Journal of Current Pharma Research
(An Official Publication of Human Journals)
An International Peer Reviewed Journal For Pharmacy, Medical & Biological Science
DOI: 10.25166 CODEN: JCPRD6 NLM ID: 101744065
ISSN: Print: 2230-7834 Online: 2230-7842
SJIF Impact Factor: 6.913

Human Journals
Review Article
May 2023 Vol.:17, Issue:4

Ecopharmacovigilance and Pharmaceutical Waste Management

Journal of Current Pharma Research
(An Official Publication of Human Journals)
An International Peer Reviewed Journal For Pharmacy, Medical & Biological Science
DOI: 10.25166 CODEN: JCPRD6 NLM ID: 101744065

Ravi Menon*[1], Sangamesh Puranik[2]

[1]*Research Scholar Sunrise University, Alwar, Rajasthan, India*

[2]*Research Guide Sunrise University, Alwar, Rajasthan, India*

Submitted: 05 May 2023
Accepted: 20 May 2023
Published: 25 May 2023

Keywords: Ecopharmacovigilance, healthcare system, pharmaceutical pollution

ABSTRACT

Ecopharmacovigilance (EPV) is a new area of interest in the current healthcare system. Presently, very little focus or debate is made on this branch of science in our country. Contrary to Pharmacovigilance (PV) no stringent regulation are made in this topic. EPV is the science related to understanding, detection and assessment activities for prevention of adverse effects or other problems due to the existence of pharmaceuticals in the environment. As India became the pharmacy of the world making stellar growth over the years, more discussions are needed in this area as it is the need of the hour. Pharmaceutical pollution has become a serious concern to our eco system, affecting small animal species to even human beings who stand in the top of the food chain. According to World Health Organization (WHO), unscientific disposal of expired, leftover, substandard, spurious and adulterated medicines is one of the most significant causes for antimicrobial resistance among animals and human beings. Other issues reported include declining population of vultures, feminization of male fishes, sterility in frogs were also reported.

INTRODUCTION:

Ecopharmacovigilance (EPV) is a new area of interest in the current healthcare system. Presently, very little focus or debate is made on this branch of science in our country. Contrary to PV no stringent regulation are made in this topic. Ecopharmacovigilance (EPV) is the science related to understanding, detection and assessment activities for prevention of adverse effects or other problems due to the existence of pharmaceuticals in the environment. As India became the pharmacy of the world making stellar growth over the years, more discussions are needed in this area as it is the need of the hour. Pharmaceutical pollution has become a serious concern to our eco system, affecting small animal species to even human beings who stand in the top of the food chain. According to WHO, unscientific disposal of expired, leftover, substandard, spurious and adulterated medicines is one of the most significant causes for antimicrobial resistance among animals and human beings. Other issues reported include declining population of vultures, feminization of male fishes, sterility in frogs were also reported.

A large percentage of the medicines produced are not consumed by the patients and get expired. For example, data from Germany showed approximately 10% of medicines sold in the country were disposed of in household waste.[1] Unused medicines can be stored by many individuals for later use when needed, especially for minor ailments. This behavior may not always be appropriate and depends on the type of medicines, duration of use and instructions from the provider. Stored in households can be helpful in emergencies and reduce physician visits and are thus considered as cost-effective and convenient. There are many reasons for medicines not being completely used such as patient's recovery from a disease, greater number of medicines bought as compared to the need, death of the patient, fear of the medicine's adverse effects, poor patient compliance, and forgetfulness. These unused medicines are stored in homes and may ultimately lead to wastage of medicines.[2–4] There is a high probability that these unused medicines may be discarded in an inappropriate manner that can harm the environment. Long-term exposure to various types of medicines in the environment can cause toxic effects to the water system and can even affect aquatic animals, plants and microorganisms.[5] This may result in the emergence of antibiotic resistance due to the availability of traces of antibiotics in the water system.[6] In addition, unused medicines can become a source of accidental and intentional poisoning and can contribute to self-medication practices.[7] To address these problems leftover medicines should be properly handled to avoid

