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Antibiotics in the environment: A review

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Abstract

Due to overuse and misuse of antibiotics in human medicines, veterinary medicines, agriculture, aquaculture and their persistence, before the covid-19 pandemic, antibiotics were considered as most emerging pollutants of the 21st century. Due to population growth, economic development and longevity during the last 25 years in the low and middle-income group countries the prescription and use of antibiotics have increased many folds. This results in presence of antibiotics in all the compartments of the environment i.e. surface water, groundwater, soil, milk, plants, vegetables, fruits and fish. Wastewater generated from hospitals, households, aquaculture is the hotspot of the residual antibiotics. Human health is adversely affected by consuming antibiotics contaminated plant and animal food and by drinking antibiotics contaminated water. Antibiotics not only causes the development of antibiotic-resistant bacteria and genes resistant to antibiotics but also affects the ecosystem, biogeochemical cycling, microbial growth and microbial population. The major threat to humans due to the indiscriminate use of antibiotics is the development of multiple antibiotic-resistant bacteria.

The concentration of the antibiotics in the aquatic environment, milk samples, plants, vegetables, and fruits consumed by humans and their impact on animals and humans are documented in this review.

Keywords: Antibiotics; Human; Environment; Milk; Vegetables; Fruits; Fish; Aquaculture

1. Introduction

Antibiotics which were first clinically used in the 1940s in the form of Penicillin are natural, semi-synthetic or synthetic compounds having the ability to stop infections caused by bacteria by either killing them(bactericidal); or preventing their reproduction (bacteriostatic) and supporting the body's natural defense to eliminate them. Technically antibiotics are compounds that in the living body can kill germs. Globally antibiotics are not only prescribed and used for the treatment of infectious diseases in humans and animals but are also used in livestock, aquaculture for their growth and meat production. Antibiotics affect biomass and enzymatic activities in the bacteria. The annual consumption of antibiotics in 2020 is approximately 1.8 lakh tonnes (China's contribution in the consumption is more than 55%) out of which approximately 1.31 lakh tonnes are used for the food animals (including fish), and it is estimated that by 2030 the global consumption of antibiotics will be approximately 2.37 lakh tonnes. United States of America, France, Italy are the main consumer of the high-income countries segment while in low and middle-income countries segment China, India and Pakistan are the main users. Globally till 2020 (before the Covid-19 pandemic), it was estimated that about 300 million people of the age group15-64 takes antibiotic at least once a year.

Due to misuse and overuse of the antibiotics by the clinical settings, private sector, primary healthcare providers and pharmacies the antibiotics residues and their metabolites are reported in all the compartments of the environment, viz., air, groundwater, surface water, soil, food chain, urine, breast milk, fruits, vegetables, cereals, grains, animal feeds by

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the number of food scientists which adversely affects the living organisms. In Pakistan, the inappropriate usage of antibiotics in the primary health care sector is about 88% [1] followed by China (61%) [2] and South Africa (55%) [3]. Globally, scientists are also worried about the impact of antibiotics on non-target organisms [4]. The presence of antibiotics in low amounts in the environment promotes the development of antibiotic-resistant bacteria [5]. So, now antibiotic residues in the environment are considered environmental pollutants [6]. Antibiotics even at a very low concentration impact nitrogen transformation, organic matter decomposition, sulphate reduction, nutrient cycle and methanogenesis in the environment [7-9]. World Health Organization before Covid-19 has reported that the occurrence of antibiotic-resistant bacteria and genes resistant to antibiotics are the most worrying health problems of the 21st Century [10-11]. Human resistance to bacteria *Staphylococcus* spp., *Salmonella* spp., and *Campylobacter* spp are due to consumption of animal origin antibiotics contaminated food [12].

The soil, which is the natural source for plant growth/food production is an integral part of the environment and ecosystem possess strong binding capacity acts as a sink for the antibiotics released in the environment [13]. Soil quality, which directly affects human health, food quality, and social development, is deteriorated by the presence of these undesirable organic chemicals beyond their normal concentrations [14-15]. Globally soil pollution is considered a major threat for the ecosystem as residues of the antibiotics in soil provides favourable conditions for bacteria to become antibiotic-resistant resulting in adverse immunological effects [16]. Accumulation of the antibiotics beyond their limit affects the soil enzyme activity, overall microbial activity and soil microorganisms' population, and nitrogen cycling and carbon mineralization. Due to water scarcity in low and middle-income countries untreated wastewater is used by farmers for agricultural usages which cause accumulation of the antibiotics in food plants/ crops [17] and leaching to groundwater.

This work aims to provide the latest review on the concentration of antibiotics in different environmental compartments.

2. Classification of Antibiotics

Antibiotics can be classified as:

2.1 Based on the chemical structure

2.1.1. Aminoglycosides

These antibiotics are used for septicaemia, urinary tract infection, ocular infection, severe pelvic inflammatory disease, Complicated skin, bone or soft tissue infection, Peritonitis and other severe intra-abdominal infections common examples are Garamycin, Gentamicin, Nebacin, Streptomycin, Zemdri.

2.1.2. Beta lactum

Used against bacterial infections, breast cancer, as anticancer commonly used are Penicillins, amoxicillin, Cephapirin, Cefuroxime.

2.1.3. Tetracyclines

Generally used against syphilis, endocervical, rectal, gonorrhoea infections. Chlortetracycline, Doxycycline, Oxytetracycline, Tetracycline is the most widely used tetracyclines.

2.1.4. Sulphonamides

Sulfadiazine, Sulfadimethoxine, Sulfadimidine, Sulfamethazine, Sulfamethizole, Sulfamethoxazole, Sulfapyridine, Sulphonamide are antibiotics that are prescribed for high blood pressure, diabetes, pain and inflammation.

2.1.5. Macrolides

Macrolides are used for Mycoplasma pneumonia, Cystic fibrosis, Rhinosinusitis, Pertussis, Diphtheria, Bronchiectasis, Pharyngitis, Tonsillitis, Acute exacerbation of COPD, Genital ulcer disease, COVID-19 etc, most commonly macrolide antibiotics used are Azithromycin, Clarithromycin, Erythromycin, Tylosin.

2.1.6. Quinolones

Quinolones are used for urinary, abdominal, respiratory tract infections and against STDs. Ciprofloxacin, Enrofloxacin, Norfloxacin, Ofloxacin are mostly used quinolones.

