



Antibiotic resistance and wastewater: Correlation, impact and critical human health challenges

Awanish Kumar^a, Dharm Pal^{b,*}

^a Department of Biotechnology, National Institute of Technology Raipur, India

^b Department of Chemical Engineering, National Institute of Technology Raipur, India



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ABSTRACT

The spread of bacterial antibiotic resistance (due to over and non-judicious use of antibiotics) is an apprehensive subjects matter and the role of wastewater treatment plants has been attracting particular interest. These stations are a reservoir of resistant bacteria, and the amount of bacteria released into the environment is very high and dangerous. The reuse of treated wastewater for irrigation is a practical solution for surmounting scarcity of water, but there are several health-related and environmental risks associated with this practice. It may increase antibiotic resistance (AR) levels in soil and water. Wastewater treatment plant effluents have been recognised as significant environmental AR reservoirs due to selective pressure generated by antibiotics that are frequently discharged in water. It also enhanced the possibility of horizontal gene transfer by increasing the abundance of the resistance gene. This review focuses on the emergence of antibiotic resistance in waste water, waste water treatment, challenges and their impact on human health. Based on the current state of the art, we conclude that the improvements in wastewater treatment technologies are required that not only remove solids, organic matter, and nutrients but also they could remove AR element and bacteria.

1. Introduction

The whole world is facing an ever increasing shortage of water and in most part of the world; the reuse of treated or untreated wastewater is the main source of water for agriculture as freshwater availability is not sufficient. Nevertheless, numerous environmental and health risks are associated with reuse of wastewater. Therefore, pollution measures are necessary to avoid biological risks and ensure the safe use of wastewater. In the recent past, personal care, pharmaceuticals, and human health related products containing antibiotics have been identified as emerging contaminants and threat of aquatic environment. Presence of antibiotics in our environment has been reported throughout the globe in groundwater, sediments, surface water [1–3]. Water bodies are getting contaminated with antibiotic due to their unsafe disposal and its concentration is increasing day by day due to increase in the population, urbanization, industrialization, and wrong agricultural practices.

Therefore, treatment of wastewater is carried out for the purpose of reducing the pollutants by removing pathogens, biodegradable substances, nutrients to ensure public health and protecting the environment. Furthermore, with the increase in water demand, the recycling of wastewater has been brought into question and efficient functioning of sewage treatment is needed. Many surveys revealed the presence of

antibiotics in wastewater treatment plants. Surveys were carried out by taking frequent samples, including influent, the supernatant of the primary sedimentation tank, the mixed liquid in the aeration tank, effluent after disinfection, rejected water from sludge dewatering, supernatant in the secondary sedimentation tank, etc. Increasing concentration of multiple antibiotics led to the proliferation of resistant bacteria in the environment. High concentrations of multidrug-resistant bacteria have also been detected in hospital wastewater, domestic sewage, and drainage from livestock feeding process which is a severe threat to the human health [4–6]. Recently, the impact of antibiotic residues on ecosystem has been recognised as an international threat [7]. Aquatic and terrestrial organisms have been affected by the extensive presence of antibiotics in the environment [8], besides, alteration in microbial activity and community composition [9], and prevalence of bacterial resistance to antibiotics [10]. Moreover, antibiotics produced from anthropogenic sources may lead to entering into the environment via wastewater treatment plants if the removal is not complete, or wastewaters are untreated [11]. The excretion of incompletely metabolized antibiotics by humans and animals is the primary source of antibiotics in the environment. Other sources may include the disposal of unused antibiotics and waste from pharmaceutical manufacturing processes. Residential (private residences, dormitories,

* Corresponding author at: Department of Chemical Engineering National Institute of Technology Raipur, Chhattisgarh, 492010, India.
E-mail address: dpsingh.che@nitrr.ac.in (D. Pal).

hotels, and residential care facilities) and commercial facilities (including hospitals) are known contributors of antibiotics to municipal wastewater [12].

The development of antibiotic-resistant bacteria has poses an increasing concern. The widespread and often inappropriate administration of antibiotics in livestock, pets, and humans has been shown to result in the development of antibiotic-resistant bacteria and is generally accepted to be a primary pathway for their proliferation in the environment. There is further concern that antibiotic-resistant bacteria might develop from long-term environmental exposure to low concentrations of antibiotics (ng/L– μ g/L), such as those present in wastewater and surface water. One study has shown the increased prevalence of antibiotic-resistant *Acinetobacter* spp. in sewers receiving hospital and pharmaceutical plant wastewater effluent [13]. Genotoxic substances are often mutagenic and carcinogenic and are, therefore, the potential suspect in the development of antibiotic resistant organisms. Although several studies have detected the occurrence of antibiotics in hospital effluent [12,13], little is known about their persistence in conventional wastewater treatment processes or their fate or effects in the environment [14]. The resistant organisms may enter into human bodies directly or indirectly, and the resistance genes are distributed in various environmental media and disseminated widely by horizontal gene transfer mechanism in the environment [15]. Discharged factors in waste water, such as gene cassettes, integrons, plasmids, and heavy metals, play important roles in the exchange of resistance and contribute to resistance retention [16]. Therefore, the focus of research should be shifted on the study that will have significant implications for the elimination of antibiotics from the environment. Effective approaches (additional treatment steps, downstream of conventional biological process, such as membrane processes [17], adsorptive treatment processes [18], advanced oxidation processes [19], and the combined ones [20]) have been suggested to limit/eliminate the occurrence of antibiotics and multi-drug resistant bacteria in the aquatic environment and to monitor their concentration properly. This review compiles useful information on various sources for antibiotics, wastewater treatment techniques to remove antibiotics, antibiotic resistance in waste water and its impact on public health and mechanism of antibiotic resistance and prevention of its spread.

