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A REVIEW OF THE EFFECTS OF PHARMACEUTICAL WASTE ON THE ENVIRONMENT AND HUMAN HEALTH

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ABSTRACT

Pharmaceutical wastes include a wide range of antibiotics, painkillers, and cancer drugs that cause environmental pollution and disrupt the natural functioning of ecosystems. In this review study, the effects of pharmaceutical waste on the environment and human health were investigated. The results obtained from the review of various studies showed that pharmaceutical waste has environmental risks and destructive effects. The review of various studies showed the negative effects of pharmaceutical waste on human health, including mortality, the prevalence of respiratory and lung diseases, cancer, and negative effects on the soil of agricultural products and water. Research evidence showed the harmful environmental effects of pharmaceutical waste on surface and underground water, soil plants, and agricultural and aquatic products, serious damage to people's health, respiratory diseases, cancer, neurological disorders, and transmission to food chains. However, this evidence requires a more detailed and comprehensive evaluation so that the results can be interpreted more confidently.

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Introduction

Medicines play an important role in the treatment and prevention of diseases in animals and humans [1, 2]. But pharmaceutical residues may have unwanted effects on animals and microorganisms in the environment [3, 4]. Although the side effects of drugs on human and animal health are usually fully investigated in safety and toxicology studies, the potential environmental effects of drug residues have been less studied. Some pharmaceutical residues, including painkillers, antidepressants, and antibiotics, can affect humans and animals [5, 6]. Many researches show that one of the effects of the industrialization of societies is the pollution of soil and underground water and hazardous pharmaceutical waste all over the world [7, 8].

Medicines are known as hazardous waste whose generic or chemical name is included in part 33 of the list of wastes published by the United States Environmental Protection Agency under the title of hazardous waste in 40CFR261 [9, 10] and also has characteristics of flammability, corrosiveness, reaction acceptability, and toxicity that are given in the same list (40CFR261) [11, 12].

In European countries in 2014, according to estimates, 342,000 landfills of contaminated pharmaceutical waste were identified (5.7 per 10,000 population) [13, 14]. According to the data collected from 33 countries in 2011, the most pollutants that lead to soil and surface and underground water pollution were hazardous waste [15, 16], including urban and industrial waste and industrial and commercial activities, and pollution caused by pharmaceutical waste and hospital waste [17]. In seven Asian countries, 679 areas were identified as places contaminated with pharmaceutical and chemical waste [18]. According to the report of the World Health Organization, one-third of the disease burden in Africa is related to environmental risk factors [19, 20]. Environmental pollution by pharmaceutical waste is reaching an alarming level, and the burden of diseases related to the effects of waste in low-income countries is increasing and is not sufficiently recognized [21]. A wide variety of human drugs,

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including antibiotics, statins, or cytotoxins used in cancer treatment, as well as large amounts of veterinary drugs such as antibacterials, antifungals, and antiseptics, reach the environment through various pathways [22, 23] and lead to soil, surface water, and agricultural land pollution.

After being released into the environment, pharmaceutical wastes are deposited in surface water and rivers, air, soil, and agricultural lands. A wide range of other factors such as physical properties and chemical compounds and characteristics of the receiving environment affect their distribution in the environment [24]. Adsorption coefficients of pharmaceutical residues in soil for several veterinary drugs have been reported from 1 liter per kilogram to more than 6000 liters per kilogram [25]. In addition, the degradation of pharmaceutical residues varies significantly depending on the chemistry, biology, and weather conditions. For example, the half-life in winter conditions is six times higher than in summer, and this compound is absorbed faster in loamy sandy soils [26]. Recent studies have measured a wide range of drugs, including hormones, steroids, and antibiotics, with small amounts in different soil, surface, and underground water samples, and the effects of these pharmaceutical residues on environmental organisms and human health are worrisome [27]. A wide range of harmful effects of pharmaceutical residues, including physiological effects, inhibition or stimulation of growth in aquatic plants and algae species, and effects on the fertility and growth of fish, reptiles, and aquatic invertebrates have been identified [28]. In addition to the structure and function of DNA in tumor cells, anticancer drugs and chemotherapy or cytostatic drugs directly or indirectly affect non-target cells and tissues in living organisms [29]. Considering the above contents and the need to investigate the role of pharmaceutical waste as a dangerous environmental pollutant, our main goal in this research is to investigate the effects of pharmaceutical waste on the environment and human health.

Results and Discussion

Pharmaceutical residues in the environment usually appear as complex compounds, and therefore even if the concentration of a compound is low, it may be important for environmental toxicity [30]. In the study of Mishik *et al*. investigating the genotoxic properties of anticancer drugs, it was found that even low concentrations of these drugs have toxic effects on the ecosystem [31]. The concentration of medicinal compounds has been observed several times higher than the predicted concentration in the environment, so these results suggest the possibility of adverse effects of medicinal residues in plants [32]. Kennedy *et al*. reported that compared to the effective concentrations of a binary compound, a combination of pharmaceutical waste drugs, including anticancer drugs, can pose a serious risk to the environment. Because their effects occur in very low concentrations, which are in the range of concentrations encountered in aquatic systems. According to Al-Rashak *et al*.'s reports, the effects of some pharmaceutical residues are synergistic even at low concentrations.

