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Antibiotics: A Potential Source of Pollution in the Environment

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Abstract: *Since their discovery antibiotics have been central to modern healthcare and have been extensively and effectively used to prevent and treat infections in humans and animals. They have also been used in agriculture, aquaculture, and in livestock as growth promoters. In the last several years, antibiotic usage has received a lot of attention due to their emergence as a potential source of pollution. This paper collects information from other published articles on the sources and occurrences of antibiotics in various natural and artificial systems. Almost all antibiotics have been reported for their occurrences in natural water bodies, soil, sediment, manure, sludge, and effluents from industries and hospitals across the globe. Transformation of antibiotics and their fate in wastewater treatment plants have been discussed in detail. The adverse effects of these pollutants other than development of resistance have also been discussed and necessary suggestions have been highlighted for effective monitoring and mitigating pollution, which may provide scope for future research.*
Keywords: *Antibiotics, ecotoxicity, genotoxicity, sources, pollution, wastewater treatment plants*

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I. Introduction

Antibiotics are therapeutic agents which restrain or annul the growth of microorganisms. Their era began in 1930s with the discovery and isolation of bactericidal compounds from soil dwelling actinomycetes. Atleast 65 antibiotics in nine classes were found and introduced into medicine during what has been called as the 'golden era' of antibiotic drug discovery. Today, antibiotic research and development focuses on derivatives of older classes of antibiotics and discovery of novel compounds, both natural and synthetic using innovative discovery platforms (Lewis, 2013). Antibiotics have become central to modern healthcare since their introduction into medicine. Their role has expanded from treating serious infections to preventing infections in surgical patients, protecting cancer patients and patients with compromised immune system, and promoting growth and preventing diseases in livestock and other food animals.

II. Sources

With the production of antibiotics, thus began the entering of their effluents into the environment. Antibiotics enter the environment through several sources, such as wastes of manufacturing plants (Babíc *et al.,* 2007; Larsson *et al.,* 2007), improper disposal of unused medication (Bound and Voulvoulis *et al.,* 2005), and landfill leachates (Holm *et al.,* 1995). However, according to Hirsch *et al.*, (1999) patients undergoing treatment are the prominent sources of antibiotics in the aquatic environment. Hence, there are two routes through which antibiotics reach the aquatic environment: urban and agricultural.

Urban route comprises of antibiotics excreted [for some compounds as much as 90% in the form of parent compound (Jjemba, 2006)], washed off (in case of topical application) or discarded by people in households, hospitals or industries which end up in sewers. Once in wastewater, antibiotics and their metabolites are either directly discharged into nearby surface waters or transported via sewers to wastewater treatment plants (WWTPs). Antibiotics may also reach surface waters directly because of leaking or overflowing sewers. In WWTPs during treatment, substances having lower affinity for solids will subsequently be discharged into streams (Roberts and Thomas, 2006) while substance with higher affinity for solids will be adsorbed to sludge during treatment and will reach the environment by the application of sewage sludge as manure in agriculture fields or by leaching in landfills.

In case of agricultural route, antibiotics present in animal excreta may reach the aquatic environment by drainage and runoff to surface water and by percolation to groundwater. Many studies have shown that antibiotics are transported either by the aqueous phase or in suspension bound to particles (Kay *et al.,* 2004, 2005), and this pathway is mainly enhanced by land application of manure laden with antibiotics (Alexy 2004; Kumar *et al.,* 2005). Antibiotics which have been retained or which have progressively accumulated in soils over the years may be gradually released into the aqueous phase; therefore agricultural soils may act as environmental reservoirs for antibiotics (Rooklidge, 2004; Lee *et al.*, 2007). These compounds can also reach natural water bodies directly either from leaking manure storage structures or constructed lagoons (Meyer, 2004) or through dust (Hamscher *et al.,* 2003). Antibiotics used in aquaculture find their way in surface waters through leaching from food pellets, fish faeces or pond sediments (Cabello, 2006; Lee *et al.,* 2007). Antibiotics sprayed on fruit plants may reach the aquatic environment; however this pathway has not been studied in detail. Therefore, agricultural activities may be considered among the main non-point sources of antibiotics in the aquatic environment.