2.1.7. Lincosamides

These antibiotics are most effective against gram-positive bacteria and are used for persons which are allergic to penicillins. These antibiotics are also effective against pelvic inflammatory disease, abdominal infections, abscesses, acne, and anaerobic infections. Clindamycin, Cleocin, Evoclin Lincomycin, Pirlimycin are some examples of Lincosamide antibiotics.

2.2 Based on their spectrum

2.2.1. Narrow-spectrum

These are those antibiotics that are active against a selected group of bacterial types, act either on gram +ve or on the gram – ve but not on both. These antibiotics do not disturb beneficial bacteria. So, the collateral damage to the microbiota is minimum. These antibiotics have a very low tendency to develop antibiotic-resistant infections. Commonly used narrow-spectrum antibiotics are Azithromycin, Clarithromycin, Erythromycin, Clindamycin.

2.2.2. Broad-spectrum

The broad-spectrum antibiotics are effective against gram-positive, gram-negative bacterias and disease-causing bacteria. Broad-spectrum antibiotics have generally prescribed when either infection is caused by multiple bacterial groups or when the infection causing bacterial group is unknown. These antibiotics have a very high tendency to develop antibiotic-resistant infections. Besides ampicillin commonly used broad-spectrum antibiotics are Doxycycline, Minocycline, Aminoglycosides (streptomycin is the exception), Amoxicillin/ clavulanic acid, Piperacillin/tazobactam, Ciprofloxacin, Tetracyclines, Chloramphenicol Carbapenems, Trimethoprim /sulfamethoxazole.

Globally broad-spectrum antibiotics are mostly prescribed and used antibiotics.

3. Sources of the antibiotics in the environment

In the last 15 years for economic development, to feed the increasing population and to cure ageing citizens in low and middle-income countries the use of antibiotics has grown vastly. Antibiotics are the most prescribed medicines worldwide. In low and middle-income countries the antibiotics can be very easily procured from hospitals, pharmacies, drug stores, roadside stalls even from peddlers [18]. There are five different sources from which antibiotics enter the environment: a) humans b) animals c) agriculture d) aquaculture e) pharmaceutical industries. Almost 80-90% of the consumed antibiotics are excreted by humans/animals in the unaltered or as active metabolites via urine and faeces because of partial sorption by the guts of humans or animals and the antibiotics are released in waste system [19-20]. Improper disposal by the hospital, medicinal institutions, slaughterhouses, animal houses, dairy farms and household wastes, pouring of unused/ expired medicines in the drain, flushing in the toilet and waste dumping by the research institutions and drug manufacturing units, causes accumulation in large amount in wastewater. The sludge generated from wastewater contains antibiotics residues and globally are used as a soil conditioner in agricultural fields, the application of fertilizers, irrigation of crops by wastewater causes accumulation of the antibiotics in soils and plants/ edible parts. The leachate containing antibiotics from the soil after rainfall contaminates the groundwater. The main point source of the contamination of the environment by antibiotics is wastewater/ sewage sludge.

4. Antibiotics in the aquatic environment

Hospital, domestic and pharmaceutical industrial wastewater/ sewage water and effluent from landfills are the major entry sources of antibiotics in the aquatic environment. The concentration of the antibiotics in the wastewater depends on antibiotic properties and water solubility as most of the antibiotics cannot be evaporated and are water-soluble can be easily passed from wastewater to surface water, river water, groundwater and agricultural fields [21, 22].

With the increasing population and urbanization there is a stress on the water bodies and as assumed, by 2050 the global population will be about 9.8 billion and with 70% the urban population there will not only be very serious stress on the water bodies but in low-income group countries, it may also cause civil war. A survey of the literature denotes that concentration of the antibiotics in wastewater ranges from ng/L to 100 ug/L; in river water ranges from few ng/L to 2.5 mg/L; in hospital effluent the concentration of the single antibiotic ranges from 0.1 ng/L. to 62.5 ug/L. The effluents of pharmaceutical industries in developing and developed countries like India, China, the USA, Korea and Israel are contaminated with antibiotics ranging from ug/L to several mg/L [23] and it was also reported that the amount of the antibiotics on surface water bodies near pharmaceutical industries is more than in the blood of patients undergoing treatment.

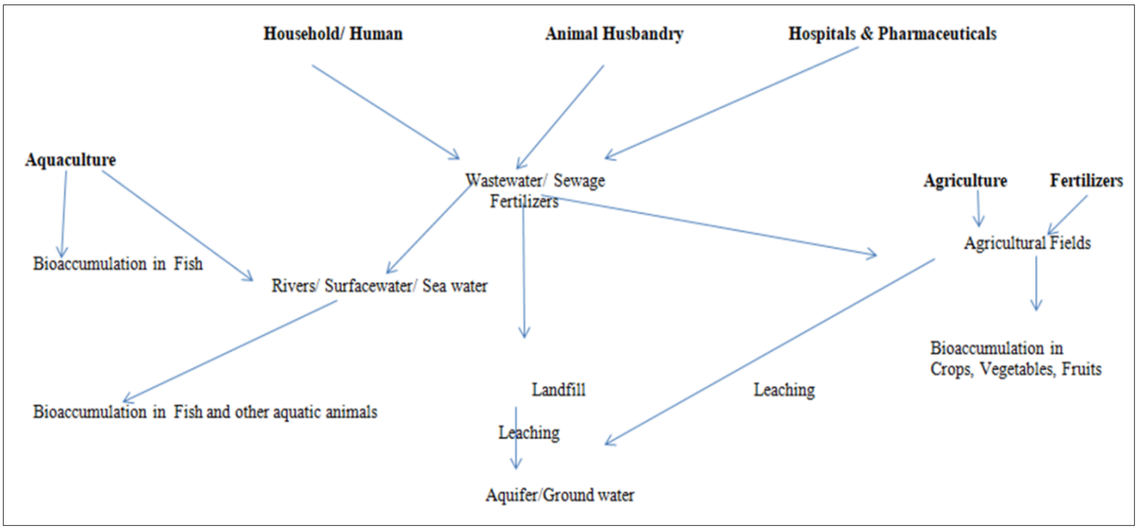

Figure 1 Sources of the antibiotics in the environment

Antibiotics in the aquatic medium adversely affect aquatic fauna/ flora (bacteria, fungi, algae, fish etc) and earthly organisms [24-25]. Antibiotics in the environment alter the ecological functions of the ecosystem; structure of the community also affects survival, reproduction, the population of the microbes. The development of the antibiotic-resistant bacteria and antibiotics resistant genes are the most serious impact on the environment and human health due to the occurrence of the antibiotics in the aquatic system. Wastewater became the hotspot for the bacteria to generate antibiotic-resistant genes if even the traces of antibiotics are in the wastewater.

