

**Communication**

Antibiotics Resistance in Water Mediums: Background, Facts, and Trends

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To cite this article:Djamel Ghernaout, Nouredine Elboughdiri. Antibiotics Resistance in Water Mediums: Background, Facts, and Trends. *Applied Engineering*. Vol. 4, No. 1, 2020, pp. 1-6. doi: 10.11648/j.ae.20200401.11**Received:** December 18, 2019; **Accepted:** December 25, 2019; **Published:** January 7, 2020

Abstract: From human and animal provenances, antibiotic-resistant microorganisms come into water mediums. Such bacteria are capable of diffusing their genes into water-indigenous microbes, which as well hold resistance genes. Conversely, several antibiotics from industrial sources spread in water mediums, greatly modifying microbial ecosystems. During the last decade, hazard evaluation protocols for antibiotics and resistant bacteria in water, founded on better programs for antibiotics discovery and antibiotic resistance microbial origin tracking, are more and more enhanced. Techniques to decrease resistant bacterial charge in wastewaters and the number of antimicrobial agents, in most cases originated in hospitals and farms, involve regulation of disinfection methods and running of wastewater and manure. For avoiding mixing human-originated and animal-originated microorganisms with ecological organisms, a procedure is more than recommended. This work reviews the facts and future trends of this new open and imposed field in dealing with domestic wastewater. It is vital to elevate efficient barrier measures such as membranes processes, like reverse osmosis and nanofiltration, avoiding the integration of resistant and pathogenic bacteria into nature. Techniques have to be developed for cheap and reliable: first, bacterial clones and resistance genes origin tracking; second, detection of antibiotics in water mediums; third, disinfection of water from antibiotic-resistant populations and the resistance gene pool, and elimination of antibiotics from wastewater; and fourth, prevention policies for mixing human–animal-originated and soil–water bacteria.

Keywords: Antibiotic-resistant Bacteria (ARB), Antibiotic Resistance Genes (ARGs), Wastewater Treatment, Disinfection, Oxidation, Drinking Water

1. Introduction

Water mediums receive both human and animal pathogenic and greatly pathogenic bacteria are permanently liberated with wastewater [1]. Many of such microorganisms [2, 3] bear antibiotic-resistance genes, in the end, incorporated into genetic mobile platforms (plasmids, transposons, integrons) capable of diffusing among water and soil bacterial groups [4]. Water makes not only a path of dispersal of antibiotic-resistant organisms among human and animal communities since potable water is mainly originated from surface water but as well the road by which resistance genes are entered in natural bacterial ecosystems. In these aquatic mediums, the

nonpathogenic microbes may serve as a tank of resistance genes and platforms. Further, the entry (and cumulative collection) in the nature of antimicrobial agents, detergents, disinfectants [5-7], and residues from industrial pollution [8], like heavy metals, participate in the growth and dispersal of these resistant organisms in the water medium. The intense usage of prophylactic antibiotics in aquaculture [9] is especially pertinent. Reciprocally, ecological bacteria operate like an indefinite exporter of genes that could work as resistance genes while coming into pathogens. Several such genes are not foremost resistance genes; however, they are a member of the unobserved 'resistome' [10], the series of genes capable of being transformed into antibiotic-resistance genes.

There is an increasing focus on the human health hazard evaluation procedures for antibiotics and resistant bacteria in water [11, 12]. Definitely, it is hard to accept the fact that public health officers and ecotoxicologists have neglected for more than a century to really intend the decisive necessity of prohibiting the blend between microbes from human-animal and ecological settings [1].

2. Main Genetic Reactors for Antibiotic Resistance

Antibiotic resistance incubates in bacteria due to the impact of industrially formed antimicrobial agents on bacterial populations and groups. Genetic reactors are spaces in which the opportunity takes place for genetic growth, especially due to elevated biological connectivity, generation of variation, and the existence of specific selection. On the other side of mutational phenomena, a crucial genetic shift happens because of recombinatorial incidents, often deriving from genetic commutations between organisms inside populations and groups. Antibiotic resistance develops (Figure 1) in four major genetic reactors [1].