III. Occurrence Of Antibiotics In The Environment:

Extensive research has been done regarding the presence of antibiotics in the environment. Almost all antibiotics and their metabolites have been found in sewage influent and effluent samples, in surface waters, ground and drinking waters, sludge, sediment and soil. It has been found that the concentrations of antibiotics measured in different compartments such as sewage, surface waters etc. are in the same range in different countries (Hernándaz *et al.,* 2007; Chang *et al.,* 2008; Martins *et al.,* 2008).

3.1 Occurrence in industrial and hospital wastewaters:

Wastewaters are the most studied for the presence of antibiotics since reported concentrations in this matrix are obviously the highest, but may vary by upto ten orders of magnitude. This huge variability in reported concentrations of antibiotics is due to diverse origin of the wastewaters, which may come from industries, hospitals, municipal wastewater treatment plants, farm lagoons, field run off etc. The concentrations of antibiotics are also affected by the different treatment processes applied to wastewaters which in some case may be non-existent (as in the case of direct discharges of urban or agricultural origin) and in others very advanced e.g. tertiary wastewater treatment systems like reverse osmosis, micro and nano filtration as well as ozonation.

Pharmaceutical industries often generates highly contaminated sewage for e.g. wastewater generated from oxytetracycline manufacturing industry had antibiotic level as high as 920 mg/L (Li *et al.*, 2008a) which are several times higher than the EC_{50} for some aquatic species such as *Microcystis aeruginosa* (EC_{50} = 20.7 µg/L) or *Rhodomonas salina* (EC_{50} = 160 µg/L) (Holten-Lützhøft *et al.,* 1999). Other compounds such as quinolones have also been reported in effluents from drug manufacturers with concentration of ciprofloxacin upto 30 mg/L which are well above EC_{50} values for several aquatic species as well (Larsson *et al.,* 2007). Another study has reported 153 µg/L of benzylpenicillin in the effluent of β-lactum manufacturing plant which is comparable to the minimum inhibitory concentrations (MICs) (Li *et al.*, 2008b).

Hospitals are considered one of the most important sources of antibiotics in the aquatic environment (Gòmez *et al.,* 2006). The maximum concentration of ciprofloxacin found in hospital effluents (124.5 µg/L) (Hartmann *et al.,* 1998) is considered higher than the lowest effect concentration of ciprofloxacin for genotoxicity (LOEC = 0.2 µg/L) or the EC_{50} of some pathogens (Kümmerer *et al.*, 2000). In other studies, Pham Thi (2003) investigated the presence of fluoroquinolones in the hospital wastewater in Switzerland and detected ciprofloxacin and norfloxacin in the range of 17.2-29.4 µg/L and 2.6-7.9 µg/L respectively. In another such study, concentrations of β-lactums in hospital wastewater were 20-80 µg/L during a day course (Cerovec, 2000). β-lactums were also detected in the lower µg/L range in hospital effluents and in the influent of municipal sewage treatment plant (Christian *et al.,* 2003).

3.2 Occurrence in wastewater treatment plants (WWTPs):

Urban wastewaters have been extensively studied for the presence of antibiotics because of the preponderant role of wastewater treatment plants on the antibiotic contamination of surface waters. Hirsch *et al.*, (1999) investigated the occurrence of several representatives from main groups of antibiotic in WWTP effluents and in river water. They described the analysis of various water samples for 18 antibiotics from classes: macrolides, sulphonamides, penicillins and tetracyclines. They observed the frequent occurrence of erythromycin-H2O, roxythromycin and sulfamethoxazole with concentrations upto 6 µg/L in WWTPs. Neither tetracyclines nor penicillins could be detected at concentrations above 50 and 20 ng/L respectively. Effluents of nine sewage treatment plants (STPs) over Italy were analyzed and four antibiotics (ofloxacin, erythromycin, lincomycin and clarithromycin) were detected in high concentrations. They were persistent enough to remain in substantial quantities in river waters too (Calamari *et al.,* 2003). Analyses in raw sewage and WWTP effluents applying different types of processes have demonstrated the failure of the commonly used wastewater treatment technologies to completely remove antibiotics present in wastewaters.

