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Review Paper

A review on biodegradation of pharmaceuticals through microorganisms

Neha Kamal*, Alok Sinha and Vipin Kumar
Dept. of Environ. Sci. and Engineering, Indian Institute of Technology (IIT) Indian School of Mines (ISM), Dhanbad - 826004, Jharkhand, India
nehakamal9@gmail.com

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Abstract

Pharmaceuticals are one of the most critical evolving contaminants. The highest source of the pharmaceuticals contamination is the hospitals, household and pharmaceuticals manufactures. Numerous methods for example physico-chemical and biological methods have been employed in the degradation of pharmaceuticals. As physico-chemical methods are expensive, biological methods- thorough microorganisms are extensively used. A better understanding of the mechanism of biodegradation has a high ecological significance that depends on the indigenous microorganisms to transform or mineralize the organic contaminants. The present review gives a short discussion on the role of microorganisms in degradation of pharmaceuticals.

Keywords: Biodegradation, Microorganisms, Pharmaceuticals.

Introduction

The significance of the pharmaceutical industry has continuously improved over the last 50 years replicating the increasing demand for pharmaceuticals. Finally, these drugs are either evacuated by human, or simply prepared of, and end up in the environment. Hence, the growth into the environment of pharmaceuticals is currently accepted as a serious problem[1]. Pharmaceutical have been widely used in many fields such as medicine, industry, aquaculture and people's everyday life they are becoming abundant in the environments due to their wide applications and poor removal by the conventional biological wastewater treatment plants. They can be classified into several classes based on their various purposes[2]. The specific classes, corresponding purposes and main properties of pharmaceuticals were listed in Table-1. Pharmaceuticals have been received increasing attention since 2000s. The worldwide production of Pharmaceuticals was over $1x10^6$ tons in 1993[3]. In 2003, the annual production of penicillin was 28,000 tons amounting 60% of the world total consumption of antibiotics[4]. The pharmaceuticals can be introduced into the environment by direct and indirect pathways. The way of Pharmaceuticals entering to the environment was reviewed by Mompelat et al[5]. According to literatures, Pharmaceuticals can enter the surface water through directly discharging into the surface water by industries, hospitals, households and wastewater treatment plants and through land runoff in case of bio solids spread on agricultural land, which can reach the groundwater by leaching or bank filtration. Within the surface water compartment, sediment can adsorb the Pharmaceuticals because it has a variety of binding sites[6]. Soil can be also one of the sink for Pharmaceuticals. Pharmaceuticals can pass into the soil by the irrigation with the treated or untreated wastewater containing Pharmaceuticals. For some Pharmaceuticals, they can transfer to soil by atmospheric wet deposition[7]. Many studies have exposed that Pharmaceuticals occurred in the surface water with the range of concentration from ng/l to mg/l [18-13]. In the ground water at level of concentration ng/l to mg/l [14-16], in sediment with the concentration reaching mg/kg and in soil achieving mg/kg[17-18]. The main aim of this paper is to review the current knowledge on Biodegradation of Pharmaceuticals through Microorganism.

Source and persistence of pharmaceuticals

The main sources of pharmaceutical removal into the environment is through waste water treatment plant and sewage treatment plants (STPs). The existence of pharmaceuticals in wastewater treatment plants had been reported in different countries all over the world, generally in the levels of ng $L^{-1}$to μg L^{-1}, such as USA[19], United Kingdom[20], Spain[21], Finland[22], and Japan[23]. According to literatures also reveal that the removal efficiency of pharmaceuticals by the wastewater treatment procedures (flocculation, sedimentation, and active sludge treatment) is restricted[24-27].

After discharging from STPs, pharmaceuticals in sewage would cause successive contamination to the getting water bodies. For their chemical properties, the fraction which enters into the atmospheric environment will be limited. Their circulation will primarily occur in the aquatic environment. Pharmaceuticals may also be adsorbed into the active sludge in STPs and then introduced into the environment through sludge land soil and water application[2]. As a group of novel emerging contaminants, Pharmaceuticals shows different properties with the conventional persistent organic pollutants their sources may

have been banned or limited. The input pharmaceuticals with STPs as the main source of pharmaceuticals contamination in environment, resulting in a steady-state concentration in aquatic systems, which has been called as "pseudo-persistent"[3]. Persistent disclosure by pharmaceuticals even at low concentration levels can be important.

Table-1: The classification, functions and main properties of pharmaceuticals[59].

