

Open Access

Pharmaceutical Substances in India are a Point of Great Concern?

Senthil Kumar Kurunthachalam*

Avinashilingam University, Coimbatore 641043, Tamil Nadu, India

The annual global pharmaceutical trade is worth about 300 billion US\$, this number is projected to increase to 400 billion US\$ in the span of 3 years [1]. India's 3.1 billion US\$ pharmaceutical industry growth rate is 14% per year. After North America and Europe, India has a third largest pharmaceutical industry in the world and its turnover rate is expected to touch 74 billion US\$ per year by 2020 [2]. Consequently, India can be considered "is the country of great concern" in terms of pharmaceutical substances related issues. Because pharmaceutical substances are wide array of complex chemical formulations and are very synthetic in nature and tend to react within the environment. The major environmental pharmaceutical substances are; antibiotics (e.g., enoxacin, gentamicin, neomycin, ciprofloxacin), antidepressants (e.g., citalopram, escitalopram), analgesics (e.g., paracetamol, ibuprofen, diclofenac), beta blockers (e.g., atenolol, metoprolol), anti inflammatory (e.g., naproxen, aspirin), narcotics/anesthetics (e.g., propoxyphene, morphine, heroin), antimycotic (e.g., terbinafin, clotrimazole, miconazole, fluconazole, amphotericin), antihistaminic (e.g., cetirizin, benadryl, tavest, drixoral), hormones, vitamins and supplements (e.g., zostavax, golimumab, ascorbic acid 'vitamin C', biotin 'vitamin D', antioxidants 'vitamin E', carotinoids 'vitamin A'), cholesterol, lipid regulators and triglycerides reducers (e.g., gemfibrozil, lipitor, zocor, vytorin), birth control pills (e.g., demulen, desogen, norinyl, yasmin), and sexual stimulators (e.g., cialis, viagra, kamagra, penegra). The studies demonstrated that very high concentrations of antibiotics and antibiotics resistant bacteria were found in effluents from a sewage treatment plant in India. Particularly, high concentrations of terbinafin, citalopram, cetirizine, ciprofloxacin and enoxacin were found in drinking water [3].

Pharmaceutical chemicals play a significant role in modern history of humans and veterinary sector by providing an ideal health in prescription drugs, over the counter (OTC) therapeutic drugs as well as medicine for veterinary. The Indian pharmaceutical industry is also one of the very familiar sectors of the global terms due to their cheap production and marketing. Therefore, Mr Jim Worrell a chief executive of Pharma Services Network, North Carolina in USA pointed "There is a lot of good talent at a much lower price in India, What I see happening now is manufacturing and even packaging and even formulation is moving to India". Furthermore, innovative technology with low cost production, skilled human power, operations, and potential in the design of high technology makes India a center of attraction also in pharmaceutical part of the world. Therefore, India is considered to be a potential global outsourcing hub for pharmaceutical products accompanying with China and Israel. The water quality monitoring for the year 1995-2009 conducted by the Central Pollution Control Board indicated organic, inorganic and bacterial contamination was critical in the water bodies of India [4]. The main cause of water contamination is due to the domestic and industrial wastewater mix in the environment without pass through treatment plants as only 31-32% of the wastewater gets treated (except Delhi and Mumbai in which 69% of wastewater gets treated). So, Is the toxic impact of pharmaceutical substances a point of major concern in India? "I would say, YES" despite of the fact that current levels in general environment are still probably low. However, we cannot ignore the levels in hot spot/point source regions such as hospital waste/discharge, and sewage treatment plants since the direct impact can be found in hospital from the former and the entry of the substances in drinking water from the latter.