3.3 Occurrence in surface and ground waters:

Occurrences of antibiotics have been well documented in both surface and ground waters. Rivers, lakes, creeks, estuaries, basins, sea water and wells have been reported to be contaminated by several of these compounds. The first reported case of surface water contamination by antibiotics was in England more than two decades ago when Watts *et al.,* (1982) detected at least one compound from the macrolide, sulphonamide and tetracycline group of antibiotics in river water at concentrations of 1 µg/L. Following this, a series of antibiotics were also detected in surface water. For example, a German group detected residues of chloramphenicol in one small river in southern Germany at concentrations of 0.06 µg/L (Hirsch *et al.,* 1999).

Also, Sacher and his co-workers (2001) analysed 105 groundwater wells in Baden-Wuerttemberg, Germany. Among 60 pharmaceuticals they found erythromycin-H2O and sulfamethoxazole, which were the only antibiotics out of the eight compounds detected in at least three ground water samples. In 2002, Koplin *et al.* published a study which showed the presence of 95 organic wastewater contaminants including pharmaceuticals in 139 streams across the USA. Among the 31 antibiotics from the groups of tetracyclines, macrolides, sulphonamides and fluoroquinolones; erythromycin-H2O and sulfamethoxazole were detected in concentrations of upto 1.7 and 1.9 µg/L respectively. These observations were later confirmed by Focazio *et al.,* (2008) who showed that 6 antibiotics from the 25 initially targeted were found in 26 of the 74 untreated drinking water sources across the United States. Ground waters are affected by a variety of sources, with landfills, septic systems, and agricultural fields representing the most significant potential sources of antibiotic contamination. Also, landfills containing WWTP bio-solids or discarded antibiotics contaminate ground waters because leachate plumes may reach nearby aquifers. Studies on the disposal of pharmaceuticals in the United States and the United Kingdom (Kuspis and Krenzelok 1996; Bound and Voulvoulis 2005) showed that a significant proportion of people (54% in the United States, 71% in the United Kingdom) disposed off unused medication in the trash. Hence, the role of landfills in the contamination of ground waters should be reassessed, as disposal of antibiotics is usually considered only a minor source of contamination (Boxall, 2004).

3.4 Occurrence in drinking water:

Occurrence of antibiotics in drinking water is the least reported so far. This can be due to the low limits of quantification necessary to achieve their determination in drinking water, which often must be less than 0.001 µg/L. Antibiotic concentrations in contaminated tap water range from 0.0003 to 0.005 µg/L, with a median concentration of 0.002 µg/L (Segura *et al.,* 2009). Antibiotics reach drinking water, albeit in very low amounts, because they are able to persist in natural water sources and resist purification processes in drinking water treatment plants (DWTPs). However, antibiotics seem to be more affected by purification processes than other, more frequently reported organic wastewater contaminants (OWCs). In a study on the fate of 106 OWCs (including 25 antibiotics) in a conventional DWTP using several physicochemical processes in sequence, from the 42 OWCs detected above their reporting limit in stream and raw water samples, only five were antibiotics. In finished waters, only 17 OWCs were detected, and none of them were antibiotics (Stackelberg *et al.,* 2004). A study on the effectiveness of several treatment processes used in DWTPs showed that activated carbon sorption, reverse osmosis, and oxidation (chlorination or ozonation) were among the most efficient treatments to remove antibiotics from source water (Adams *et al.,* 2002).