Classification of pharmaceuticals	Functions	Representatives frequently detected	Molecular weight	Log *Kow*
Antibiotics	Kill bacteria	Sulfamethoxazole Trimethoprim Amoxicillin Erythromycin Ofloxacin Ciprofloxacin	253.3 290.3 365.4 733.9 361.4 331.3	0.89 0.91 0.87 3.06 -0.39 0.28
Lipid regulators	Regulation of triglycerides and cholesterol in blood	Clofibrate Benzafibrate Clorfibric acid Gemfibrozil Simvastatin Furosemide	242.7 361.8 214.6 250.3 418.6 330.7	3.02 3.61 2.88 4.77 4.68 1.51
Nonsteroidal anti-inflammatory drugs	Reduce pain and inflammation	Ibuprofen Diclofenac Acetaminophen Aspirin Indomethacin Naproxen	206.3 296.1 151.2 180.2 357.8 230.3	3.97 4.5 0.46 1.19 4.27 3.18
Beta-blockers	Inhibit the hormone adrenalin and the neurotransmitter noradrenalin	Atenolol Metoprolol Nadolol Pindolol Acebutolol	266.3 267.4 309.4 248.3 336.4	0.16 9.7 -0.6 1.75 1.71
Antidepressants	Improve the physical disorders	Diazepam Doxepin Imipramine Amitriptyline Fluxetine	284.7 279.4 280.4 277.4 309.3	3.08 3.84 4.28 4.81 3.96
Anticonvulsants	Treat mood disorders	Carbamazepine Primidone Dilantin Phenobarbital Gabapentin	236.3 218.3 252.3 232.2 171.2	13.9 1.12 2.47 1.47 -1.1
Antidepressants	Improve the physical disorders	Diazepam Doxepin Imipramine Amitriptyline Fluxetine	284.7 279.4 280.4 277.4 309.3	3.08 3.84 4.28 4.81 3.96
Antineoplastics	Control or kill neoplastic cells	Epirubicin Ifosfamide Methotrexate Tamoxifen Cyclophosphamide	543.5 261.1 454.4 371.5 261.1	1.85 0.86 -1.28 6.3 0.73

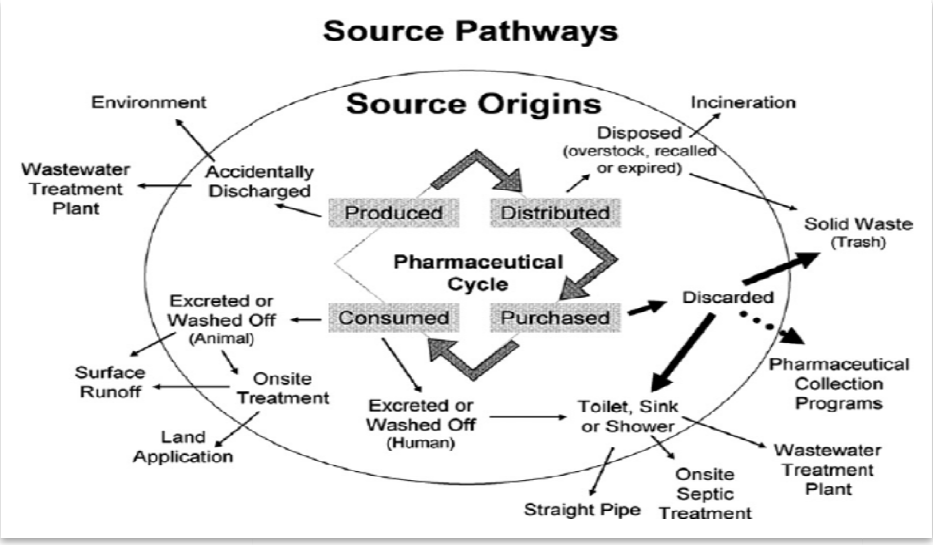

Figure-1: Exposure pathways of pharmaceuticals in the environment[28].

Removal of pharmaceuticals by biodegradation processes

Biodegradation (degradation through micobes) is the main subtraction mechanism for organic pollutants in the environment, which has many benefits such as low cost and mild operational situations. Microorganisms can remove the pollutants by using for metabolic functions and in some cases different microorganisms can cooperate together to remove the pollutants.

Pure cultures: Pure cultures of microorganisms isolated from activated sludge, wastewater, soil or sediment can be used to remove the repeatedly identified pharmaceuticals, such as carbamazepine[29,30], sulfamethoxazole[31,32], iopromide[33], ibuprofen[34,35], paracetamol[36,37], diclofenac[38] and triclosan[39,40]. Some pure cultures isolated from the activated sludge and also abilityto reduce a wide-range of pharmaceuticals. For example, *Achromobacter denitrificans* degrade the sulfamethoxazole as well as degrade the other sulfonamides[32]. Several pure cultures use as sole carbon and energy source, through different degradation mechanism[34-36]. For instance, *Delftia tsuruhatensis, Pseudomonas aeruginosa* and *Stenotrophomonas* can degrade paracetamol. For the specific pharmaceuticals, pure cultures use as carbon and energy source. In this situation, other substrates have to be supplied to provide the carbon and energy for their metabolic functions. For example, carbamazepine has stable structure resulting in poor biodegradability. But two unknown pure cultures, *basidiomycete*[29] and *Streptomyces* MIUG[30] can degrade the carbamazepine in the presence of glucose. In carbamazepine. According to Liu et al[33] iopromide drugs only degraded with the extra substrate. *Pseudomonas sp. I-24* strain proved that it has capacity to remove iopromide with starch use as primary substrate. The enzyme induction of the microorganisms is important point for biodegradation of pharmaceuticals[39]. The biodegradation of pharmaceuticals depends on whether microorganism can produce the specific enzyme to decompose them. For example, triclosan can induce *Nitrosomonas europaea* to produce ammonia monooxygenase, which can degradetriclosan[40]. Some pharmaceuticals such as tetracycline, trimethoprim and ciprofloxacin, they cannot induce microorganisms to produce the specific enzyme which leads to their poor biodegradability.