The histopathological parameters of the host tissues are altered in presence of antibiotics. The concentrations of the antibiotics in the aquatic environments (wastewater, surface water, hospital effluents, river water, and aquaculture) are recorded in Table 1.

5. Antibiotics in the fish and other aquatic organisms

Due to the population increase, urbanization and economic development the production of fish, which is a major source of food for humans and the good source of animal protein, is growing rapidly worldwide. The average per capita consumption globally is approximate 21 kg [26] which was 9 kg in 2013. Antibiotics present in the aquatic medium are bioaccumulated in the aquatic biota especially in gills, liver, lungs and intestine of fish via organic matter, the food they consume [27-29]. Accumulation of antibiotics in fish damages cardiovascular, metabolic and developmental systems. Bioaccumulation of the antibiotics in fish organs causes' cellular damage by affecting the fish immunity system, antioxidant and detoxification processes induce oxidative stress which results in host-microbiota dysbiosis. The accumulation of the antibiotics in the fish initiates gluconeogenesis and anaerobic glycolysis (retards the aerobic glycolysis). The concentrations of antibiotics in fish are recorded in Table 1.

6. Antibiotics in the Plants and Vegetables

Since the early days of evolution vegetables and fruits are an essential part of the human diet as it provides essential nutrients. During the last two decades due to changes in dietary habits and population explosion, the demand for vegetables and fruits is increasing globally [30]. Due to scarcity of drinkable water, the wastewater (treated or untreated) in all the developing countries and some developed countries is used for irrigation of the agricultural fields. The literature denotes that approximately 20 million hectares of land are irrigated by raw wastewater or partially treated wastewater containing antibiotics, their metabolites, antibiotics resistant genes and genes of resistance to antibiotics globally. Livestock manures that contain unmetabolised antibiotics are amended in soils for essential nutrients in agriculture. Due to these anthropogenic resources, the vegetables and fruits are contaminated with antibiotics. Globally 10% of the world population consumes the food which is grown on the wastewater irrigated/ manure amended soils.

Table 1 Concentration of different antibiotics in sewage wastewater, hospital effluent, ground water, aquaculture water, river water, sediments and manure/compost

Compound	Wastewater/ Sewage water	Hospital Effluent	Freshwater/ Surface water	River water	Others	Vegetables/ fruits	Soil
Amoxicillin	172.6ng/L [42];62.5 ng/L (outlet) [42];17.7µg/L [43]; 13.8µg/L[43]; 0.0-33800ng/L [44]; 147-1670 ng/L [45]; 16.2-189 ug/L [46]; 0-5.9 ng/L [17]; 99400 ug/L [47];0-6940 ng/L [19]	0.16-0.79µg/L[48]; 0.001-0.023ppm [49]; 5.86µg/L[50]; 2-57ng/L [51]; 2.0-6.0 ng/L [17];0-900 ng/L [19]	0.06-0.36µg/L[48]; 4-17 ng/L[52]; 0.0-0.501 ug/L[20]; 0.0-1.3 ng/L [17]; 0-200 ug/L [19]	0.0-16.7ng/L [53]; 0.0-2.7ng/L [17]	Aquaculture- 0.0-0.06µg/mL [54]; 0-40 ng/L [51]; Milk- 68-802 ug/kg [55]	0.81-0.91 mg/kg[56] ; 13.7-33.6 ng/g (Lettuce) [18]; 14.3-45.2 ng/g (Carrots) [18]	
Ampicillin	139ppb[57];51-556 ng/L [17]; 75.4-1805 ng/L [58]; 70600 ug/L [47]; 23.5-263.3 ng/L [19]	131ppb[57]; 0.09-0.54 µg/L [48]; 0.001 - 0.024ppm [50]; 1.24 mg/L [59] 107-324 ng/L [17]	0.0-0.16µg/L[48]; 30-74 ng/L [17];16 ug/L [60]	40-164 ng/L [51]; 21-184 ng/L [17]; 0-13700 ng/L [19]	Aquaculture - 0.0-0.20µg/mL [54];Milk- 0.5-92 ug/kg [55]	12-22 ng/L [17]	
Azithromycin	160-1866 ng/L[61];112-274 ng/L [61]; 130-505.5 ng/L [62] ; 390 ng/L [63]; 0-592 ng/L [64]; 45.2-597.5 ng/L [65]; 1083ng/L [66]; 728-1890 ng/L[45]; 88-680 ng/L [67];3020-4120 ng/L [68]	85-113 ng/L [64]; 189-62507ng/L[69]	0.0-16.7 ng/L [70] ; 2356ng/L [69] ; 4.86-13.01 ng/L [1]; 0.61 ug/L [72]; 6810 ng/L [73]; 0.03 ug/L [74]	0.0-25.7 ng/L[70]; 0.0-67 ng/L [75]; 0.0-1620 ng/L [76]; 0-67 ng/L [64]; 240 ng/L [77]; 19-2270 ng/L [51]; 2819 ng/L [78]	Sediments- 43.2ng/g[78] Milk-9708.7ug/ kg [79]		
Carbamazepine	57-240 ng/L [80]; 0.04-378 ug/L [81]; 21-832 ng/L [82]; 940ng/L [63]; 60.58ug/L [83]; 132	0.54-2 ug/L [90]; 3ng/L [91]; 30-70 ng/L [88]	0.02-8.05ug/L [92]; 0.0-5.90 ng/L [70]; 566 ng/ L [93];0.42 mg/L [94]; 595 ng/L [95]; 1238	0.0-11.5 ng/L [70]; 1-30 ng/L [75]; 0.0-136 ng/L	Sediments- 6.35/g [78]	52ug/g (radish);33 ug/g (ryegrass)	