3.5 Occurrence in soil and sediment:

Human and veterinary antibiotics are also found in soil and sediments. Antibiotics reach soils mostly from the use of contaminated excrements (manure or sewage sludge) as fertilizer on agricultural land or directly through grazing livestock. Kim and Carlson (2007) detected tetracyclines, sulphonamides and macrolides in soil. Antibiotics reach soil mostly from the use of contaminated excrement (sludge or manure) as fertilizer for agricultural land or directly through grazing livestock. It has been estimated that loads of upto kilograms per hectare may enter agricultural soils and that a concentration level of antibiotics similar to pesticides is easily reached (van Gool, 1993; Winckler and Grafe, 2000). Due to intra-corporal administration of antibiotics, they are frequently found in dung and manure of farm animals. For example, manure samples from pigs contained upto 3.5 mg/Kg of sulphonamides and upto 4 mg/Kg of tetracyclines (Höper *et al.,* 2002; Hamscher *et al.,* 2002a). In another study, Campagnolo *et al.,* (2002) detected antibiotic from a multitude of different classes in all the manure samples procured from eight pig farms, with single substances often exceeding 100 µg/L and the sum of all antibiotics approaching 1000 µg/L. In soils, under conventional land farming fertilized with manure and monitored for two years, average concentrations of upto 199 µg/Kg tetracycline, 7 µg/Kg chlortetracycline (Hamscher *et al.,* 2002a) and 11 µg/Kg sulfadimidine (Höper *et al.,* 2002) were detected. Another significant source of antibiotics in the environment is their use in aquaculture for fish production. This results in residual concentrations of several hundred mg/Kg of antibiotics in aquatic sediments (Coyne *et al.,* 1994). For example, residual oxytetracycline at concentrations ranging from 500 to 4000 µg/Kg was observed in marine sediment following the chemotherapy in fish farms in the US (Capone *et al.,* 1996).

IV. Transformation And Fate In Wastewater Treatment Plants (WWTPs):

4.1 Removal pathways in WWTPs:

In wastewater treatment plants the major removal pathways for antibiotics includes biodegradation, disinfection and membrane separation. Other removal pathways include processes such as hydrolysis, photolysis and volatilization but these processes play a minor role in the reduction of antibiotics in WWTPs. For example, *β*-lactums are considered as the most unstable antibiotics due to the presence of a *β*-lactum ring which is susceptible to hydrolysis. However, they undergo hydrolysis before reaching the WWTPs. In some other studies it was observed that the half-lives of *β*-lactums were longer at neutral pH (as in WWTPs): amoxicillin, >5days (Andreozzi *et al.,* 2004); meropenem, 52 hr (Alexy *et al.,* 1999) and ceftiofur, 8 days (Gilbertson *et al.,* 1990). Therefore, although hydrolysis occurs in WWTPs but its contribution in removal of antibiotics from WWTPs has to be neglected due to short hydraulic retention time (HRT) (8-20 hr) of treatment processes.

Sunlight-photolysis or UV-photolysis also helps in the degradation of some antibiotics like amoxicillin, quinolones, macrolides and tetracyclines. However, this process is of minor significance because sunlight or UV rays cannot reach deep into the wastewater in WWTPs due to high concentrations of suspended solid or sludge (Golet *et al.,* 2003). Also, the half-lives of most antibiotics are longer than the HRT of WWTPs and this also results in the negligible effect of photolysis.

Volatilization can be estimated according to the vapour pressure of target antibiotics. The removal of antibiotics through volatilization can be neglected in WWTPs (Pérez *et al.,* 2005) due to two reasons first is the availability of limited data for most antibiotics and second, is that the vapour pressure listed in different reference papers were very low ($<5.75 \times 10^{-6}$ Pa).

4.2 Transformation and fate of antibiotics in conventional WWTPs:

4.2.1 Transformation and fate of antibiotics in primary treatment:

A primary treatment unit usually consists of screens and primary clarifiers. When coagulants like aluminium salts, ferric iron salt or polymers are added it is known as chemically enhanced primary treatment (CEPT) processes. Till date, no significant elimination has been observed in primary treatment processes for many antibiotics like sulfamethoxazole, sulfapyridine, clarithromycin, trimethoprim, erythromycin azithromycin, roxythromycin, amoxicillin, clindamycin and lincomycin (Gulkowska *et al.,* 2008; Radjenovic *et al.,* 2009; Sui *et al.,* 2010).

