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Review Article

Environmental pharmacology: an emerging science

Anuradha T. Deshkar*, Ujwala P. Gawali, Prashant A. Shirure

Department of Pharmacology, Dr. Vaishampayan Memorial Government Medical College, Solapur, Maharashtra, India

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***Correspondence to:**
Dr. Anuradha T. Deshkar,
Email: anuradhatdeshkar@gmail.com

ABSTRACT

With continuous rapid expansion of the human population there is escalating demand for resources, including human and veterinary pharmaceuticals. This has lead to rapid development of global pharmaceutical industry and with that increase in issues caused by pharmaceutical products. In recent years a great concern has been expressed over the occurrence and persistence of pharmaceutical products in the environment and their potential impact on environment. Owing to this the new branch of science called environmental pharmacology has sprouted. Environmental pharmacology deals with dispersion and impact of pharmaceutical products on environment. Solutions need to be suggested to save this only liveable planet from ill effects of these pharmaceutical products. This has given birth to the science of Ecopharmacovigilance (EPV).

Keywords: Environmental pharmacology, Ecopharmacovigilance, Pharmaceutical products

INTRODUCTION

Every cloud has a silver lining and every rose has its thorn, drugs are no exception. Drugs have been a blessing for the mankind in curing the ailments although not completely but to a great length.[1] Along with advantageous effects they also impart some adverse reactions sooner or later.[2] In recent decades there is expeditious development of global pharmaceutical industry and with that an increase in consumption of pharmaceutical products. In past few years a great concern has been expressed over the occurrence and persistence of pharmaceutical products in the environment with their diverse biological effects.[3] Human pharmaceuticals from various therapeutic classes have increasingly being detected in the environment typically at ng/L to low mcg/L in surface water. In 2009 Edward HL and others stated that there is presence of widely dispersed drugs and drug metabolites in the environment which possess a potential direct and indirect risk to humans.[4] The pollution of water and soil bodies with pharmaceutical residues is an emerging environmental problem. Many of these substances, including human pharmaceuticals, may have little, if any, impact on human health or the environment; though for some substances there may be a significant risk.[5]

The alarming reduction in number of vultures in Indian subcontinent shook the environmental scientists and activists.[6] Prior to this observation, research on the impact of chemical pollution was restricted to persistent organic

pollutants.[7] At this verge, attention has been drawn to the environmental impact of chemicals used in small concentration, that is, drugs giving birth to the subject of Environmental Pharmacology.[8] Environmental pharmacology is defined as the effect of pharmaceuticals and house care products on the environment and ecosystem. It involves the study of gene-environment interaction, drug-environment interaction and toxin-environment interaction. The different terminologies have been used interchangeably with environmental pharmacology includes 'ecopharmacology' and 'ecotoxicology'.[9]

Sources of entry of drugs into environment

Excretion

Drug use in both the human and veterinary population is escalating day by day. According to one estimate 100,000 tons of antimicrobials are consumed every year.[10] More than 30 billion doses of nonsteroidal antiinflammatory drugs (NSAIDs) are consumed annually in the United States only.[11] Consumed drug passes out of the system either as metabolites or unchanged through excretion. Drugs are usually water soluble and therefore find their way into the sewage.[12] Many pharmaceutical chemicals are nondegradable to resist the acid environment in the stomach or long-lasting, thus present a special risk when they enter, persist, and disseminate in the environment including water supplies and the food chain leading to an unwitting re-entry of drugs into humans.[1,3,13] Excretion dominates the global input of medicines into the environment and are a much more difficult source to control.[14]

Waste from pharmaceutical companies

Waste of the pharmaceutical companies also contributes toward the entry of drugs into the environment. Though such industries adopt the sewage treatment process before disposal but because of their obsolete processes the contamination of environment by drugs continues. Few drugs are not entirely removed by treatment process leaving their traces to go into water in environment.[12]

Hospital waste

Waste water from hospitals also constitutes a major source of entry of drugs into the environment.[15]

Terrestrial deposition

For examples via sludge application to land, leaching from Solid waste landfills or treated or untreated waste water use for agricultural purpose.[16]

Irrational disposal

Leftover and expired drugs constitute another dominating cause of environmental contamination with drugs. Improper disposal of leftover medication usually contaminates the environment to a great extent. Drug residuals from the formulations like transdermal patches also leave the significant amount of drug in environment.[17]