	ug/L [84]; 73-151 ng/L; 327-949 ng/L [45]; 43.4-672.5 ng/L [85];60-276000 ng/L [86]; 1035-11478 ng/L [87]; 0.30 ug/L [46]; 5-1680 ng/L [88]; 340-482.5 ng/L [89]		ng/L [69];0.01-4.5ug/L [96]; 12.6-659 ng/L [97]; 69 ng/L[98]; 229-390 ng/L [46]	[76]; 92-186 ng/L [93]; 72-1090 ng/dm^3[99]; 2-388 ng/L [100]; 8.8 ng/L [101]; 13.9 ng/L [102];1346 ng/L [103]; 14-2900ng/L [87]; 0-354 ng/L [78]		[104]; 1.7-216 ng/g dry plant weight [105];52 ug/g(Plant Leaves)[104]	
Cefadroxil	18.25ug/L[106]	3.24mg/L [59]					
Cefixime		10.85μg/L [50]					
Cefpodoxime		0.28mg/L [59]					
Cefprozil							
Cefuroxime	0.6μg/L [42]; 1.7 μg/L [43]; 49-24380 ng/L [97];58-1277 ng/L [17]; 0-9500 ng/L [19]	0.0-246 ng/L [51]; 1052-1557 ng/L [17]	21-65 ng/L 17]	195-7800 ng/L[51]; 32-868 ng/L [17];0-1700 ng/L [19]		11-27.3ng/g[17]	
Cephalexin Beta -lactum	0.0-3.23 ug/L [106]; 0.0-308.0 ng/L [97] 1020-5640ng/L [19]		11-29 ng/L [52]				
Chloroamphenicol	0.0-23ng/L [45]; 0.99 ng/L [108] ;400.2ug/L [107]; 3.30ug/L [109]	0.06-0.59 μg/L [48]	0.0-0.08μg/L [48]; 355 ng/L [110]; 0.36 ug/L [96]	0.70 ug/L [107]; 0.40 ug/L [96]	Aquaculture- 5-32ng/L[111]	6.2-142.1 ng/g [108]	1.0-10.5 ng/g [108]

Chlortetracycline	44µg/L [112]; 6.0-83 ng/L [17]; 0.14-420 ng/L [19]	0.37-17.7 ng/L [69] ; 16-24 ng/L [17]	8.4-15.4 ng/L[70]; 690 ng/L[69]; 690 ng/L[110];4.3-14 ng/L [17]; 0-600 ng/L [19]	8.8-19.7 ng/L [70]; 5.3-44 ng/L [17]; 0.10 ug/L [96]			120 ug/kg [113]; 2668.9 ug/kg [114]; 10967 ug/kg [115]; 222 ug/kg[116]; 1590.2 ug/kg [118]; 0.9 ug/kg [112]; 0.29-161.5 ug/kg [117]; 1.3-101.5 ug/kg (Farm soil); 1.3-4.3ug/kg (Organic farm soil); 1.4-4.9 ug/kg (Sewage sludge)[119]
Ciprofloxacin	1.5mg/L [43];1.4 µg/L [43];231-371 ng/L (Ghosh et al., 2016); 258-398ng/L [61]; 3.0-5.45 mg/L [32]; 41µg/L [51]; 45-260ng/L [80]; 211-630 ng/L [62]; 24000 ng/L [63]; 2180-5600 ng/L [83]; 27ng/L [120]; 222-27100 ng/L [121]; 38.4-584.9 ng/L [65]; 0.82-6453 ng/L [122]; 199-2950 ng/L [45]; 2.54-26.2 ng/L [123]; 446-1070ng/L [68]; 48-1450 ng/L[124]; 135-165.8	218-236 µg/L[127]; 0.07-0.08µg/L [48] ;1.35 mg/L [59] ; 0.03-125 ug/L [90] ;1.3-33.9ng/L [128]; 1.99ug/L[129]; 5329-7494 ng/L [121]; 1400-26000 ng/L [62]; 53300 ng/L [130];3.2-19715 ng/L [69] ; 11352-	0.0-0.06µg/L [48]; 0.2 ng/ [32]; 0.001-6500 ug/L [92];0-6500,000 ng/L [94]; 1.27 ug/L[20]; 0.85 ug/L [21]; 116ng/L [69]; 30 ng/L [110] ; 0.0- 323.7 ng/L [131]; 0.6-12ng/L [52]; 30.0-298.3 ng/L [71] ; 0.4-224.4 ng/L [108]; 1.27-1.344 ug/L [20]; 47-146 ng/L [17]; 15 ug/L [60]; 0.90 ug/L [132]; 0.01- 0.20 ng/L [32];14-15000900 ng/L [19]	10,000-2,500,000ng/L [94]; 5015 ug/L [133]; 6-20 ng/dm^3[99]; 14300 ng/L [121] 14.9-21.3 ng/L [134] 0.2-18.8 ng/L [108];25-1168 ng/L [17];0.50 ug/L[125]; 0-5015000 ng/L [19]	Aquaculture-250 ng/L[130]	1.2-545.2 ng/g [108]; 28.5-92.8 ng/g (Lettuce) [17]	0.3-18.2 ng/L [108]; 104.4 ug/kg [33]

	ng/L [89]; 0.9-99.3 ng/L [108];27-2371 ng/L [17]; 330.3-639 ng/L [65]; 0.07 ug/L [125]; 0.30 ug/L [107]; 0.01ug/L [126]; 0.82-4540000 ng/L [19]	15733 ng/L [17];0-15000 ng/L [19]					
Clarithromycin	1129-3077ng/L[61];377-762 ng/L [61]; 1-10ug/L [135]; 280-1213.5 ng/L [62]; 88 ng/L [63]; 60ng/L [91]; 38-83 ng/L [83]; 0.0-313.2 ng/L[65]; 0.0-122ng/L [66]; 33-501 ng/L [45]; 87-160 ng/L [67]; 0.01ug/L [126]	0.85-2 ug/L [90]; 1.51-159732 ng/L [69]	443 ng/L [95]; 72 ug/L [69]; 276 ng/L [29];8000 ng/L [73]; 0.30 ug/L [74]	0.9-1497ng/L [136]; 0.0-48 ng/L [75]; 2-21 ng/L [76]; 0.0-85 ng/L [70]; 1.1-8.3 ng/dm^3[99]; 159 ng/L [137]; 0.10 ug/L[96]			
Cloxacillin	0-320 ng/L [19]	0.31mg/L [59]					
Doxycycline	0-2.37 ng/ L [138]; 1.58-6.75 mg/L [32]; 1-11 ug/L [135] ; 5.3-9 ng/L [62] ; 1.8-264 ng/L [108]; 12.6 ng/L [89]; 1.8-264.4 ng/L [108]; 14-153 ng/L [17]; 119400 ug/L [47];100-10900 ng/L [19]	0.1-7 ug/L [90]; 24-120 ng/L [17]; 1.2-62.6 ng/L[69]; 1.20-32.8ng/L [89]	0-234ng/L [113]; 0-47.3 ng/L [139];0.48ng/L [140] 0.8ng/L[32]; 0.0-10.1 ng/L [70]; 80 ng/L [69]; 9.4-25 ng/L [17];0.04 - 0.8 0 ng/L [141]	0-103.1ng/L [142]; 10-110ng/L [29]; 0.0-12.8 ng/L [70]; 1.9-68 ng/L [17]; 32.9 ng/L [143]; 1.9-3.5 ng/L [108]; 8.3-68 ng/L [17]			0.23-13.5ug/kg [144]; 495ug/kg [115]; 870.5 ug/kg [118]; 105 ug/kg [145]; 365 ug/kg [[146]; 1.1-5.5ng/L [108];333.6 ug/kg [16]; 0.87-184.8 ug/kg [117]; 1.1--256 ug/kg (Farm soil); 0.8-