4.2.2 Transformation and fate of antibiotics in biological treatment units:

Biological treatment unit comprises of biodegradation and adsorption as the dominant transformation pathways for antibiotics. Junker *et al.,* (2006) used ^{14}C-labelled antibiotics to study the fate of two antibiotics: benzylpenicillin (28 µg/L) and ceftriaxone (14 µg/L) in activated sludge. He found that benzylpenicillin was mineralized upto 25% whereas no mineralization was observed for ceftriaxone. These results were similar to the results obtained in closed bottle test (CBT) (Al-Ahmad *et al.,* 1999; Alexy *et al.,* 2004). For example, benzylpenicillin was removed upto 27% via biodegradation whereas ceftriaxone kept unchanged under the same condition (Al-Ahmad *et al.,* 1999; Alexy *et al.,* 2004). Studies on the biodegradability and removal efficiency of sulfamethoxazole have been controversial since there are studies which demonstrate poor removal of sulfamethoxazole in biological treatment process (Brown *et al.,* 2006; Watkinson *et al.,* 2007). While there are some studies showing high elimination efficiencies of sulfamethoxazole (Carballa *et al.,* 2004; Radjenovic *et al.,* 2007, 2009).

Many studies have demonstrated that the most dominant removal pathway for antibiotics like quinolones and tetracyclines is adsorption rather than biodegradation (Batt *et al.,* 2006a; Batt *et al.,* 2007; Xu *et al.,* 2007). As a result of adsorption antibiotics like ciprofloxacin, ofloxacin and norfloxacin were removed upto 85% (Batt *et al.,* 2007), 75-77% (Brown *et al.,* 2006; Radjenovic *et al.,* 2009), and 87%–100% (Lindberg *et al.,* 2005; Vieno *et al.,* 2006), respectively. Tetracycline of 10 µg/L can be removed rapidly in activated sludge unit via adsorption, and the removal efficiency was up to >95% in 6 hr (Batt *et al.,* 2007). On the other hand, macrolides could not be significantly removed in biological treatment process (Göbel *et al.,* 2005b; Göbel *et al.,* 2007). For example, at an environmentally relevant concentration (3 µg/L), no removal was observed for clarithromycin during 48 hr in an activated sludge process (Joss *et al.,* 2006).

4.2.3 Transformation and fate of antibiotics in digestion tanks:

Only a few studies have been conducted on the fate and transformation of antibiotics in anaerobic conditions. Antibiotics like ciprofloxacin and norfloxacin were found to be quite stable and no significant removal of these antibiotics was observed under anaerobic conditions. Degradation of nine antibiotics was studied using ISO standard method 11734 (1995). The results showed that only benzylpenicillin had certain ultimate biodegradation after a lag phase of 40 days (Gartiser *et al.,* 2007).

4.3 Transformation and fate of antibiotics in advanced treatment process:

4.3.1 Filtration:

Some WWTPs use advanced techniques like sand filtration or membrane filtration to obtain high effluent quality. During sand filtration, clarithromycin and trimethoprim were partly removed upto 15% and 60% respectively (Göbel *et al.,* 2005b). However, the elimination of sulfapyridine and sulfamethoxazole was very low, with the removal efficiency of about 14.6% and 26.9% respectively. A study showed that reverse osmosis removed 94% antibiotics and only eight antibiotics were present in the permeate (Watkinson *et al.,* 2007). A study conducted by Koyuncu *et al.,* (2008) showed that nano-filtration process worked efficiently for antibiotics with molecular weight >300 (such as tetracyclines) as removal efficiencies were higher than 95%.

4.3.2 Disinfection:

Ozonation was applied in most of the disinfection studies. During ozonation, antibiotics can be oxidized either by O_3 directly or by hydroxyl radicals (·OH), which are generated as a consequence of O_3 decay. Dodd *et al.* (2006) found that only four (Penicillin G, cephalexin, amikacin, and N(4)-acetylsulfamethoxazole) among 14 antibiotics tested were oxidized predominantly by ·OH and the other 10 antibiotics reacted predominantly with ozone. Trimethoprim was not degraded when another disinfectant species HOCl was used (Dodd and Huang, 2007). On the other hand, 3-amino-5-methylisoxazole, SO_4^{2-}, and N-chloro-*p*-benzoquinoneimine were generated after reaction of sulfamethoxazole with HOCl, indicating its degradation (Dodd and Huang, 2004).

