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Review article

Role of eco-pharmacology in pharmaceuticals

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ABSTRACT

More than thousands of decades pharmaceuticals and mankind have accompanied together and been helpful. Eco-pharmacology a novel concept of emerging science. Safe disposals are emerging concerns to be found. Pharmaceuticals can enter the surroundings through any route or any contact. The major issue is unused medications. Pharmaceuticals are useful in both in human and veterinary population day after day. Drugs like erythromycin are detected within the soil. Pharmaceuticals and personal care products are active at very low concentration and they are often found in waterways. It is mainly to evaluate the environmental risk for every new drug. It aims zero waste which will offer great benefits to eco-system. Take the prescription drugs out of the original container. Do not dispose the medications in the toilet or sink it will result in the aquatic system.

Keywords: Environment, Pharmaceuticals, Hazards, Unused drugs, Disposals.

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INTRODUCTION

More than thousands of decades pharmaceuticals and mankind have accompanied together and been very helpful, however they have caused hazards to the people living [1,2]. There is growing debate between environmentalist and research scientists about drugs leading to the habitat which is causing an unanticipated hazard to the consumers. Till today the effect of drugs in the environment haven't been a region of analysis or investigation. A lot of pharmaceutical brand products within the surrounding areas is a danger to the general public and even the species primarily living within the aquatic ecosystem is a concern to be noted. The environment is polluted not only with pharmaceutical products also with heavy metals, pesticides, emissions, gasolines etc. This attention has been drawn where the impact of drugs to the environment leading to the subject on Eco-Pharmacology [3]. Eco-pharmacology a novel concept of emerging science is the study of any pharmaceutical products or chemicals within the surroundings through any route or any concentration interrupting the ecosystem and causing adverse impacts of pharmaceutical active ingredients towards the environment. It is also mentioned as environmental pharmacology, p'coenvironmentology or ecopharmacoste wardship [4].

This is a new discipline that brings an understanding about gene-environment interactions, drug environment interaction and toxin environment interaction [5,6]. The major route is probably through excretion from human residues undergoing therapeutic management. In south east Asia a well-documented issue on decrease of predators such as vultures, after eating remains of animals which have been treated with diclofenac and oestrogens have caused adverse impacts [7].Data's have proven that household wastes are either thrown in the garbage or rinsed them down in the toilet or sink which is resulting in the surroundings causing an impact which are harmful to the public and species living. Active ingredients of drugs are mainly excreted as metabolites from the person into the eco-system thereby entering via food and move into large predators [8]. Majority of the public about 7% buy medication and consume them but do not dispose the medication in the right way. An emerging concern in today's world is safe disposals of medicines which can also lead to ignorance if not disposed in the correct way which is causing a stockpile of medications which includes expiry drugs and unused medications at households can also pose hazards leading to accidental ingestion when consumed [9-12].

Certain measures like proper destruction of drugs, disposing the medications in right way can reduce the exotoxin effects for both human, predators and species living in aquatic environment. With only limited sources available in this sector, in depth review or research of evaluating this topic can be considered.

Entry of pharmaceuticals in the environment

Pharmaceuticals are useful to both in human and veterinary population day after day. It is noted that on an estimate level around 100,000 of antimicrobials are consumed every year by each and every individual.

Human source

Pharmaceuticals can enter the surroundings by any route or contact. Through human contact it can enter through body sweat, washing the skin by having any medical residues applied onto the skin. One example is transdermal patches because it contains 28%of fentanyl which remains in the skin and when in contact the residues are excreted and enter to the environment [13].

Households

The major issue is unused medications. The reason why this happens is because people do not know how to dispose the medication in the proper way. Due to this the drugs go unused which includes those drugs which are expired or outdated or doctors prescribing medications sometimes gets discontinued and the doctor might add a new drug. Sometimes so much of medications the patient feels is to better avoid thinking that it might cause them an allergic reaction and even if the person feel that the medications makes them feel better, they have a stockpile of medications which can also lead to accidental ingestion causing major adverse effects and lead to fatality [14]. Most of the household have practiced to throw the medications in the garbage or they are rinsed them down in the toilet. This way the environment is getting polluted.