Mixed cultures: Mixed cultures are easier degrading the pharmaceuticals as compared to pure culture because in some cases it is too difficult to grow the pure culture. According to literatures, only one study has been showed to investigate the removal of pharmaceuticals by mixed culture[56]. Mixed culture also has capacity to remove the pharmaceuticals. In a mixed media, the mixed culture of ammonia oxidizing and heterotrophic bacteria has been demonstrated to be capable of enhancing the removal of the 17a-ethinylestradiol[56]. In fact, the most commonly used biological treatment process activated sludge-in the WWTPs, depends on the synergy effect of mixed culture to remove the Pharmaceuticals. In some cases activated sludge exhibits low removal capacity to the Pharmaceuticals. Thus, steps have been use to improve the removal of Pharmaceuticals by the activated sludge. Enhanced removal of Pharmaceuticals by adding mixed culture into the activated sludge has been reported[40]. The mixed culture has been showed to have higher microbial degradation rate in removing the mixed pharmaceuticals compared to removing specific pharmaceuticals[57].

This might be due to the reason that some of Pharmaceuticals can be used as carbon and energy source by mixed culture, and to further support the decomposition of other Pharmaceuticals. Established on the results achieved in the previous studies, it can be determined that mixed culture could be a potential option for enhancing the removal of Pharmaceuticals.

Table-2: Pharmaceuticals degrading microbial strain.

Compounds	Strains	Substrates	References
Hormone Estriol	*Novosphingobium tardaugens ARI-1*	Acetone	41
	Rhodococcus equi/Rhodococcus zopfii	-	42
17b-Estradiol	*Stenotrophomonas maltophilia strain ZL1*	-	43
	Dyella spp. strain	-	44
	Sphingomonas strain KC8	-	46
	Rhodococcus equi/ Rhodococcus zopfii	-	42
	Novosphingobium tardaugens ARI-1	Acetone	41
Antibiotics Sulfamethoxazolea	*Achromobacter denitrificans PR1*	-	32
Ofloxacin	*Labrys portucalensis F11*	Acetate	46
Ciprofloxacin	*Labrys portucalensis F11*	Acetate	46
Tylosin	*Citrobacter amalonaticus*	-	47-48
Sulfadiazine	*Trametes versicolor*	-	49
Cefalexin	*Pseudomonas sp. CE21 and CE22*	-	50
Lipid regulator Simvastatin	*Nocardia s.p.*	-	51
Nonsteroidal anti-inflammatory drugs Ibuprofen	*Sphingomonas sp. strain Ibu-2*	-	34
Diclofenac	*Phanerochaete sordid*	-	38
Paracetamo	*Pseudomonas aeruginosa strain*	-	52
Naproxen	*Trametes vesicolor*	-	53
Ketoprofen	*Patulibacter sp. strain I11*	-	35
Beta blocker Metoprolol	*Rhodococcus rhodochrous*	Glucose	54
Antidepressant Diazepam	*Bjerkandera sp. R1, Bjerkandera adusta and Phanerochaete chrysosporium*	-	55
Anticonvulsants Carbamazepine	*unidentified basidiomycete BNI*	Glucose	35

Conclusion

Microbial actions and degradation through microbes are most an essential for the restoration of the environment and protection of global carbon cycle. These technique known as biodegradation. Most of the elements that can be degraded or changed by microorganisms are an enormous number of synthetic compounds as well as chemicals which are uncontrollable co toxicological for example hydrocarbons and heavy metals. However, in most cases this statement concerns potential degrade abilities which were assessed in the laboratory by using selected microbial cultures and with perfect growth conditions. As a result of a some factors: struggle with microorganisms, not sufficient supply for the necessary substrates, and some important external conditions (aeration, moisture, pH, temperature), and low bioavailability of the pollutant, biodegradation in natural situations is reduced pharmaceuticals contaminated water. So, environmental biotechnology has the

objective resolving these problems with the use of microorganisms in biodegradation technologies. For this reason, it is required to sustenance the activities of the original microorganisms in polluted biotopes and to enhance their derivative facilities through biodegradation. Genetic engineering is also used to recover the biodegradation capabilities of microorganisms. However, there are many hazards related to the use of GE Min the field. Whether or not such methods are initially successful in biodegradation of pollutants may selection a difference in our competence to reduce pharmaceutical wastes and help for the removal of industrial pollution.

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