V. Effects Of Antibiotics In The Environment:

5.1 Ecotoxicity:

The widespread occurrence of antibiotics in aquatic habitats has raised a novel and intricate environmental issue. The risk associated with the presence of these contaminants in surface waters is mostly unknown. Compared with soil, the water environment has a more direct and intimate contact with human life due to the wide usage of water and the continuity of the water body that may transport antibiotic/resistance to every corner of the world, posing threat to public health and ecosystems. Also, evidence has shown that even in sub-inhibitory level concentrations, antibiotics may still exert their impact on microbial community (e.g., by influencing transcription in microbes) (Davies *et al.,* 2006), and long-term effects of exposure to low concentrations of antibiotics are still largely unknown.

Investigating how antibiotics might act on aquatic photosynthetic organisms, a paper reported the effects of erythromycin and tetracycline on the growth of the cyanobacterium *Synechocystis* sp. and the duckweed *Lemna minor* (Pomati *et al.*, 2004a). The compounds were chosen as they were widely present in several types of European surface waters and sediments, with concentrations up to μg/L (Hirsh *et al.*, 1999, Zuccato *et al*., 2000). Significant differences were observed in their effects on *Synechocystis* and *Lemna*. While erythromycin affected the growth of both organisms, tetracycline had a slight inhibitory effect on *Synechocystis* and promoted growth in *Lemna* at the level of 10 μg/L.

Also many antibiotics, both human and animal are especially harmful to aquatic organism such as algae, *Daphnia*, and *Artemia* in freshwater and marine environments. In another such study conducted by Wollenberger *et al.,* (2000) acute and chronic toxicity of nine antibiotics used both therapeutically and as growth promoters in intensive farming was investigated on the freshwater crustacean *Daphnia magna*. The acute toxicities (48-h EC_{50} value, mg/L) in decreasing order were oxolinic acid (4.6), tiamulin (40), sulfadiazine (221), streptomycin (487), tylosin (680) and oxytetracycline (approx. 1000). No observed effect concentrations (NOECs) were 340 mg/L for tetracycline and 1000 mg/L for metronidazole and olaquindox. Toxic effect on reproduction occurred generally at concentrations, which were one order of magnitude below the acute toxic levels. The chronic toxicity (EC_{50} values, mg/L) in the *D. magna* reproduction test in decreasing order were tiamulin (5.4), sulfadiazine (13.7), tetracycline (44.8) and oxytetracycline (46.2). The NOECs (mg/L) obtained in the reproduction test with oxolinic acid, streptomycin, tylosin and metronidazole were 0.38, 32, 45 and 250 respectively. The observed toxicity of oxolinic acid to *D. magna* indicated that this substance, which is a commonly used feed additive in fish farms, has a potential to cause adverse effects on the aquatic environment.

In 2011, Zounkova *et al.* studied the ecotoxicity and genotoxicity of widely used veterinary antimicrobials oxytetracycline and flumequine with six model organisms (*Vibrio fischeri, Pseudomonas putida, Pseudokirchneriella subcapitata, Lemna minor, Daphnia magna* and *Escherichia coli*). *Pseudomonas putida* was the most sensitive organism (EC_{50} values for 16-h growth inhibition were 0.22 and 0.82 mg/L for oxytetracycline and flumequine, respectively), followed by duckweed *Lemna minor* (7-d growth inhibition, EC_{50} 2.1 and 3.0 mg/L) and green alga *Pseudokirchneriella subcapitata* (4-d growth inhibition, EC_{50} 3.1 and 2.6 mg/L). The least sensitive organism was *Daphnia magna* (48-h immobilization, lowest-observed effect concentration [LOEC] of oxytetracycline of 400 mg/L). Oxytetracycline showed limited genotoxicity (SOS-chromotest with *Escherichia coli*, minimal genotoxic concentration of 500 mg/L), and flumequine was genotoxic at 0.25 mg/L. González-Pleiter *et al.,* (2013) studied the individual and combined toxicities of five antibiotics (amoxicillin, erythromycin, levofloxacin, norfloxacin and tetracycline) in two organisms representative of the aquatic environment, the cyanobacterium *Anabaena* CPB4337 as a target organism and the green alga *Pseudokirchneriella subcapitata* as a non-target organism. It was found that the cyanobacterium was more sensitive than the green alga to the toxic effect of antibiotics. Erythromycin was highly toxic for both organisms; tetracycline was more toxic to the green algae whereas the quinolones: levofloxacin and norfloxacin were more toxic to the cyanobacterium than to the green alga. Amoxicillin also displayed toxicity to the cyanobacterium but showed no toxicity to the green alga.