Drugs identified in global environment

In recent years, drugs from numerous therapeutic classes have increasingly been detected in the environment, in surface waters in different studies conducted in different parts of the world.[5] A study in Spain found that 19 drugs of the 27 human drugs investigated have been identified in the aquatic environment. Metabolites of carbamazepine, diclofenac, and atorvastatin were detected in flow proportional 24 h composite samples of wastewater effluent collected from the Norwegian cities of Oslo and Tromsø at higher concentrations than the parent drugs.[3] Studies in USA have even detected very low levels of drugs in finished drinking water.[18] Studies have also found several drugs in tap water in several countries in Europe, including Germany, the Netherlands and Italy.[19] Two separate studies in Germany found phenazone and propylphenazone in Berlin drinking-water. In the Netherlands, traces of antibiotics, antiepileptics and beta blockers were detected in the drinking-water supply.[5] Even Ground waters are affected by a variety of sources, with landfills, septic systems, and agricultural fields representing the most significant potential sources of anti-infective contamination. A recent study of groundwaters in the United States detected three anti-infectives of the twenty one targeted.[20] Following list shows different group of drugs present in the global environment.[3,5]

Antibiotics

- Erythromycin,
- Roxithromycin,
- Azithromycin,
- Clarithromycin,
- Lincomycin,
- Sulfonamides,
- Trimethoprim,
- Chloramphenicol,
- Doxycycline,
- Cefalexin,
- Ketoconazole,
- Clotrimazole,
- Triclosan,
- Triclocarban,
- Amoxycillin,
- Sulfamethoxazole

NSAID

- Diclofenac,
- Ibuprofen,
- Indomethacin,
- Mefenamic acid,
- Paracetamol,

- Naproxen

Beta blockers

- Propranolol,
- Atenolol,
- Metaprolol

Hormonal drugs

- Tamoxifen,
- Ethinylestradiol,
- Levonorgestrel,
- Endogenous estrogen excreted from women

Antidepressants

- Fluoxetine,
- Norfluoxetine,
- Citalopram

Miscellaneous

- Carbamazepine,
- Bezafibrate,
- Gemfibrozil,
- Clofibrate,
- Theophylline,
- Dextropropoxephene,
- Cetirizine,
- Cocaine

Hazards of environmental pollution by drugs on wild life

Although there is no systematic study to show the definite hazard or toxicity to humans from environmentally present medicines, the potential effects of drugs on wildlife species has been demonstrated.[21] Some of them are listed below.[5]

Diclofenac

- Abdominal gout and acute kidney failure leading to death of gyps vultures
- Histological changes in the liver, kidney and gills of fish

Oral contraceptives

- Sterility in frog

Ivermectin

- Death of dung beetle

Sex harmone

- Feminisation of male fish

Possible hazards of environmental pollution by drugs

Microbial resistance

It is one of the most important consequences. Continuous exposure to low dose of antimicrobials through drinking water may bring resistance.[1] Decreasing interest of pharmaceutical companies in development of new antimicrobials in favour of developing "lifestyle" drugs may add on to the problem.[22]

Greater risk to special population

Special populations like pregnant women, children, geriatric population, and person with renal or hepatic insufficiencies may remain at a greater risk to such exposure because in these categories the pharmacokinetics gets altered and even minor doses may also prove to be toxic.[23]

Chronic toxicity

The long-term exposure to these environmental pharmaceutical pollutants could be responsible for chronic toxicity and subtle effects in animals and plants including:

- Endocrine disruption
- Growth inhibition
- Disruption of microbial ecosystems
- Cytotoxicity
- Mutagenicity
- Teratogenicity and so on.[3]

Synergistic action and type B adverse drug reactions

Some drugs in these micro doses may also show synergistic actions and type B adverse drug reactions.[24]

Remedial measures: Ecopharmacovigilance

Ecopharmacovigilance has been sprouted as a solution to this environmental pollution by drugs. The definition of EPV by Holm et al, based on the World Health Organization (WHO) definition of pharmacovigilance is "the science and activities associated with the detection, evaluation, understanding, and prevention of adverse effects of pharmaceuticals in the environment".[3]

Approaches of EPV

- Green drug design
- Green chemistry in process development
- Development of biodegradable products
- Minimization of manufacturing emissions
- Education over rational use of drugs
- Improved prescribing practices
- Management of unused and expired drugs
- Transparency and availability of the environmental data[3]

CONCLUSION

Pharmaceutical pollution has posed serious threat to the environment worldwide. Now we should come forward and shoulder the responsibility for our own people along with the world ecosystem. Ecopharmacovigilance has emerged as a good solution for this. There is a need for individual and collaborative research between industry, academia and government acting in a proactive manner to improve the scientific understanding and implementation of Ecopharmacovigilance. It will now be pertinent for regulatory as well as scientific society to work hand in hand to address this vital issue.

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