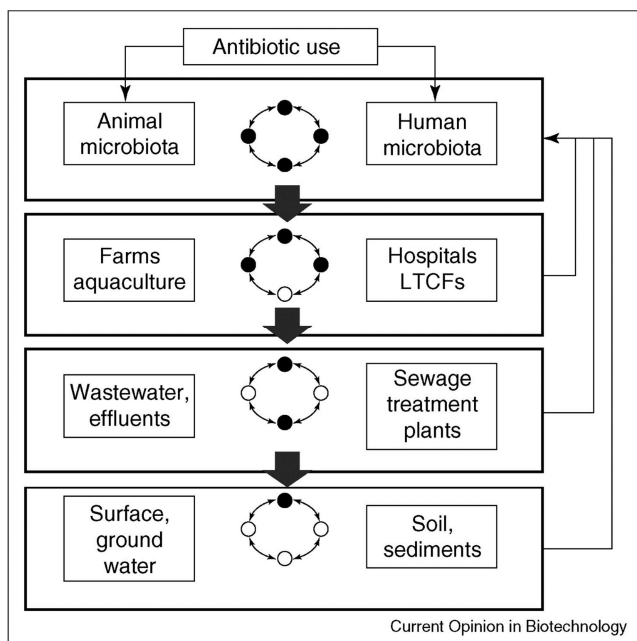


Figure 1. The four genetic reactors in antibiotic resistance, where genetic exchange and recombination shapes the future evolution of resistance determinants. Particularly in the lowest reactors, bacteria from human-associated or animal-associated microbiota (in black) mix with environmental bacteria (in white), increasing the power of genetic variation and possible emergence of novel mechanisms of resistance that are re-introduced in human or animal environments (back arrows) [1].

The first reactor is formed by the human and animal microbiota, with more than 500 bacterial species implied, in which therapeutic or preventive antibiotics employ their works. The secondary reactor implicates the hospitals, long-term care facilities, farms, or any else medium in which susceptible individuals are crowded and exposed to bacterial

exchange. The tertiary reactor corresponds to the wastewater and any kind of biological residues formed in the secondary reactor, comprising, for example, lagoons, wastewater treatment plants [13-18], or compost toilets, in which bacterial organisms from many diverse individuals have the occasion to mix and genetically respond. The fourth reactor is the soil and the surface or groundwater mediums, where the microorganisms [19] formed in the former reactors combine and counteract with ecological organisms. Water is implied as a critical factor in all the four genetic reactors; however, especially in the last ones. The probability of diminishing the evolvability of antibiotic resistance is a function of the potential of humans to restrain the flow of active antimicrobial agents, bacterial clones, and genetically founded biological information along with these genetic reactors [1].

3. Industrial Antibiotics in the Soil-water Mediums

Water solubilizes commercial antibiotics that are fixed to environmental matrices. Fixing to soil solids (and sediments) makes late their biodecomposition and interprets the long-term stability of the pharmaceuticals in nature. Evidently, soil solids also eliminate antibiotics from water; consequently, a type of water-soil pharmacokinetics has to be taken into account. Antimicrobial chemicals are kept in soil by their bond with soil chemicals. As an example, Elliot soil humic acids [20, 21] form the complexation of antibiotics [22]. More importantly, heavy metals (like methyl-mercury) also incorporate with humic acids [23, 24]; as a result, in the water film linked to soil organic solids, different antimicrobial impacts might be concurrently existing. In fact, it seems that in the existence of humic substances, in both solubilized and mineral-bound forms, ecological mobility of antibiotics [22] might augment. Aluminum and iron oxides [25-27] might modify these interactions by converting surface charge [28]. For example, sorption to such oxides conducts to diverse sorts of ciprofloxacin-surface complexes [22] possibly altering the reactivity of fluoroquinolones in the soil-water interphase. In addition, global modifications in water or in soil (since pH varies, or ionic strength) might adept these antibiotic-soil-water interactions, forming diverse degrees of antibiotic liberation (solubilization) from soil solids. For erythromycin or oleandomycin, half-lives in soil have been evaluated in 20-30 days [1].

4. Commercial Antibiotics in Water-sludge Mediums

Antimicrobial chemicals like sulfonamides, macrolides, trimethoprim, cephalosporins, or fluoroquinolones can be observed at greatly dynamic levels in activated sludge treatment; further, the antibiotic charge during the year is linked to the change in annual consumption information, being more important in the winter [29]. The wastewater level of antimicrobials is a function of the sludge-wastewater

partition coefficient; however, with fluoroquinolones field tests of sludge implementation to agricultural land proved prolonged stability of such chemicals, even if with restricted mobility into the subsoil [30]. Extremely elevated levels of sulfonamides (20×10^3 ng/mL) have been detected in pig farm wastewater and the discovery of sulfamethazine has been proposed to act as a marker for livestock-source pollution in Vietnam [31]. In Japanese urban rivers, an elevated number of antibiotic chemicals may be found, comprising sulfonamides, trimethoprim, and macrolides. In Hong Kong and Shenzhen, in urban wastewater samples, penicillin concentrations (as penicillin V) were unnoticeable; however, that was not the situation for cephalosporins, since cefalexin or cefotaxime attained levels surpassing 1 µg/mL [32], possibly enough to select organisms generating extended-spectrum beta-lactamases, as CTX-M enzymes. If the selection of ESBL organisms will form a decrease in the antibiotic level, this will be debatable. In compost toilets, amoxicillin degradation is minor, surprisingly in the existence of beta-lactamase-producing bacteria. Hydrophobic antibiotics, like tetracycline or ciprofloxacin, were found in all sludge samples from two Oslo city hospitals; however, not in the collected influent samples, proposing fixation to effluent solids [33]. In an identical manner, fluoroquinolones were systematically detected in hospital effluents [34]. The widespread utilization of antibiotics in human medicine, animal farming, and agriculture conducts to antibiotic pollution of manure, which may be employed as fertilizer [1]. Leaching trials show that largely less than 1% of fluoroquinolones in the sludge attained the aqueous phase, which might illustrate a relatively decreased mobility if sludge is employed to fertilize soil [30]. For all that, that does not eliminate centralized biological influences on particulated material. In fact, elevated levels of fluoroquinolones were detected in secondary sludge (sorption). Macrolides were so resistant to the techniques realized in wastewater treatment plants [35-38] in South China, and unexpectedly levels that are more important were detected in the final effluents than in the raw wastewaters [39].