hazardous effects. Irrational prescribing may promote wastage of medicines, and future prescribers should be knowledgeable about proper medicine disposal procedures and associated harmful effects if medicines are not disposed of properly. The future health professionals are also expected to be knowledgeable about ecopharmacovigilance, defined as "the science and activities associated with the detection, evaluation, understanding and prevention of adverse effects of pharmaceuticals in the environment".[8] Pharmacy, Medical and dental students have an important role to educate and advise family members and the general public on the safe and appropriate use of medications and their appropriate disposal practices. A study from Malaysia had shown that university going health science students were storing different medicines like analgesics, antipyretics, vitamins, antibiotics, and gastrointestinal medicines.[9] Students purchased medicines from community pharmacies operating near the hospitals and stored these in their rooms for future use. This process may increase the likelihood of sharing the medicines with their friends, and accidental poisoning. The issue of safe disposal of medicine is of global interest. There are specific programs in developed countries for proper medicine disposal whereas; the situation is different in developing countries like Nepal.

A study from Bangladesh has also revealed less knowledge among pharmacy students about medicine disposal techniques. About 58% of students disposed of liquid medicines via toilet or sink and which eventually reached a wastewater disposal system.[10] Another study done among the Pharmacy, medical and dental students from India has mentioned throwing medicines in domestic trash was the commonest method for disposing of the expired medicines. The study also highlighted a lack of awareness among respondents of the consequences of improper drug disposal practices and the best place for educating about these issues would be the pharmacies from where the students obtain their medicines.[11] Safe and proper medicine disposal issues have to be addressed in the curriculum of the medical, dental, nursing and pharmacy graduates and also should be considered by the legislative authorities. A study from Nepal has shown that even pharmacists are unaware of and have inadequate knowledge regarding the safe disposal of medicines.[12] Medicine takeback system is the secure system for safe and environment-friendly disposal of leftover and expired medicines wherein medicines are returned back to pharmacies or law enforcement bodies where they are destroyed without harming the environment.[13] Medicine takeback systems are well established with government support in countries like Australia and Canada. Similarly, countries like the United States of America and Sweden are also having a proper system of

pharmaceutical waste management.[14, 15] Different methods for waste disposal are recycling, incineration, chemical, physical and biological treatment processes. WHO has developed guidelines for pharmaceutical waste management that do not recommend the openair burning of healthcare waste as it can be toxic to the environment. A study done in Pokhara, Nepal mentioned that more than half of the participants used improper practices for medicine disposal. Hormones, antibiotics, lipid-lowering agents, analgesics and anti-inflammatory medicines, antihypertensive, tranquillizers, antidepressants, antiepileptics and anticancer medicines were present in water bodies in different parts of the world which impact human health as well as the environment.

Improperly disposed medicines can affect human health by releasing various pollutant gases, and undegraded and toxic chemical substances. So far there are no studies in Nepal evaluating health professional students' knowledge and practice on medicine disposal and hence the present study was conducted to obtain knowledge on unused and expired medicines and medicine disposal techniques from the undergraduate Pharma, medical and dental students and to explore the medicine storage process, and their practice patterns.

Among the respondents, two thirds "always" checked the expiry dates of medicines. In a study conducted in Chennai, India, among pharmacy and medical students, only 6% did not check expiry dates and in the same study, 60% of respondents considered the medicine to become toxic after the expiry dates. In another study from India among dental residents, 61% mentioned expired medicines must be returned to the manufacturer. Once expired, medicines can have poor efficacy leading to suboptimal therapeutic concentrations or can be even toxic. At times, certain drugs like tetracycline can even cause dangerous adverse effects like Fanconi syndrome. Often expiry dates of medications are not clearly displayed on the medicine packs. This can be a major issue in the case of elderly patients or patients with poor health literacy and cognitive disorders. In the present study, nearly two third of respondents mentioned the expiry dates being not clearly visible. This finding suggests that while dispensing medications the pharmacists must explain to the patients about the product expiry dates, especially the ones with near expiry dates. A proper label clearly mentioning the expiry date can also be beneficial. Safe disposal can reduce poisoning of children with medications, protect the environment and natural resources from chemical constituents of medicines, and prevent unauthorized use. In the present study 44.7% of the responding students stored medicines at their home/hostel till expiry.