							1.94.3.3ug/kg (Organic farm soil); 0.8-21.5 ug/kg (Sewage sludge) [119]
Enrofloxacin	50-78ng/L [61]; 20-34 ng/L [61]; 28ng/L [37]; 0.86-3579.6 ng/L [108]; 400.2 ng/L [65]; 10-270 ng/L [19]	60-100 ng/L [19]	0-25,000 ng/L [94] ; 15ng/L [69]; 02-11.2 ng/L [108]; 60-100-181600 ng/L [19]	0-30,000 ng/L [94]; 2.9 ng/L [143]; 0.2-52.2 ng/L [108]	Aquaculture- 680 ng/L [130]	1.5-29.7 ng/g [108]; 78.8 ug/kg [33]	0.4-5.5 ng/g [108]
Erythromycin	0.14-10 ug/L [81]; 182.7 ng/L [62]; 7000 ng/L [63]; 9-249 ng/L [147]; 2.4-271.3 ng/L [85]; 18-359 ng/L [148]; 47-1931 ng/L [17]; 0.01ug/L [126]; 12-4740 ng/L [19]	0.001-0.008 ppm [49]; 27-83 ug/L [90]; 7.2 ug/ L [129]; 1200 ng/L [130]; 0.01-101 ng/L [69]; 7944-10613 ng/L [19]	0.0-27.69 ng/L [70]; 137 ng/L [95]; 438 ng/L [69]; 0-568 ng/L [149]; 1.00 ug/L [96]; 57.6 ng/L [150]; 6.7-136ng/L [17]; 13.6- 20 ug/[64];1.41-15.9 ng/ [19]	0.7-85.3ng/L [22]; 0.0-63.7 ng/L[70]; 9-423 ng/dm^3 [99]; 24-145 ng/L [77]; 1.9 ng/L [137]; 32.9-38.8 ng/L [151] ;7.0-1149 ng/L [17]; 1.0 ug/ [96]	Aquaculture- 4 ng/L[130] 5.5-57.4 ng/L[152]	41.4-56.7 ng/g [17]	
Florfenicol	2.4-6.8 ng/L [108]; 3.30ug/L [109]		3.3-26.1 ng/L [108]	1.6-15.3 ng/L [108]			
Fluoroquinolone					Fish- 38-81 ng/g w/w ; 0-15 ng/g w/w (Biota); 92-330 ng/g w/w		

					(Invertebrates)[28]		
Gatifloxacin	3.7µg/L [42];0.48 µg/L [43]); 0-840 ng/L[19]			0-42 ng/L [19]			
Levofloxacin	532-1425ng/L [61]; 600-6800ng/L[61];0-6.2mg/L [32]; 41.75 ng/L [62]; 5-2247 ng/L [153]; 38.2 ug/L [46]; 0.5-19981.6 ng/L [108]; 1.60 ug/L [107]; 86700 ng/[19]	0.414 ug/L [20]	5-2247 ng/L [153]; 0.0474-0.209 ug/L [20]; 0.020-0.123 ug/L [20]; 0.02- 0.20 ng/L [141]; 414 ng/[19]	0.0-10.5 ng/L [154]; 0.3-6 ng/L [108]; 0.04 ug/L [107]	Milk-87.4 ng/L ; 5-2247 ng/L [153]		0.2-6.5 ng/g [108]
Lincomycin	37-54ng/L [61]; 884-1136 ng/L[61]; 15.2-730 ng/L [19]	0.3-2 ug/L [90]	860.7ng/L [155]; 0.0-40.5 ng/L [70]; 730ng/L[69]; 730 ng/L [110];339-2840ng/L [150]; 3.13-248.9 ng/L [19]	0.0-59.2 ng/L [70]; 20-24.4 ng/dm^3[99]; 10.1ng/L [143]	Aquaculture-2.9-226 ng/L [152]		
Metronidazole	28 ng/L [62]; 0.0-93.2 ng/L [65]; 13-392 ng/L [45];0.6-1.45 ng/L [108];3-24ng/L [17]; 3 ug/L [107]	0.1-90 ug/L [90]; 130400 ng/L [130]; 247-420 ng/L [17]	5.46 ug/ L [129]; 3-33 ng/L [17]; 0.2 ug/L [64]	0.4-1.6 ng/L [108];0-363 ng/L [17] ; 4 ug/L [107]		13.5-44 ng/g [17]	
Nalidixic acid	68-79ng/L [61];224-358ng/L [61] ; 0.0-50.3 ng/L[65]; 2.80 ug/L [107]		23.516 ug/L [60]	3 ug/L [156]			
Norfloxacin	155-514ng/L [61]; 2554-2775ng/L [61];20.6-150 ng/L [62]; 0.0-5411 ng/L [122]); 0.6-24.6 ng/ [108]; 11.1-18200ng/L [19]	0.03-44 ug/L [90] ; 0.8- 4.4 ng/L[128]; 3300-37000 ng/L [62];1500 ng/[130]; 90-1620 ng/L [19]; 0.037	441.9 ng/l [157]; 0.004-520 ug/L [92], 0.0-520,000ng/L [94]; 120ng/L [69]; 0.0-367 ng/L [131]; 0.7-4 ng/L [52] ; 0.4-3.6 ng/L [108]; 30-25100 ng/L[19]	.0-4700 ng/L [94]; 251 ug/L [133]; 40-88 ng/dm^3 [99]; 0.0-518 ng/L [158]; 0.2-78.1 ng/L [108]; 0.87-	Aquaculture-6060000ng/L [130]	2.1-145.7 ng/g [108]; 18.2-658.3 ug/kg [33]	0.2-4.6 ng/L [108]; 65.8 ug/kg [33]; 1.5-102 ug/kg (Farm soil); 1.4-83.4ug/kg (Organic farm