2. Sources of antibiotics

Traditionally, antibiotics are being used since the 50s to control certain bacterial diseases of valuable flora & fauna such as apple, pear, and related ornamental trees. Even today use of streptomycin with oxytetracycline is very common. Numerous antibiotic of different types is being used with world-wide estimated consumption ranging from 0.1 to 0.2 million ton per annum [21]. It has been estimated that (in the USA) half of the antimicrobials use is for humans and rest is for animals, agriculture and aquaculture mainly to promote the growth of cattle, hogs, and poultry [22]. Extensive use of antibiotics is prevalent both as human and veterinary medicine, in addition, to plant agriculture and aquaculture for treating microbial infections and for prophylaxis. It is also found that β -lactam antibiotics, including the sub-groups of penicillins, cephalosporins, carbapenems, and others make up the largest share (50–70%) of total human antibiotic consumption. Moreover, excretion rates for the unchanged active compound cover a broad range of 10–90%, with an average metabolic rate estimated to be 30% [23], that is seventy percent is excreted unchanged into waste water. In general, the high water solubility of metabolites as compared to parent compounds causes their excretion with urine. Nevertheless, formed metabolites may be more toxic to humans as compared to the parent compound.

In view of precise risk assessment antibiotics of natural origin is highly crucial. Soil bacteria may produce different antibiotics like aminoglycosides, streptomycins β -lactams etc. In addition, the free water phase also contains bacteria, though the concentration is lower

than sewage sludge or soil due to low movement of bacteria in both soils and sediments as compared to the free water phase. Besides, it has been reported that antibiotics emanated from its production plants ranges to several mg/L and may contribute significantly; however, it was considered of less concern [24,25]. It is worth to mention here that, in contrast to general expectation, hospitals are not the main source of pharmaceuticals in municipal sewage [26,27]. Now a day's to promote the growth or for the prevention or therapy of animal, antibiotics are used in modern breeding and fattening to achieve a lower percentage of fat and higher protein content in the meat [28]. Some antibiotics are used in bee-keeping and for other purposes such as streptomycins are being used for growing fruits. The main purpose of antibiotics use in aquaculture is therapeutic and also as a prophylactic agent. Antibiotics such as oxytetracycline, florfenicol, premix, sarafloxacin, erythromycin, sulphonamides are commonly used in aquaculture [29,30]. It has been noted that, selection of resistance in pathogenic bacteria may arise even due to low amounts of antibiotics.

3. Wastewater treatment and reuse

Wastewater treatment is conventionally a combination of a primary, secondary and infrequently a tertiary process. Each treatment stage consists of different biological and physicochemical processes. Primary treatment is generally common in most of the treatment plants and mainly consists of filtration and sedimentation with primary objective is to remove the solid content of the wastewater (oils & fats, sand, and settleable solids etc) [31]. Whereas the main purpose of secondary treatment is to remove organic matter (nutrients) with aerobic or anaerobic systems through the biological process such as membrane bioreactors, moving bed biofilm reactor, or fixed bed bioreactors etc; most common being the conventional activated sludge. In the plants based on activated sludge, for the growth of biological floc dissolved oxygen is utilized, that substantially removes the organic material and nitrogen. Tertiary wastewater treatment processes can be applied at the last stage for the precipitation of phosphorus on a filter [32]. Disinfectant such as chlorine, UV radiation, and ozonization is also applied in few cases for the wastewater disinfection processes before its release into the environment.

3.1. Biological treatment

During the biological treatment, antibiotics removal and modification can be biotic (mainly bacterial and fungal biodegradation) and abiotic (e.g. sorption, hydrolysis, homo or hetro photolysis). Sorption on the sewage sludge and their degradation or transformation during the treatment is the main mechanism involved in removal of antibiotics. For few cases hydrolysis is the key step, whereas, photolysis is less common due to low light exposure of the substances during wastewater treatment. Hydrophobic (or non-polar) antibiotic residues have a greater affinity to solids and thus, remain concentrated in the organic-rich sewage sludge [33]. For the removal of antibiotics from aqueous solutions, techniques such as polar hydrophilic interactions, complex formation with metal ions, and ion exchange may be employed [34]. Generally, sludge sorption constants, K_d (L/kg) is used as the measure of the affinity of antibiotics sorbed to sludge. Higher sorption to sludge is marked by the higher K_d values [35]. According to Rogers (1996) sorption potential of organic contaminants could be estimated using octanol-water partition coefficient (K_{OW}) and can be classified as: (i) low sorption potential ($\log K_{OW} < 2.5$, such as sulfonamides, tetracyclines, aminoglycosides etc.), (ii) medium sorption potential ($2.5 < \log K_{OW} < 4.0$, such as macrolides, β -lactams etc.), and (iii) high sorption potential ($\log K_{OW} > 4.0$, like glycopeptides) [36]. Nonetheless, antibiotics mainly remain in the aqueous phase of the wastewater by virtue of their hydrophilicity and biological resistance. In the wastewater treatment, influential operational parameters for the removal of antibiotic from biological residues are, (i) biochemical

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