A study from Saudi Arabia reported 37.6% of pharmacy students and 52.5% of nursing students followed the same approach of storing the medicines till it got expired. Unused medicines can also promote self-medication among family members although our study did not correlate self-medication practices with medicine storage behavior. Studies in Nepal had reported the existence of self-medication practices among the general public and students, and naturally, the presence of unused medications can promote self-medication practices.

Over one third of the students disposed of unused medicines in the garbage. Other studies worldwide also reported a considerable number of medicines being disposed of in the garbage. It is also crucial to know the reasons for storing excess medications which can eventually help develop strategies to reduce this practice. In one review, the major reasons for unused medicines were nonadherence to the drug regimen due to various reasons, death of the patient, change in medication regimen, fear of medicine shortage, inappropriate dispensing, etc.

Only one tenth of the medicines were returned to the pharmacies. Refund for returned medicines in Nepal is not provided as approximately 80–90% of total medicines used in the country are imported from foreign countries mainly from India and hence the importers and distributors discard the expired medicines under their supervision. In Nepal, the pharmacies dispense the exact number of unit doses with even medicine strips being often cut. This helps in minimizing the wastage of medicines. However, this process also limits barcoding and allows medicines to be stored without the original pack and thus compromises the stability and safety. Based on the study findings, one can assume that the respondents were unaware of the exact procedures for disposing of unused and expired medications in their location.

The United States Food and Drug Administration (US FDA) guidelines on medicine disposal clearly emphasize the various methods of drug disposal based on the nature of the medications. A study from Various Countries of the world conducted among the general public also showed improper disposal of unused and expired medications and the authors recommended a government funded drug takeback system in the country. There has been a steady increase in online pharmacies in Various Countries of the world wherein medicines are delivered based on a scanned copy of the prescription uploaded in a smartphone application, and considering this, more stringent measures have to be put in place for managing unused and expired medications.

The curriculum of these students does not provide education on topics related to safe medicine disposal. While the storage of medicines was common, there were also self-medication practices noted. For instance, nearly one sixth of the respondents less commonly followed the Doctor/Pharmacists advice while taking medications. If unused medications are stored at home, this can contribute to self-medication. Nearly half the study respondents had practiced self-medication for common illnesses such as fever and headache.

As mentioned earlier, self-medication by students is a common problem reported in Nepal and elsewhere. A probable reason for self-medication among health professional students is the easy availability of drug information sources and medicines.

In addition, since these students consider themselves knowledgeable about medicines and health conditions, they consider it appropriate to self-medicate and often even suggest over the counter (OTC) medications to neighbours, friends and family members. Storage of medicine varies depending upon the nature of the medicine. For example, specific types of medicines like antibiotics must be taken for the full course and opioid analgesics can be used on a need basis. Regarding antibiotics, the risk of improper diversion and adverse effects is lower, but this is a high risk for opioid analgesics.

Authors examined the storage and disposal of medicines as a general category. However, these nuances should be considered while interpreting the study findings. The present research reported a high knowledge score among female students. It may be because female students more commonly self-medicate than males and hence are likely to be more knowledgeable about safe medicine disposal. There is a hospital waste management guideline in Nepal according to which the wastes are managed by landfill, burial, incineration and inertization of the pharmaceutical waste product. But there are no safe medicine disposal guidelines adopted in community pharmacies.

A drug takeback system where patients can return the medicines to the pharmacies who will then send it back to the distributors has been proposed but has not been widely adopted. Knowledge about this system is low and it is not widely adopted in the country. There is the added trouble of bringing the medicines back to the pharmacy from where it was purchased and of providing the proper documentation. Respondents checked expiry dates of medicines but sometimes the information was not easy to find. Nearly half the respondents/family stored medicines for future use.