5.2 Genotoxicity

Apart from ecotoxicity, another serious concern regarding the presence of antibiotics in the environment is their genotoxic effect on humans and organisms present in the environment. Although limited studies are available in this respect as it has recently caught the attention of the researchers. One of the early researches in this area was by Hartmann *et al.,* (1998), who suggested that ciprofloxacin in the hospital wastewater, detected at ranges between 3 and 87 µg/L was mainly responsible for observed genotoxicity. Another such study conducted in 1997 suggested that quinolones (pipemidic acid and norfloxacin) have the ability to induce point mutations using the Ames test and DNA damage on *E.coli* Pol A^-/Pol A^+ (Arriaga-Alba *et al.,* 1997).

In different studies, a number of antibiotics were found to be genotoxic. Antibiotics streptonigrin and streptozotocin were found to be genotoxic (Bolzán and Bianchi, 2001, 2002). Isidori *et al.,* (2005) tested genotoxic potential of six antibiotics (erythromycin, oxytetracycline, sulfamethoxazole, ofloxacin, lincomycin & clarithromycin). It was found that ofloxacin was the only genotoxic compound and sulfamethoxazole, ofloxacin and lincomycin were mutagenic. Different short term bioassays were used to determine the genotoxic potential of antibiotics. Kümmerer *et al.,* (2000) used SOS-Chromotest to determine the genotoxicity of antibiotics while micronucleus test on *Vicia faba* root was done to assess the genotoxicity of three antibiotics (nalidixic acid, ciprofloxacin and enrofloxacin) (Khadra *et al.,* 2012). The results showed that high concentration of the antibiotics resulted in significant micronucleus (MN) induction while low concentration resulted in non-significant MN induction. Also when a mixture of these three antibiotics was tested, significant MN induction even at low concentration (0.02 mg/kg) was observed indicating a clear synergism of these molecules on *Vicia faba* genotocixity. Therefore, a number of antibiotics like quinolones, floroquinolones, ofloxacin, lincomycin etc. were found to be genotoxic using a variety of animal and microbial assays. (McQueen *et al.,* 1991; Hartmann, 1998; Isidori *et al.,* 2005; Khadra *et al.,* 2012). Despite these studies, knowledge on the genotoxic potential of antibiotics is still limited.

VI. Conclusion And Future Scope:

Antibiotics pollution has been detected around the globe in almost all compartments of the environment. Major research studies and regulatory developments happened significantly in areas like North America, Europe and China. While much less information is available from other parts of the world like Africa, South America and other parts of Asia. So, a development of the world database with a wider range of climate ranging from tropical to arctic is necessary to carry out necessary steps in regulating and mitigating the pollution. WWTPs are considered as the most common source and pathway of antibiotic transport to surface water, ground water, drinking water, sea water and soil. Pharmaceutical manufacturing plants and hospital effluents are also a major source of antibiotics in local areas. Application of WWTPs sludge, sewage and manure to land has become a controversial issue as this activity leads to antibiotics entering into food chain via grazing animals and agricultural practices

The behaviour of antibiotics in conventional as well as advanced WWTPs is not completely understood despite identifying biodegradation, adsorption, ozonation and filtration as the major elimination pathways. Presently, very little information is available about the metabolites excreted by humans and transformation products in WWTPs. Identification of metabolites, transformation products and their potential ability to form more toxic products still needs to be studied. A concoction of parent compound, their metabolites and transformation products together with other toxic organic and inorganic compounds that are present in WWTPs and the biological potency of these mixtures is still an open question. Hence, the synergistic effects of these compounds altogether with other environmental conditions will have an entirely different toxic effect on non-target organisms.

The impact of antibiotics on the environment has become a major concern lately and therefore it is necessary to understand its interaction with the ecosystems. Most of these studies conclude that non-target organisms would be exposed to sub-lethal concentration which can likely cause any acute toxicity, but may induce toxicity at the cellular/DNA level. Hence, effects of the antibiotic stress on target organisms should be detected by using biomarker tools.

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