India has shown to be a breeding ground for around 50 drug resistant microbes ("super bugs" or "genetically modifying microbes") due to extensive usage and improper disposal of pharmaceutical drugs into the environment [5]. The "super bugs" were found in patient blood and urine from more than 40 countries including India [5]. Furthermore the tropical, hot and humid weather in India would provide an ideal condition for several microbial species' development. Based on our research in India (led by Dr. K. Kannan from Wadsworth Health Center, NY, USA and co-investigator Dr. N. Yamashita from AIST, Tsukuba, Japan), we found high occurrence of pharmaceutical drugs in drains, sewerages and rivers and they signalled to be future disaster [6]. Also our team found out there is no medicine developed for the disease arises from the genetically modified bacteria. Elevated occurrence (31,000 μ g/L) of an antibiotic ciprofloxacin in a waste water treatment plant in Patancheru, India had been already reported [7]. Further, in India, bacteria resistant to ciprofloxacin have been found downstream pharmaceutical plants, genes for multi resistance were found in drinking water, and multi resistant Salmonella in water sprayed on vegetables. Besides, the analgesic diclofenac causes kidney failure in Indian vulture and therefore, population was declined drastically. All these information suggests that pharmaceutical drugs in India were well spread in several environmental as well as biological media.

Pharmaceutical chemicals can enter in to the environment by number of passage such as 1) from low cost pharmaceutical production industries in developing countries such as India (production sites in India showed elevated antibiotics concentration from the surface waters) and China; 2) direct and improper disposal by patients/ humans by unused/expired medications in to the trash and through the excretion of urine or faeces (Significant amount of pharmaceutical drugs were observed in sewage treatment plants are mainly from the human excretion because majority of them are not metabolized in the body and they may be excreted via the urine. Besides, several of pharmaceutical drugs have less assimilation capacity in the intestine to the bloodstream passage and rejected fraction will end up in the gut and finally excreted via feces); 3) release from hospital waste/trash; 4) disposal by pharmacies; 5) veterinary use as medicine as well as additives to animal food; which is excreted into soil or surface waters (such exposure may affect terrestrial organisms directly, which endanger an exposed animal/species); 6) dairy waste disposal; 7) household water/

*Corresponding author: Senthil Kumar Kurunthachalam, Visiting Professor, Avinashilingam University, Coimbatore 641043, Tamil Nadu, India, E-mail: kuruntha@gmail.com

Received September 22, 2012; Accepted September 25, 2012; Published September 27, 2012

Citation: Senthil Kumar K (2012) Pharmaceutical Substances in India are a Point of Great Concern? Hydrol Current Res 3:e103. doi:10.4172/2157-7587.1000e103

Copyright: © 2012 Senthil Kumar K. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

sewage, solid garbage mix with drug surplus; 8) leaching from defective landfills; 9) release from aquaculture which has medicated feed as well as excretion from the aquaculture; 10) release from molecular farming/ pest control drugs; and 11) disposal of euthanized/medicated animal carcasses, etc.,

Pharmaceutical substances are tended to dissolve readily with any media, shown to evaporate in normal temperature and end up in soil and aquatic ecosystems. Several of analgesics, antibiotics and anti-neoplastics are non-volatile and polar in nature. Gradual build up of pharmaceutical in aquatic environment would produce ravage of problems even at microgram levels [8]. Especially some of the pharmaceutical drugs can able to interfere with the endocrine system and produce a destructive effect (e.g., endocrine disruption or homeostasis disruption). For example, during the course of the disruption, drugs interfere with synthesis, metabolism, secretion, transportation, binding, mode of action, and elimination pathway of natural hormones found in humans and wildlife. Besides, some of the pharmaceutical substances are highly persistent and not degraded easily in the biological systems which results in a bio-accumulation potential through the food chain (e.g., same like legacy pesticides and polychlorinated biphenyls "PCBs"). In humans, pharmaceutical substances usually conjugate in bile acid, after excretion it will undergo de-conjugation in sewage treatment plants and produce high level free pharmaceutical substance [9]. Because Pharmaceutical chemicals are formulated to resist in an acid environment in stomach therefore, they are not easily degraded, and prove to be long-lasting. In addition, pharmaceutical chemicals add to the effects with other environmental chemicals and potentially produce synergistic effects (e.g., cocktail of other chemicals in humans). In general terms, the impact exposures to this mixture are hard to understand due to the multitude of the mechanism, however it cannot be ignored. On the whole, the very important threat is the adaptation or gene modification and spread of bacteria, viruses and other microorganisms resistant to the pharmaceutical substances present in the environment and possible unpredictable important negative consequences [5].