Most respondents had good knowledge about expired medicines and medicine disposal, but the practice must be improved. One-third of students disposed of medicines in the garbage and less than one-tenth of medicines were returned to pharmacies. Self-medication was also noted. The sample was broadly representative of the student population. The major area of focus is to implement a drug takeback system in the country, preferably in stages starting from the larger cities and educating the public about this system once it has been implemented. The harms of improper medicine disposal should also be mentioned.

So, the possibility that the students may have consulted external information sources cannot be ruled out. Moreover, the institution especially the department of pharmacology emphasizes rational use of medicines and rational prescribing and hence the findings cannot be generalized to other students in the country. No physical checking of drug storage was made, and the analyses and interpretation were purely based on student responses. Since the study is questionnaire based the Dunning–Kruger effect cannot be ignored. There may be the possibility that medicine storage in the homes of students may be more since they consider themselves to be future prescribers and experts in medications and hence the findings may be different from other health professional students.

Pharmacy, Medical and dental students were aware of the expiry of medicines and knew methods to safely dispose of expired medicines. However, they practiced self-medication and stored medications at home and did not provide information on how they disposed unused and expired medications. More awareness and creating a chart of disposal procedures of common medicines and popularizing the chart can be important to strengthen knowledge. The drug disposal and takeback system should be implemented in community pharmacies initially located in major cities and information about the system should be widely disseminated. Similar studies in other health professional institutions and in other regions are required.

Human and animals exposed to drugs through the environment may be affected directly or indirectly. Microbial resistance is the most talked-about topic in the recent times. Antimicrobial resistance may develop as a result of long-term exposure to very low doses of antimicrobials through drinking water. Pharmaceutical companies' falling interest in creating novel antimicrobials in favor of producing fancy medications may exacerbate the problem. Although the effect of very low doses from environmental cycling is unclear, certain populations, such as pregnant women, children, the elderly, and people with renal or hepatic

diseases, may be more vulnerable to such exposure because their pharmacokinetics are altered in these groups, and even minor doses can be harmful. In the same way, some medications in tiny minuscule quantities may have a synergistic effect. The possibility of Placebo impact from medications, even at sub therapeutic amounts in the environment, cannot be ruled out. Furthermore, adverse reactions of type B may occur at these doses. Authors conclude that some recommendations for implementing Eco-directed sustainable prescribing (EDSP) from the standpoint of introducing and strengthening ecopharmacovigilance related medical training and education are based on the aforesaid findings. Hospitals, medical centers, and colleges should create training and educational programs to educate physicians and medical students about Active Pharmaceutical Ingredient (APIs) in the environment, environmental consciousness while prescribing, the environmental impact of their professions, ecopharmacovigilance, and EDSP. Furthermore, there is a need to promote rational prescribing to control over prescription of medications, which is a fair start in implementing EPV in the healthcare system. It is also recommended that the environmental constituent be incorporated into the rational prescribing principles. Additionally, building a database would also be helpful to allow obtaining the relevant information to select the effective and more environment friendly doses rather than prescribing some non-environment friendly hazardous drugs and understand the drugs' excretion profiles.

Drugs plays important role in our day today activities in order to prevent diseases and their treatment. A mythology is famous among people that drugs become toxic and dangerous after expire date but actually it's not like that, there is simple decrease in the therapeutic effectiveness of drug dosage forms. But after expire date we cannot use them and throw them without knowing that these drugs have lethal side effects on living organisms present around us. Reuse of expired drugs that are present around us because these drugs are not safe for living organisms. To design a procedure through which we can extract API from expired drugs and reuse to synthesize such chemicals or compounds which are useful as disinfectants. In this I extract aspirin from expired drug and further this converted into salicylic acid which further undergo decarboxylation to give phenol which is an effective bacteriostatic and bactericidal. Through this we design a proper disposal method for expired aspirin tablets. Aspirin tablets when triturates and react with 0/1 M solution of Fe(NO3)3 it gives brick red color .Where acetyl salicylic acid react with 0.1 M Fe(NO3)3 it gives yellow color. In another hand when we react salicylic acid with same reagent it gives purple color.

