu, F.B. Dilek, Importance of H2O2/Fe2+ ratio in Fenton's treatment of a carpet dyeing wastewater, J. Hazard. Mater., 2006; 136: 763–769.
31. Shemer I, Holmgren C, Min R, Fulop L, Zilberter M, Sousa KM, et al. Non-fibrillar beta-amyloid abates spike-timing-dependent synaptic potentiation at excitatory synapses in layer 2/3 of the neocortex by targeting postsynaptic AMPA receptors. Eur J Neurosci., 2006; 23: 2035–47
32. Munoz, J.L., F. Garca-Molina, R. Varon, J.N. Rodriguez-Lopez, F. Garca-Canovas and J. Tudela. Calculating molar absorptivities for quinones: Application to the measurement of tyrosinase activity. Anal. Biochem., 2006; 351: 128-138.
33. T.Mandal et al, Advanced oxidation process and biotreatment: Their roles in combined industrial waste water treatment, Desalination., 2010; 250: 87–94.
34. T.Mandal et al, Treatment of leather industry waste water by aerobic biological and Fenton oxidation process, Journal of Hazardous Materials, 2010; 180: 204–211.

35. Ravina CG, Chang Cl, Tsakraklides GP, McDermott JP, Vega JM, Leustek T, Gotor C, Davies J Transcriptional and post transcriptional control of cysteine bio-synthesis in Chlamydomonas reinhardtii. Plant physiol., 2002; 130: 2076 -2084.
36. S.F. Kang, H.M. Chang, Coagulation of textile secondary effluents with Fenton's reagent, Water Sci. Technol., 1997; 36: 215–222.
37. APHA, Standard Methods for the Examination of Water and Waste water20th ed, Works Association/Water Environment Federation, Washington, DC, USA, 1995.
38. Fent, K., Weston, A.A., Caminada, D. Ecotoxicology of human pharmaceuticals. Aquat. Toxicol., 2006; 76: 122-159.
39. Suman Raj, D.; Anjaneyulu, Y., Evaluation of biokinetic parameters for pharmaceutical wastewaters using aerobic oxidation integrated with chemical treatment. Process Biochem., 2005; 40(1): 165-175.
40. Tamal Mandal, Kalyan Kr Sarkar. Cost saving treatment management of Propranolol HCl (Pharmaceutical) manufacturing waste water by fenton oxidation process. J Adv Pharm Res Biosci., 2014; 2(2): 12-15.