In India, the sewage treatment plants (STP) shown to have the very moderate performance to clean the pharmaceutical substances. Consequently, the majority of the domestic waste (e.g., human excretion), hospital waste/disposed medicines, pharmaceutical waste and industrial waste enter into the STPs. The STP water re-cycled for a drinking purpose even in developed countries and therefore uncleaned pharmacy drugs would enter humans un-intentionally. In STPs, the fate of incoming pharmaceutical substances is very complex. Few substances seem to be more or less completely eliminated, while others pass through the different processes without being changed its original chemistry [10]. Therefore, fate of pharmaceutical substances in the STP may offer a variety of additional techniques for diminishing the amount and harmful activity of its biological contents. The effluent from the STPs in India contained a multitude of antibiotics with the concentrations that produce lethality to bacteria and vegetation. Besides, the highly antibiotic tolerant bacteria such as enterococcae were present in all STPs.

There is enormous research have been conducted with regard to the ecological and physiological threat associated with pharmaceutical substances and their metabolites in the aquatic environment. Because of the lipophilic nature, high solubility and polar characteristics; most of the pharmaceutical substances are vulnerable to aquatic organisms. Antidepressant drugs shown to bio-accumulate in frogs and can significantly affect their developmental cycle. Some studies also

documented a pharmaceutical pollution and its serious reproductive impact such as feminization or masculinisation in certain fish species particularly due to the elevated occurrence of estrogens and other synthetic hormones in STPs. The rainbow trout blood plasma had a pharmaceutical dose which is equal to the human therapeutic plasma levels. In other study from Sweden, rainbow trout exposed to STP water showed 25 pharmaceutical drugs (e.g., progestin levonorgestrel levels were 8-12 ng/ml) which is higher than humans and also shown to reduce the fertility in the fish [11]. Other studies also documented that concentrations of ethinyl-estradiol can cause endocrine disruption in amphibians at the concentration <1 mg/L through vitellogenin production and structural change in their sex organs (a frequently used index for the feminization of male fish) [12]. The beta-blocking drugs such as propanolol found to cause a significant decrease in egg production in Medaka fish [13]. Blood testosterone levels in fish were decreased in Gemfibrozil (cholesterol reducers) exposed fish species [14]. Many of pharmaceutical substances were detected in the liver and blood of aquatic wildlife at µg per kg levels which is similar to humans and also shown to affect swimming ability of the mollusks [13].

Environmental pharmaceuticals chemicals are well known to have serious genotoxic effects in humans. The tetracycline's and quinolones are not metabolized in the humans and are excreted with the original form [9]. They can be toxic to other microorganisms, aquatic wildlife such as fish species. Exposure scenario of pharmaceutical substances in humans considered to be a complex which depends upon types of drugs, their concentration and their occurrence in the environment. Further pharmacokinetics, structural formation during their transformation after metabolism or natural degradation in the environment is important factors to bio-accumulate and produce a spectrum of effects. Pharmaceutical substances demonstrate to produce a number of fatal effects in humans and farm animals. The most common effects are endocrine disruption and its oriented carcinogenic, teratogenic, developmental and reproductive effects [7]. Furthermore they interfere with the hormonal balance by disrupting metabolic capacity, produce immune defects which eventually produce acute toxicity. In addition, the emerging concern for human community is the exposure of pharmaceutical drugs may have a potential to induce an antibiotic resistance. For example, over dosage of antibiotic drugs either by intentionally or un-intentionally (i.e., higher than minimum inhibitory concentrations) for a particular pathogenic microbes, a selective pressure probably may exerted which leads to promotion of antibiotic resistance [5].