		ng/mL (urine) [157]		6800 ng/L [19]			soil); 1.0-15.3 ug/kg (Sewage sludge) [119]
Norfluoxetine	0.0-10.4ug/L [159]						
Ofloxacin	2.88-384 ng/L[123];0-12.4 ng/L [138]; 400 ng/L [62]; 2.45-4.12 mg/L [32];85µg/L [51]; 0.0-305.1 ng/L[65]; 11.1-1330 ng/L [160]; 497 ng/L[161]; 2936.9 ng/L [162]; 37-1470 ng/L [124]; 81000ng/L [163]; 175-529 ng/L [65]; 0.01ug/L [126];0.14-420 ng/L[19]	1.199mg/L [155]; 23-510 ng/L [62] ; 19800 ng/L [130]; 0.28mg/L[59]; 3400 ng/L [164,165]; 0.35-35 ug/L [90]; 0.9-27.1 ng/L[128]	0.3-990ng/L [113];0.0-182.7 ng/L[139]; 0.0003-17.7 ug/L [92];43.5 ng/L [150];1547-4778ng/L [166] ; 0.0-80ng/L [140]; 1199.7 ng/L [155]; 2.1-26.4 ng/L [70]; 0-11,000 ng/L [94]; 0.0-503 ng/L [131];0.01- 0.50 ng/L [141];0-488 ng/L [19]	0.7 ng/L [167] 308 ng/L [114]; 8-23 ng/L [67];; 23-85190 ng/L [51];53-108ng/L [150]; 6.0-36.7 ng/L [70] ; 180-10,000ng/L[94]; 542.4 ug/L [133]; 0.0-6.4 ng/L[168]	Aquaculture-238.6 ng/L [130]		1.1-66.5 ug/kg (Farm soil); 1.9-41.5ug/kg (Organic farm soil); 1.5-49.8 ug/kg (Sewage sludge [119]
Ox tetracycline	664-841 ppb [57]; 9µg/L [112];9.4 mg/L [32];4.3-233 ng/L [17] ; 230 ng/L [98]; 1880 ng/L [150]; 204-233 ng/L [18]; 0.2-47000 ng/L [19]	3200 µg/L [127]; 0.01-4 ug/L [90] ; 75-1487 ng/L [17]; 0.38-31.3 ng/L; 75-252 ng/L [17]	0.4ng/L [141]0.0-30.5 ng/L [70]; 1340ng/L [69];2.2-9.2 ng/L [17]; 150ug/L [169]; 0.02-0.40 ng/L [141] ;110-4200 ng/L [19]	12.4-26.3 ng/L [70]); 3-26 ng/L [17]; 0.10 ug/L [96]	Aquaculture-0.056-0.234 µg/mL [54]; 75 ng/L [152] Milk- 223 ppb [57] ; 1.5µg/kg [112] Fish- 389-641ng/g (Rainbow Trout liver); 175-295 ng/g (fillets) [27]		1.0-8400 ug/kg (Farm soil); 2.0-47.3ug/kg (Organic farm soil); 1.7-33.6 ug/kg (Sewage sludge) [119]
Penicillin	0.0-160 ng/L [170] ; 20-13800 ng/L [19]	0.85-5ug/L [90]; 0.13 ng/mL (urine) [157]	1.8-5.9 ng/L9]		Milk-15.22 ug/L [171] ; 13-353 ug/kg [55]		0.15-59.6ug/kg [144]);423 ug/kg

							[113]);613.2 ug/kg [114];571.4 ug/kg [115]; 415 ug/kg [116]; 1398.5 ug/kg [118]; 530 ug/kg [145]; 0.7 ug/kg [112]; 200 ug/kg [172]; 338.3 ug/kg [16];0.04-31.85ug/kg [117]
Roxithromycin	234-388ng/L [61];554-785ng/L [61];1.5-290 ng/L [62]; 1.9-269 ng/L [85];870-1500 ng/L [19]		180ng/L [69]; 480 ng/L[98]	0.3-66.5ng/L [22]; 1.4-190 ng/L [67]; 0.02 ug/L [96]			0.1-4.8 ug/kg (Farm soil); 0.1-5.0ug/kg (Organic farm soil); 0.1-1.4 ug/kg (Sewage sludge) [119]
Sparfloxacin	0.5µg/L[42]; 2.1µg/L [43]; 19000 ng/L [163];0-63200 ng/L [19]			0-2090 ng/L [19]			
Streptomycin	0.0-2700ng/L [109]			Sea water-0.0-3400ng/L Organohalogen Compounds Vol. 75, 538-541 (2013)			

				[109]			
Sulfachloropyridazine							52.9 ug/kg [115]; 200 ug/kg [172]
Sulfadiazine	0.28-71.8 ng/L[138]; 1.22-41.0 ng/L[85]; 1.8-57 ng/L [67];10-37 ng/L (agricultural leachate) [173]	0.001-0.003 ppm [49]	0-520ng/L [113]; 0-45.6 ng/L [139];9-137ng/L [166];12 ng/L[174]	0.58 ng/L [99]; 0.93-68 ng/L [67]; 0.04 ug/L [96]	Aquaculture-164-3941 ng/L [37] Milk-0.001-0.004 ppm [49]		1.5-20.1 ug/kg (Farm soil); 0.5-0.9ug/kg (Organic farm soil); 1.70.5-0.9 ug/kg (Sewage sludge) [119]
Sulfadimethoxine	0.2-350 ng/L [19]		15,000ng/L [69]; 35-60 ng/L [19]		Milk-31-69 ug/kg [55]		
Sulfadimidine	0.53-89.1 ng/L [138]		0-123ng/L [113]; 0.0-9.9 ng/L [139]; nd-113ng/L [175]; nd-49ng/L [140]	0-1080ng/L [150]; 0.01 ug/L [96]			0.11ug/kg [118];0.06-6.04ug/kg [144]; 0.6-3.0 ug/kg (Farm soil); 0.6-1.3 ug/kg (Organic farm soil); 0.9-1.3 ug/kg [119]
Sulfadoxine	3.20 ug/L[107]			1460 ug/L [107]			
Sulfaguinidine	72-234ng/L (agricultural leachate) [173]						
Sulfamerazine			1.5ng/L [69]; 0.7-1.2 ng/L [176]				3.1 ug/kg [118]; 0.7-2.9 ug/kg (Farm soil); 0.8-3.7ug/kg