5. Impact of Antibiotic Levels on Disinfecting Water and Treating Wastewater

Disinfecting water using ClO_2 might participate in eliminating beta-lactam chemicals [1, 40-45]. The water-decomposition of beta-lactams (penicillin G) has been investigated, being penicilloic acid the major decomposition product [46]. Aqueous chlorination of potable water and wastewater reduces trimethoprim action [47-49]. Treating wastewater might remove almost 80% of fluoroquinolones or tetracyclines prior to they come in rivers, and are predisposed to photodegradation [30, 32]. Antibiotic reduction performances through wastewater treatment [50-52] are less important for macrolides that are comparatively enduring in nature [32]. Using methods for antibiotic elimination via coagulation [53-62] and granular activated carbon adsorption, ionic treatment or micelle-clay systems are encouraging for

diminishing tetracycline and sulfonamides [63].

6. Quantifying Antibiotic Levels in Water

The advance in instrumental analytical chemistry, employing electrophoretic and chromatographic techniques, like liquid chromatography-tandem mass spectrometry, allows us to reveal several various kinds of antibiotics at levels of nanograms/liter, following solid-phase extraction [64, 65]. On the other hand, immunochemical techniques are also helpful for cheap rapid examination [65]. Voltammetry and amperometric detection of tetracyclines employing multiwall carbon nanotube modified electrodes have been lately suggested for controlling water samples [66]. Surprisingly, commercially available test kits have been successfully employed for the quick examination of antibiotic activity in effluents and surface water samples [67]. It is to be observed that natural organic matter [68-70] might greatly influence the findings of the analysis of different antibiotics [1].

7. Decreasing Antibiotic-resistant Bacteria in Wastewater

Antibiotic-resistant microbes from humans and animals are liberated into the wastewater through polluted sites (comprising urine), feces, finally cadavers and manure. Especially, wastewater from hospitals and dense farming facilities (below-concentrated animal feeding operations) is likely the main origin of pathogenic and antibiotic-resistant microorganisms [71-73] and antibiotic-resistance genes that are liberated into nature. It is fundamental to elevate our comprehension of efficient barrier measures [74-79] avoiding the integration of resistant and pathogenic bacteria into nature (see Introduction). Wastewater may be disinfected in diverse fashions [80-84], involving chlorine (2-3 logs bacterial decrease with chlorine injection of 30 mg/L), ozone (3-4 logs removal at 100 mg/L), or ultraviolet light (efficient but costly [85]). These techniques might vary in diverse conditions, as for instance, ammonia existing in wastewaters might compete for free chlorine to form monochloramine [1, 86]. In such situations, efficient chlorine injections might need levels of 100 mg/L. Filtering techniques involving surface-modified ones activated carbon filter media are encouraging (more than 6 logs removal). The findings of many investigations [85] show the potential that chlorination might conduct to the modification of wastewater populations, with the selection of chlorine-resistant bacteria (related to *Bacillus subtilis* and *Bacillus licheniformis*), which might participate in the selection of particular resistance genes and genetic platforms. Numerous investigations have treated the impact of diverse sorts of manure controlling on the ecological fate of resistance genes. High-intensity manure management (with amending, watering, and turning) was more efficient in diminishing the permanence of resistance genes than low-intensity management. Various genes had different kinetics of maintenance [87-89], possibly in link with the organisms

harboring them.

8. Conclusions

The main points drawn from this work may be given as:

1. A great fraction of the diffusion and growth of antibiotic-resistant bacterial organisms is a function of water mediums. In aquatic mediums, bacteria from diverse sources (human, animal, ecological) are capable to merge, and resistance incubates as a result of random commutation and mixing of genes, genetic platforms, and genetic vectors. Simultaneously, antibiotics, disinfectants, and heavy metals are liberated in water and might deploy selective activities, as well as ecological demolition in water communities, conducting to antibiotic resistance. Techniques have to be developed for cheap and reliable: first, bacterial clones and resistance genes origin tracking; second, detection of antibiotics in water mediums; third, disinfection of water from antibiotic-resistant populations and the resistance gene pool, and elimination of antibiotics from wastewater; and fourth, prevention policies for mixing human–animal-originated and soil–water bacteria [1].

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