Considering those facts, stringent regulation may be expected from individuals, industries, STPs, and regulatory agencies (Central Drugs Standard Control Organization (CDSCO) and National Pharmaceutical Pricing Authority (NPPA) and Water Act) in India. For example, individuals who intake pharmaceutical drugs may dispose in safe and sound methods such as proper sealing of original drugs with the hazardous mark and trash in special containers with black mark. Individuals should have self restriction for unnecessary medication, not to flush in the drain, minimize the usage, other safety options of disposal and community collection which is very common in some developed parts of the world [7,14]. The industries should discharge the cleaned water to the drain which should be monitored by regulatory agencies regularly. The regulatory agencies can give an education to public, train them with label program and disposal information and inform pharmacies to provide leaflets for the safe disposal. The take back program to collect the drugs at a central location for proper disposal is a feasible and safe practice of the pharmaceutical drug disposal [7,14]. The World Health Organization (WHO) should implement Good

Manufacturing Practice (GMP) primarily in the developing countries like India. The pharmaceutical industry must be invited to actively work on reducing pharmaceuticals in the environment through GMP. Further after disposal, reducing environmental fate of the pharmaceutical chemicals can be done in STPs by sorption in sludge method followed by high incineration burning both in aerobic and anaerobic (the ashes should be analyzed for any other un-intentional pollutants such as dioxins, PCBs, PBDEs etc.,) Forms. In order to reduce pharmaceutical substances, STPs should also add up few techniques such as stimulating the activity of organic compound degrading strains of microorganisms, reverse osmosis techniques, micro filtration or membrane reactor, UV-treatment of the water, ozone treatment, powdered active carbon phase treatment and solar treatment of effluents. In addition, there is a basic necessity for environmental monitoring of pharmaceutical substances (e.g., pharmaceutical detection methods, global detection strategy and the current global levels) and their adverse effect either by developing a Pharmaco-Ecotoxicology department. Concentrations of pharmaceutical drugs in drinking water alone are not sufficient to assess the risk of negative environmental effects. Consideration must also be implemented in bioaccumulation potential in fish and other food intake by humans, as well as to additive and synergistic effects between pharmaceutical and other chemicals (i.e., cocktail effects) in the contaminated water.

References

- 1. (2012) Pharmaceuticals and pricing policy in Malaysia.
- 2. (2012) A brief report pharmaceutical industry in India.
- 3. Fick J, Söderström H, Lindberg RH, Phan C, Tysklind M, et al. (2009)

Contamination of surface, ground, and drinking water from pharmaceutical production. Environmental Toxicology and Chemistry 28: 2522-2527.

- 4. Murty MN, Kumar S (2011) Water Pollution in India: An economic appraisal.
- Gale J, Narayan A (2012) Drug-defying germs from India speed post-Antibiotic Era. Bloomberg Markets Magazine.
- Tripathi VK (2012) Pharma waste in the Patna sure recipe for disaster. Hindustan Times.
- Waghulkar VM (2010) Dark side of PPCP: An unconscious infiltration into environment. International Journal of ChemTech Research 2: 899-902.
- Huber M, Gobel A, Joss A, Hermann N, Loffler D, et al. (2005) Oxidation of pharmaceuticals during ozonation of municipal wastewater effluents: A pilot study. Environmental Science and Technology 39: 4290-4299.
- Ruhoy IS, Daughton CG (2008) Beyond the medicine cabinet: An analysis of where and why medications accumulate. Environ Int 34: 1157-1169.
- 10. Brar SK (2011) Emerging contaminants Small concentrations, big problems. Hydrology and Current Research.
- 11. Fick J, Lindberg RH, Parkkonen J, Arvidsson B, Tysklind M, et al. (2010) Therapeutic levels of levonorgestrel detected in blood plasma of fish: results from screening rainbow trout exposed to treated sewage effluents. Environmental Science and Technology 44: 2661–2666.
- Park BJ, Kidd K (2005) Effects of the synthetic estrogen Ethinylestradiol on early life stages of mink frogs and green frogs in the wild and *in situ*. Environmental Toxicology and Chemistry 24: 2027–2036.
- Wennmalm Å, Gunnarsson B, Eckerman I (2010) Pharmaceuticals Permanent pollutants in environment Basic facts and proposed measures to protect the public health and the environment. ISDE Document on pharmaceuticals.
- Tong AY, Peake BM, Braund R (2011) Disposal practices for unused medications around the world. Environ Int 37: 292–298.

Page 3 of 3