							(Organic farm soil); 0.8-3.4 ug/kg (Sewage sludge) [119]
Sulfamethadiazine			0.0-23.5 ng/L [70]	0.0-20.6 ng/L [70]			
Sulfamethazine	9.6 μg/L[112]; 3.2-586 ng/L [45]; 132 ng/L [88]; 10-92 ng/L (agricultural Leachate) [173];1.1-1500 ng/L [19]	19153 ng/L [130]	0.0-25.7 ng/L [70]; 220ng/L [69]; 12 ng/L [174];4.6-33ug/L[64];20-120ng/L[19]	0.0-14.1 ng/L [70]; 360 ng/L [88] 0.60 ug/L [107]	Aquaculture-29-180 ng/L [37]; 2 ng/L [130] Milk- 0.05 μg/kg [112]	0.1-1.2 mg/kg in Plant tissue [56];0.01 ug/g (radish);0.01 ug/g (ryegrass) [104]	1.7 ug/kg [113];177.9 ug/kg [115];258 ug/kg [116];11.5 ug/kg [118];0.6 ug/kg [145]; 1.1 ug/kg [112]; 20.4 ug/kg [177]; 100 ug/kg [172]; 1.3-101.5 ug/kg (Farm soil); 0.7-1.3ug/kg (Organic farm soil); 0.5-1.6 ug/kg (Sewage sludge) [119]
Sulfamethizole	10 μg/L[112]; 11-480 ng/L [148];300-350 ng/L [19]	0.03-8.55 ng/L [69]	130ng/L [69]				0.10-0.66 [144];1.2 ug/kg[113];58.1 ug/kg [115];9.3 ug/kg [116]; 1.1 ug/kg

							[112]; 2.6 ug/kg[177]
Sulfamethoxazole	0.23-1.02µg/L [178-180]; 0.16-0.9 µg/L [181]; 0.4 µg/L [112]; 0.3-36.38 ng/L [138];159-174ng/L [61];1044-1280ng/L [61]; 252 µg/L [51];62.1-88.8ng/L [54]; 5--15 ug/L [135]; 0.003-0.98ug/L [81]; 10-57ng/L [145]; 162 ng/L [63];30-132 ng/L [83]; 59.3 ng/L [120]); 98-2200ng/L [182]; 7.8 ug/L [183]; 0.0-68.5ng/L [65]; 19-43 ng/L [67]; 26-633 ng/L [148]; 1520ng/L [184];12.6 ug/L [46]; 156-984 ng/L [88]; 0.6-20.9 ng/L [108]; 27.8 ug/L [185]; 14.6 ug/L in agricultural wastewater [185]; 103-7194 ng/L [17]; 3 ug/L [125]; 10 ug/L [107]; 0.01ug/L [126;0.4-2260 ng/L [19]	4.6 µg/L [127];0.06-0.12µg/L[48]; 0.001-0.018 ppm [49]; 0.04-83 ug/L [90]; 65- 9800 ng/L[182]; 20.6 ug/L [183]; 20300 ng/L [130]; 0.15-373 ng/L [69]; 1335 ng/L [88]; 2315-3590ng/L [17];100-300 ng/L [19]	0-650ng/L [113]; 0.0-171.6ng/L [139]; 13-149ng/L [75]; 0-250 ng/L [140]; 0.0-0.08µg/L [48]; 0.001-29 ug/L [92]; 0.0-44.4 ng/L[85]; 0.17 mg/L; 1.40 mg/L [94]; 1.25 ug/L [21]; 1900ng/L [69]; 6 ng/L [120]; 608 ug/L [183]; 0.3-18.6 ng/L [108]; 1.50-2.93ug/L [96]; 0.6-2 ng/L [52]; 380 ng/L [98];25.7 ng/L [150]; 727-772 ng/L [46]; 1.7-300 ng/L [88]; 0.3-18.6 ng/L [108]; 11-56 ng/L [17]; 6-7.3 ug/L [64]; 1.31 ug/L [74]; 290ug/L[186];0-2000 ng/L[19]	2.2-764.9ng/L [142]; 0.0-68ng/L [136]; 0.0-42.6 ng/L [70]; 0.0- 56 ng/L [75]; 10-110 ng/dm^3 [99] ; 60-80ng/L [182]; 10-252 ng/L [51]; 320 ng/L [102]; 106.7 ng/L [137]; 0.3-13 ng/L [108]; 13-2861 ng/L [17]; 950 ng/L [174]; 14 ug/L[[125]; 40 ug/L [107] ; 1.50 ug/L [96];3.1-13700 ng/L [19]	Aquaculture-0.0-0.05µg/mL [54]; 2390000 ng/L [130]; 2.2-23.2 ng/L [152] Milk-0.7 µg/kg [112]; 0.001-0.002 ppm [49]	5.26 ug/Kg [187]; 1.06-1.89mg/kg [56] Roots of radish; 11.2-21.4 ng/L [17]	6.7 ug/kg [118]; 0.12-2.8 ug/kg [144]; 5.26 ug/Kg [187]; 0.4-3.1 ug/kg (Farm soil); 0.4-0.9/kg (Organic farm soil); 0.4-0.6 ug/kg (Sewage sludge) [119]
Sulfapyridine	0-210ng/L [138]; 400 ng/L [37]; 4.7-112 ng/L [65];0.4-2.2 ng/L [108]		0 -510ng/L [113];0.5 ng/L [108]	1.4-112.5 ng/L [142]; 121ng/L [53]; 0.2-3.1 ng/L [108]			

Sulfamethoxypyridazine	92-905 ng/L [[37]						
Sulphaquinoxaline	104-337 ng/L [37]						
Sulphonamide	2.8 ug/L [183]	15.7 ug/L [183]	0.4 ug/L [183]		Milk-2.5 ug/kg [188]; Fish-120-210 ng/g w/; 19-451 ng/g w/w (Biota); 68-140 ng/g w/w (Invertebrates) [28]		19.7 ug/kg [16]
Tetracycline	254 μg/L [112]; 23 ng/L [62]; 45.4 ng/L [120]; 0.0-231.2 ng/L [65]; 11-199 ng/L [17]; 0-48000 ng/L [19]	0.0-0.001 ppm [49]; 0.01-4 ug/L [90]); 13-1598 ng/L[17]; 100 ng/L [130]; 58-116 ng/L [17]; 0-80 ng/L [19]	0.0-14.7 ng/L [70]; 1.30 ug/L [21]; 140ng/L [69]; 11-16 ng/L [17];110-4200 ng/L [19]	0.0-18.9 ng/L [70]; 14 ng/L [33]; 11-30 ng/L [17]; 0.10 ug/L [96]; 31-25500 ng/L [19]	Aquaculture-180 ng/L[189]; 0.012-0.112μg/mL [54] Milk- 5460 ug/kg [79];16-134.5 ug/kg [190]	4.4-28.3 ng/g (Lettuce) [18]; 12-38.6 ng/g (Carrots) [18]	9.7 ug/kg [118];0.1-0.235 ug/kg [113];2.4-3.8 ug/kg [172];22 ug/kg [157]; 189.8 ug/kg [114]; 153 ug/kg [115]; 60.4 ug/kg [116];976.2 ug/kg [118]; 197 ug/kg [145]; 177.6 ug/kg [112]; 600 ug/kg [172]; 949.4 ug/kg [16]; 0.16-25.66 ug/kg [117]; 0.5-9.7 mg/kg 173]; 1.0-249