In addition, the previous study of the double combination of anticancer drugs showed that algae are more sensitive than cyanobacteria and these compounds can have their own cooperative or antagonistic effects [33]. In the studies of Kovács *et al*. [34], Pichler *et al*. [35], Gajski *et al*. [36], Novak *et al*. [37], and Larsson *et al*. [38], the harmful environmental effects of pharmaceutical wastes on surface and underground water, plants, soil, and serious harm to health People at risk of these pollutants have been identified. In addition to this review, various studies show that pharmaceuticals are not the only dangerous environmental pollutants, but living and aquatic organisms are at risk, from a combination of drugs and other substances, including pesticides, agricultural toxins, and industrial chemicals [39]. Many countries do not routinely monitor the presence of drugs, including antibiotics, in drinking water due to high costs. Studies conducted in Southeast Asia have reported the presence of several types of antibiotics in hospital wastewater. Studies conducted in Bangladesh, India, Indonesia, and Thailand have reported antibiotic residues in aquatic products [40]. Therefore, when wastewaters containing untreated antibiotics enter open water or soil, antibiotics, and their metabolites can enter the human food chain and endanger the health of humans and other living organisms.

The review of various studies in this research showed that indirect exposure to pharmaceutical substances through surface water, soil, and agricultural products is considered a risk for humans. A comparison of the data obtained from previous studies showed that the concentration of medicinal compounds in the groundwater levels is very low. However, the possibility of transmission from other methods, such as soil absorption by crops and biomagnification through the food chain, has not been sufficiently calculated and the possibility of transmission cannot be completely ruled out [41]. Evaluating the environmental effects of pharmaceutical waste is very difficult and complex. Since 1980, the US Food and Drug Administration (FDA) has evaluated the environmental risks of human and veterinary drugs and their effects on aquatic and terrestrial organisms before they are placed on the market. However, the harmful effects of most drugs remain unknown and there is a need for evidence-based studies [42]. Various studies have shown the environmental effects and potential negative effects of pharmaceutical residues on fish, algae, bacteria, earthworms, plants, and invertebrates [43].

However, there is a fundamental question regarding the real value of these studies; Based on the fact that in evaluating the risks of medicinal substances, they usually use standard biotoxicity tests, which are often short-term and focus mainly on mortality or respiratory diseases and cancer as the endpoint. In addition, evaluation tests focus on pharmaceutical substances remaining in surface waters and do not pay attention to pharmaceutical substances that are present in sediments [44]. The observed effects of pharmaceutical effects in the laboratory are at much higher concentrations than those which are measured in the natural environment, so the more subtle effects of pharmaceutical residues in the environment may remain unknown [45]. In addition, many organisms that affect human and animal health and are targeted by drugs play a vital role in the functioning of ecosystems [46]. While many of these observations are seen in realistic environmental concentrations and their

importance in environmental health has not yet been determined; In fact, the fact that some drugs indirectly have adaptive environmental effects will be one of the research challenges in the coming years. Also, the environmental behavior of a substance may change in the presence of other substances. For example, antibacterials act on soil microbes, which play an important role in reducing pesticides [41].

Due to the limitations of the research conducted so far, only a small part of the currently used drugs has been investigated, and there is a need to understand how other drugs affect the environment. Traditional standard tests may be inappropriate for evaluating the effects of many drugs [47]. Although they showed unpleasant effects after exposure to drugs in realistic environmental concentrations. However, the function and ecological effects of medicinal substances should be determined precisely [44]. Drugs are unlikely to affect the environment individually. Therefore, it is necessary to examine the effects of pharmaceutical residues in combination with other substances. Therefore, future research should focus on understanding the basic biological processes including the release fate and effects of drug residues [39].

Such research should lead to the development of new modeling methods, for example, Hoggett *et al*. have proposed an adaptive plasma concentration model that can connect mammalian and fish species and provide useful information about the possible effects of drugs on Offer fish. Other modeling approaches, such as quantitative and structure-activity relationships, can help us estimate the environmental effects of drugs from their chemical structure and better understand the effects of drug residues on human health and the environment. Among the limitations of this research is the lack of sufficient and evidence-based studies to determine the absorption of pharmaceutical residues in soil, surface water, and agricultural products and their transfer to the food chain. Therefore, it is necessary to conduct quantitative studies to determine the indirect effects of pharmaceutical residues on the environment and human health. Due to the complexity and difficulty of determining the effects of pharmaceutical residues in the ecological cycle, the harmful and adverse consequences of most drugs in the environment remain unknown. Also, it is difficult to evaluate the effect of a drug alone, and the effects of other dangerous chemical substances, such as electronic waste, industrial and petroleum materials, may have synergistic effects on the negative consequences of pharmaceutical waste disposal in the environment. Therefore, future research should focus on understanding the biological processes of pharmaceutical waste based on its release and fate in the environment.

Conclusion

According to the results of reviewing various studies, pharmaceutical and chemical wastes as destructive factors have harmful effects on the environment and human health. In all these studies, the mortality rate, the incidence of respiratory diseases and cancer, the prevalence of hepatitis C, poisoning, and the risk of congenital malformations in people who lived near chemical waste disposal sites and pharmaceutical waste were significantly high. Research evidence showed the harmful environmental effects of pharmaceutical waste on surface and underground water, soil plants, and agricultural and aquatic products, serious damage to people's health, respiratory diseases, cancer, neurological disorders, and transmission to food chains. However, this evidence requires a more detailed and comprehensive evaluation so that the results can be interpreted more confidently.

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