NEED FOR THE STUDY:

Drugs and Cosmetics Act in our country regulates import, manufacture, sale, quality control etc of drugs and pharmaceuticals, but this act is silent about recall of unused drugs. Major contributors of unused drugs are the expired leftover medicines in houses and adulterated, spurious. Irrational prescribing practices, over the counter purchase of drugs by public leads to this unnecessary piling of medicines. Absence of legal accountability makes the recall system of drugs ineffective.

In India, there is no one point track and trace system available in the supply chain of medicines. With the introduction of Goods and Services Tax (GST) mechanism any person can purchase any drugs from anywhere. The presence of third-party manufacturing acts as a catalyst, for the mushrooming pharma marketing companies to promote selling huge volumes of medicines subsequently leading to an exponential increase in its wastage. Scientific disposal of unused drugs is very expensive and facility for the same is also not available in many states, so people are forced to dump unused drugs in water bodies or burn it in open spaces leading to environmental pollution. A System called PROUD [Program for Removal of Unused DRUGS] was introduced in Kerala. If this system is operated throughout the country as an National Service Scheme (NSS) activity especially by pharmacy colleges, then this social menace can be prevented to a great extent.

- **Gisela Holm; etal** has discussed about Implementing Ecopharmacovigilance in Practice: Challenges and Potential Opportunities Ecopharmacovigilance (EPV) is a developing science and it is currently very unclear what it might mean in practice. Authors have performed a comparison between pharmacovigilance (PV) and EPV and have identified that there are similarities, but also some important differences that must be considered before any practical implementation of EPV. The biggest difference and greatest challenge concerns signal detection in the environment and the difficulty of identifying cause and effect. It reflect on the dramatic vulture decline in Asia, which was caused by the veterinary use of diclofenac, versus the relative difficulty in identifying the specific causes of intersex fish in European rivers. We explore what EPV might mean in practice and have identified that there are some practical measures that can be taken to assess environmental risks across product life cycle, particularly after launch of a new drug, to ensure that our risk assessments and scientific understanding of pharmaceuticals in the environment remain scientifically and ecologically relevant. These include:

- Tracking environmental risks after launch of the product, via literature monitoring for emerging data on exposure and effects.

- Using Environmental Risk Management Plans (ERMPs) as a centralized resource to assess and manage the risks of a drug throughout its life cycle.

- Further research, testing or monitoring in the environment when a risk is identified.

- Keeping a global EPV perspective

- Increasing transparency and availability of environmental data for medicinal products. These measures will help to ensure that any significant environmental issues associated with pharmaceuticals in the environment (PIE) are identified in a timely way, and can be managed appropriately.

➢ **Avisek Dutta; etal** has discussed about the impact of Pharmaceuticals in the environment have the potential to be hazardous to human beings. With each passing day it is becoming a major source of concern. Due to recent findings showing the availability of pharmaceutical components in the environment, particularly in ground water bodies, pharmaceuticals have gained a growing amount of attention from worldwide health regulatory bodies and have become one of the most significant water pollutants. The aim of this article is to review the environmental hazards of pharmaceuticals that have been reported in various literature sources to promote awareness on safe usage of medicines, to increase pharmaceutical manufacturers' knowledge on environmental safety aspects and to arrest the attention of pharmacovigilance practitioners to some of the emerging problems caused by medicines. Pharmaceutical waste has been a source of huge concern amongst environmental scientists. Pharmaceutical manufacturers and pharmacovigilance scientists should invest more attention to these increasing environmental concerns caused by medications. Ecopharmacovigilance is defined by the World Health Organization (WHO) as the science and activities concerned with the detection, assessment, understanding, and prevention of adverse events or other related problems caused by pharmaceuticals in the environment that affect people and other animal species. This review is an attempt to compile information on Ecopharmacovilance, with an emphasis on the Indian perspective.