Hospital

Hospital drug manufacturing units have significant amount of drug present which can enter the environment very easily. If we do not dispose them properly in individual colour bags and put these in an incinerator and can cause major adverse effects [15]. Mainly in hospitals antibiotics are used in large amounts for each patient because to prevent any type of bacterial infection. Careful handling of ampoules, glass and vials is important, as it results in local water bodies affecting the species.

Excretion of pharmaceutical ingredients from patients

Whether it be human or animals the medications are given orally or parentally. These medications maybe poorly absorbed in the gastrointestinal tract. Unabsorbed drugs are excreted and results in the environment after they have been excreted, they enter the food chain.

Animal carcasses

High level of certain drugs present in the animal carcasses are potentially poisonous to scavengers.

Potential exotoxic effects

Pharmaceutical active compounds

Active pharmacological metabolites enter the aquatic ecosystem by any route and once entered they undergo biodegradation [16]. These compounds are mainly discovered on the surface water in in certain countries. Long term effects on reproduction, development and behaviour of aquatic species have shown improvement. There are different classes for PhACs which include.

Anti-microbials

They have high potential to the eco-system and are specifically toxic to bacteria [17]. Drugs like erythromycin are detected within the soil. Other drugs like ciprofloxacin, a fluoroquinolone antimicrobial, are highly toxic to and is therefore of special concern with regard to ecosystem impacts. Sources of antimicrobials include agriculture which accounts about 50% of antibiotic use [18].

Synthetic hormones

They affect the endocrine system of humans and wildlife at low levels. The important synthetic hormone found in environment is 17α-ethinylestradiol (EE2), used as an oral contraceptive for humans [19].Others which include mestranol which is also an oral contraceptive but they are very rare present in the environment.EE2 is excreted by humans as an inactive glucuronide, however it is de-conjugated to the active parent in sewers and WWTPs by E.coli.

Lipid regulators

Clofibric acid is a lipid lowering drug. They were the first PhAC present in ground water. It is mainly suspected to be harmful for the aquatic ecosystem. Drugs like atorvastatin accounted for 52% of recommendations for lipid regulators in 2003. Effects of lipid regulators such as Clofibric acid, gemfibrozil, fenofibrate and bezafibrate on humans at low concentrations are unknown.

Anti-inflammatory drugs and analgesics

They are easily available as over the counter medications which are given to patients when suffering from any pain or inflammation. These drugs are mainly detected in sources of water such as ground water and drinking water. Diclofenac is a reason for increase in the number of deaths of more than 95% of the oriental white- 22 backed vulture population. Renal failure in vultures is due to the drug present in the dead livestock.

Antiepileptics

Carbamazepine is frequently found to be detected in surface water at up to 1.1µg/L and in groundwater at 900 ng/L. These are found to persist in soil more than 6 months after irrigation by reclaimed wastewater in Colorado. Some researchers have suggested that carbamazepine acts as a tracer to indicate pollution of water by sewage effluent.

Selective serotonin reuptake inhibitors

It includes such as fluoxetine are usually prescribed as anti-depressants. They can exert a wide range of effects on aquatic organisms, especially on invertebrates.

Other PhACs

These include betablockers such as metoprolol which has the maximum concentration of PhACs. Beta blockers are not always removed by WWTPs for instance, one study found that less than 50% of propranolol was removed by secondary sewage.

Different drugs with examples which is commonly observed in PhACs

Table 1: Drug examples of PhACs observed

Drugs	Examples
Beta-Blockers	Metoprolol, Propranolol, Nadolol
Steroid and hormonal preparations	Oestrogen, Progesterone, Mestranol
Antibiotics	Macrolides, Sulphonamides and Fluoroquinolones
Anticonvulsants	Carbamazepine, Primidone
Antidepressant	Fluoxetine
NSAIDs	Acetaminophen, Ketoprofen, Naproxen

Pharmaceutical and personal care products (PPCPS)

PPCPs refers individuals using any product for personal health or cosmetic reasons to enhance the growth of the livestock. They are comprised of prescriptions and over counter medications, veterinary drugs, fragrances, cosmetics, sunscreen products, diagnostic agents. The major sources of these include human activity, residues from pharmaceutical and hospital settings, illicit drugs and steroids. In recent years researchers are bringing attention towards this sector of study to fully understand PCCPs entering into the environment. Studies of PPCPs are mainly included irrespective of their doses and route of entry into the environment. They are active at very low concentration and they are often found in water. Most of the substances do not get metabolised they get excreted via urine. Around 30 to 90% of oral medicines are excreted via urine which will reach the aquatic environment. There are new screening methods for PPCPs and therapeutic drugs on terrestrial using laboratory animals which include collecting animal urine and excreta every day for one-month and toxicological studies can be performed according to the ICH guidelines [20,21].