							ug/kg (Farm soil); 1.1-2.9ug/kg (Organic farm soil); 1.0-22.1 ug/kg (Sewage sludge) [119]
Tindidazole		0.26 mg/L [59]					
Trimethoprim	121-165ng/L [61]; 1088-1578ng/L [61];107µg/L [51]; 24.71-24.99 ng/L [54];23-552ng/L [37]; 0.06-6.8 ug/L[81]; 265 ng/L [63]; 2.6 ug/L [183]; 15.2-190.6ng/L [65]; 42-635 ng/L [45]; 4500 ng/L [98]; 33-788 ng/L [148]; 31-1668 ng/L [17];0.07 ug/L [125]; 4 ug/L [107];1.93-4010 ng/L [19]	2.2 µg/L [127]; 0.01-15 ug/L[90]; 6.6 ug/L [183]; 7100 ng/L[130]; 0.06-273 ng/L [69];94-4826 ng/L [17]	0.004-13.6 ug/L [92]; 0.0-15.3 ng/L[70]; 0.018mg/L [95], 8.0mg/L [94]; 710ng/L [69]; 0.4 ug/L[183]; 0.40-5.5 ug/L [96]; 1-7 ng/L [52]; 274-633 ng/L [46]; 6000 ng/L [73];0.8- 3.7 ug/L [64]; 1.20 ug/L [74];3-710 ng/L [19]	0.0-20.2 ng/L [85]; 3-26 ng/L [[75]; 0.0-9 ng/L[76]; 5-100 ng/dm^3[99]; 17.2 ng/L [101]; 196 ng/L [137]; 16-106.5 ng/L [51]; 19-98 ng/L [17]; 2.70 ug/L [125]; 7 ug/L [107]; 0.40 ug/L [96];17-4000 ng/L [19]	Aquaculture-1040000 ng/L[130];1.5-94 ng/L [152]; 17-820 ng/L [17])	3.40 ug/kg [187]; 32.7-104 ng/L [17]; 2-17 ug/kg in plant tissues [56]	0.62 ug/Kg [187]

Antibiotics are translocated from soils to the edible parts of vegetables (fruits, leaves, stems, tubers) through xylem and phloem [31]. Hussain et al [32] during their research studies found that wheat, spinach and carrot samples were contaminated with levofloxacin, ofloxacin, oxytetracycline and doxycycline. They also found that accumulation of the antibiotics was maximum in the leaves part and minimum in the fruit part and the order of accumulation was leaves > stem/shoot > root > fruit. Li et al., [33] during their work on fluoroquinolones found that accumulation of the fluoroquinolones was more in the solanaceous fruits than the leafy vegetables. Table 1 denotes the amount of antibiotics accumulated in the plants, fruits and vegetables.

7. Antibiotics in the Milk

With the increasing population, economic prosperity and change in dietary habits milk consumption per capita in both developed and developing countries are increasing, to cater for this demand the use of veterinary medicines for therapeutic and prophylactic purposes for farm animals is also increasing. This results in the global presence of antibiotics in the most of the Milk samples, dairy products and dairy wastes. India is ranked first in milk production and contributes approximately 18% of total global milk production. Several researchers [34-36] have reported antibiotics in milk and dairy products beyond the permissible limits. β –lactum antibiotics are found in approximately 12 % milk samples of the United Kingdom and 11% milk samples of the USA.

If the antibiotics contaminated milk, cheese and Yoghurt are consumed by a human for a longer period microflora of the intestine become antibiotic-resistant. Consumption of antibiotics contaminated milk in humans cause allergies, alteration in intestinal function [37, 38].

Photosensitivity reaction, pigmentation on nails and discolouration of teeth occurs in humans when the tetracyclines contaminated milk is consumed for a longer period, while consumption of chloramphenicol contaminated milk causes optic neuropathy, brain abscess [39]. The cardiovascular and immune system in the citizenry is affected by azithromycin contaminated milk. β –lactum contaminated milk causes food allergic reactions e.g. urticarial, anaphylaxis, bronchospasm, haemolytic anaemia, thrombocytopenia, acute interstitial nephritis, serum sickness, Stevens-Johnson syndrome; toxic epidermal necrolysis [40, 41] The data of the concentrations of the antibiotics in the milk samples are reported in Table 1.

8. Conclusion

- Antibiotics are considered the most toxic pollutants of the 21st century as they are present in all the compartments of the environment (groundwater, surface water, river water, hospital effluents, soil, manure, milk, vegetables, crops fruits and fish).
- In manure and biosolids, the concentration of the antibiotics ranged in ug/g level. River water near pharmaceutical industries contains antibiotics up to mg/L.
- In the agro-system, antibiotics are introduced via manure amendments and irrigation by contaminated wastewater and impacts ecological balance in soils.
- As the antibiotics contain hydroxyl, carboxyl, amine groups glycosylation of the antibiotics in the plants occurs.
- Wastewater is mainly responsible for the development and selection of antibiotics resistant bacteria and the transfer of antibiotics resistant genes.
- Globally antibiotics are bioaccumulated beyond their permissible limits in the liver and fillet part of the most consumable fish (rainbow trout)
- Ingestion of the antibiotics via animal and/or plant-based food and drinking of antibiotics contaminated water impacts human health. Besides the production of antibiotic-resistant bacteria and genes resistant to antibiotics, the uptake of the antibiotics causes allergies, alteration in intestinal function, optic neuropathy, brain abscess, urticarial, anaphylaxis, bronchospasm, haemolytic anaemia, thrombocytopenia, acute interstitial nephritis, serum sickness, Stevens-Johnson syndrome; toxic epidermal necrolysis in human.

Future Suggestions

- It is a need of the hour to develop effective technology to remove antibiotics from wastewater.
- Efforts must be made to remediate antibiotics from hospital effluent, veterinary effluents and poultry effluent before entering into the wastewater.
- Efforts must be made to create awareness to the citizenry regarding the negative impacts of antibiotics and their misuse must be minimised.

Compliance with ethical standards

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Disclosure of conflict of interest

No Conflict of interest.

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