➢ **Bikash Medhi and Rakesh K. Sewal** has discussed about Ecopharmacovigilance: An issue urgently to be addressed, to protect the mother environment from the harmful effects of

residual pharmaceutical left unnoticed. Every rose has its thorn" and so have the drugs too. Drugs have been a boon for the humanity in curbing the ailments though not fully but to a great extent. Along with beneficial effects they also impart some adverse reactions sooner or later. Owing to this fact, a new branch of science called "Pharmacovigilance" sprouted in 1960 after the incidence of thalidomide disaster. Pharmacovigilance became well accepted and practiced in developed world but developing part of globe consumed decades to it. At present, India has also started a national program to monitor the adverse effects of drugs. Unfortunately, however, despite this achievement worldwide, the effect of drug use on environment remains unaddressed. The exorbitant decline in number of vultures in Indian subcontinent shook the environmental scientists and activists. Prior to this observation, research on the impact of chemical pollution was restricted to persistent organic pollutants. 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 ecopharmacovigilance. Ecopharmacovigilance can be defined as science and activities concerning detection, assessment, understanding, and prevention of adverse effects or other problems related to the presence of pharmaceuticals in the environment, which affect human and other animal species.

REFERENCES:

1. Stüvel H. Kann man nach dem Verfallsdatum Medikamente nutzen [Can medicines be used after expiry]. Gesund Magazin; 2012,
2. Bound JP, Voulvoulis N. Household disposal of pharmaceuticals as a pathway for aquatic contamination in the United Kingdom. Environ Health Perspect. 2005;113(12):1705–1711. doi:10.1289/ehp.8315
3. Vogler S, Leopold C, Zuidberg C, Habl C. Medicines discarded in household garbage: analysis of a pharmaceutical waste sample in Vienna. J Pharm Policy Pract. 2014;7:6.
4. Daughton CG. Cradle-to-cradle stewardship of drugs for minimizing their environmental disposition while promoting human health. II. Drug disposal, waste reduction, and future directions. Environ Health Perspect. 2003;111(5):775–785.
5. Boxall AB. The environmental side effects of medication. EMBO Rep. 2004;5(12):1110–1116.
6. Costanzo SD, Murby J, Bates J. Ecosystem response to antibiotics entering the aquatic environment. Mar Pollut Bull. 2005;51
7. Beirens TM, van Beeck EF, Dekker R, Brug J, Raat H. Unsafe storage of poisons in homes with toddlers. Accid Anal Prev. 2006;38(4):772–776
8. Holm G, Snape JR, Murray-Smith R, Talbot J, Taylor D, Sörme P. Implementing ecopharmacovigilance in practice: challenges and potential opportunities. Drug Saf. 2013;36(7):533–546.
9. Ali SE, Ibrahim MIM, Palaian S. Medication storage and self-medication behaviour amongst female students in Malaysia. Pharm Pract (Internet). 2010;8(4):226–232.
10. Labu Z, Al-Mamun M, Harun-or-Rashid M, Sikder K. Knowledge, awareness and disposal practice for unused medications among the students of the Private University of Bangladesh. J Biomed Pharm Res. 2013;2:26–33.
11. Sirisha A, Janardhan M, Karuna SP, Rao VY, Raikar SR, Patil S. Knowledge, attitude and practice on safe disposal of medicines among medical and dental undergraduates. J Basic Clin Res. 2016;3:5–9.

12. Paudel E, Choi E, Shrestha N. Pharmaceutical waste management in private pharmacies of Kaski District, Nepal. Int J Innov Sci Res Technol. 2019;4(8).
13. How medicine take-back works. Available from: http://www.take backyourmeds.org/why/how-medicine-take-back-works/.
14. Wu M, Atchley D, Greer L, Janssen S, Rosenberg D, Sass J. Dosed without prescription: preventing pharmaceutical contamination of our nation's drinking water. NDRC. 2009;60. Available from: https:// www.nrdc.org/sites/default/files/hea_10012001a.pdf.
15. Persson M, Sabelstrom E, Gunnarsson B. Handling of unused prescription drugs–knowledge, behaviour and attitude among Swedish people. Environ Int. 2009;35(5):771–774.