Environmental persistent pharmaceutical pollutants (EPPP)

They are outlined as compounds that can withstand biodegradation of organisms and remain in the surroundings. EPPPs are detected in ground water causing genetic, immunological and hormonal effects in humans and other species.

Approaches on drugs in the environment

Reducing the quantity of pharmaceutical waste

The first step is to find out the root cause of drugs present within the environment. Many people are not aware of how polluting our environment with pharmaceuticals can cause serious major changes in ecosystem. The more we pollute the more it affects the other species living below so, we should reduce it by not dumping the waste in waterbodies or lands which cause landfills that get accumulated and cause adverse effects.

To increase sewage treatment plants

These are not driven to remove medicines but certain measures should be brought out to reduce the sewage from the waterways.

Use of green pharmacy

Green pharmacy includes pharmaceutical products to significantly reduce the hazardous substances and to protect the environment. It is considered as an eco-friendly approach which is designed for chemical products to eliminate the use of toxic substances. It aims zero waste which will offer great benefits to ecosystem. It ensures that individuals buying medications should not dispose them down in sink [22]. If any unused medications can be given to non-profit organizations where they redistribute these medications. Anti-epileptics like valproate is a commonly used pharmaceutical product that can biodegrade quickly [23]. Carbamazepine can be biodegraded using microorganisms as bio remediation agents.

Developing better drug disposal programs

Medications are not supposed to be disposed in the sink whether be it over the counter or prescribed medications because wastewater treatment is ideally not designed to remove pharmaceuticals compounds that may end up in the local water ways. Proper disposal of unused, unwanted, expired drugs in garbage can result in safe and healthy environment also further eliminate the abuse of medications [24].

In order to minimize these issues, there are certain guidelines that can be followed which include:

Return the medications to the donor or manufacturer

Some people think returning the medications back to pharmacy is not possible, but practically it is possible. It is good initiative to return unused medications rather stocking them at the household [25].

Landfills

Landfill means to place waste directly into a land disposal site without prior treatment or preparation.

Waste immobilization

Immobilization of pharmaceutical waste can be done by following three ways:

- **Encapsulation:** Packing of pharmaceuticals in non-reactive sealed steel or plastic containers.
- **Inertization:** Mixing of pills out of their packaging with cement. It is a form of encapsulation.
- **Incineration:** These are high temperature ideally meant for disposing pharmaceutical.

Regulatory framework- globally-Europe

Environment risk assessment (ERA)

It is mainly to evaluate the environmental risk for every new drug. The main goal of ERA is to safeguard both the terrestrial and aquatic ecosystems along with groundwater and microbes in waste water treatment plants. Once evaluation is completed the datas are submitted to the European Medicines agency for evaluation to check on the quality, safety and efficacy required for market authorization of medicines intended for both human and veterinary use and further outcome of this sector can minimize the risk of medicines entering into the environment [26].

Water framework directive (WFD)

This framework by European environmental legislation commits all its member nations to attain a better qualitative and

quantitative estimation of water resources by extending the spectrum of water conservation to all specific types of water [27].

Knowledge and need assessment on pharmaceutical products in environment waters (KNAPPE)

It focuses on the information regarding the occurrence and the impact of pharmaceutical products in the environment

Sweden

Pharmaceutical firms have to adhere to the national environmental guidelines, health legislation, control discharges within land and water.

United States of America

Drug enforcement administration (DEA)

It mandates the drug disposal listed in CSA (Controlled substance act) either by returning medication back to the producer or by developing it with certain guidance and proper recording.

Table 2: Methods of safe disposals of pharmaceuticals

Category	Disposal methods	
Tablets, Capsules	Soak 50 tablets in tea and coffee grind in a polythene bag in about 100ml of water. Seal and discard in an incinerator at high temperature (Temp. 850°C to 1200°C).	Big quantity-pulverize using a heavy-duty crusher
Liquids	Dilute the liquid with water and drain it or transfer to ETP if the quantity is big.	Dispose in an incinerator
Ampoules	**Injectables-Ampoules/Vials:** Break ampoules/ vials (up to 10 ml) and pour the liquid in a polythene bag containing used Tea/Coffee grind. Seal it and discard. **Powder injectables (in Vials/Ampoules):** Discard it in an incinerator	Broken glass, ampoules, vials and rubber stoppers should be thrown into individual colour bags
Anti-infective drugs	**β-lactams:** β-lactam antibiotics dissolved in small quantities by soaking in 1N sodium hydroxide for 30 minutes and discard. **Tetracyclines-**Soaked in 10% of calcium hydroxide/any other calcium salt in Water for 30 minutes and trash. **Macrolides-(erythromycin, clarithromycin):** Soak in 1N hydrochloric acid and trash. **Aminoglycosides- (gentamicin, amikacin):** Dilute small amounts with huge quantity of distilled water.	Liquid antibiotics may be diluted with water, allowed to stand for few weeks and discharged to a sewer
Anti-neoplastic agents	Return to donor or manufacturer	It will not lead to landfills
	Waste encapsulation	This method will not lead to the sewer
	Waste Inertization	No medium temperature
	Medium and high-temperature incineration	-
Steroidal agents	These agents are soaked in one normality sodium hydroxide for half an hour and discarded	-
Hormonal medications	Exposed to UV light for 20 minutes and trash.	Expose in a sonicator for one hour and trash.

Resource conservation and recovery act (RCRA)

The toxic waste in the form of chemicals or formulations which are so detrimental to surroundings, that they must be separated for special disposals and cannot be introduced into sewers and landfills. RCRA monitors appropriate safe practices in the manufacturing, storage, transportation, treatment and removal of toxic drugs.

India

Ministry of environment, India classified that pharmaceutical industry as 'red category' as it emits hazardous waste to our environment.

Risk migitative strategies

The first step is to decrease the quantity of drug waste. In accordance with RMMs they are divided into three categories,

a) **Short-term measures:** e.g., Improved disposal and sewage treatment techniques, refusal of the spreading of contaminated manure

b) **Mid-term measures:** e.g., Modified risk perception and risk communication of producers and consumers of medicinal compounds

c) **Long-term measures:** e.g., Decisions that foster the idea of feasible pharmacy [28].

Household disposal steps

As per national drug control policy, U.S.A, the following steps can be adopted for removal of meditative products.

- Take the prescription drugs out of the original container. Do not add them in different containers and create multiple number of drugs [29].
- Mix the pills in tea and coffee grinds or cat litters in a polyethene bag.
- Do not over stock the medications at your household as it can result in accidental ingestion.
- Remove any personal information such as drug name, Rx number by scratching with a permanent marker pen or covering it with a duct tape.
- Do not dispose the medications in the toilet or sink, it would result in the aquatic system.

Safe methods on drug disposals for different pharmaceutical products

These are medications which are commonly used in hospitals, household to safely dispose them in the correct manner to prevent further pollution of pharmaceuticals in the environment.

CONCLUSION

Eco-Pharmacology is a broad area where abundant information is not given. Nowadays our planet earth is being impure with toxic waste, pharmaceuticals, chemicals, garbage waste etc causing an impact to the humans, terrestrial and aquatic ecosystem. People are not educated and not being aware on the impact of unused

and expired medicines in our environment and health effects. Still there are not much effective measures on how to dispose pharmaceuticals present at our households. Therefore, it is important as pharmacist to advise and take measures in educating the patients about stocking medications, keeping away expired medications at home and not properly disposing can cause aquatic species to die. Since the waters are polluted, it is not safe for human beings to drink water that is not purified. It is necessary to start taking proper strict measures in ways to dispose medications and toxic substances and make our environment cleaner and safer place to live.

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CONFLICT OF INTEREST

There is no conflict of interest between the authors.

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