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Review Article

Perception and impact of micropollutants in urine-based liquid fertilizer on crop production: A comprehensive review of Eco-sanitation practices

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ABSTRACT

Large-scale sustainable agriculture presents a formidable challenge globally, resulting in severe food insecurity for approximately 52% and 48% of people living in rural and urban areas, respectively. An estimated 690 million individuals suffer from hunger annually due to the high cost of chemical fertilizers and other factors. To reduce costs, source-separated urine offers a promising alternative for crop production, despite containing more nitrogen and phosphorus than traditional fertilizers. However, human urine also contains pharmaceuticals and micropollutants with adverse effects on human health and the environment. Human urine provides essential micronutrients for plant growth, with studies showing similar nutrient concentrations between concentrated urine and mineral fertilizers. Nevertheless, the presence of heavy metals and other contaminants in urine raises safety concerns. While urine diversion toilets can safely collect urine, their use as a liquid fertilizer requires careful consideration due to the presence of disease-causing organisms, pharmaceuticals, and metabolites that contribute to water and soil contamination. Consumers and farmers alike worry about the safety of crops fertilized with urine, given the perception of disease-causing pathogens. This review explores the impact of urine and chemical fertilizers on plant yield as well as the effects of heavy metals, pharmaceuticals, and microplastics on human health and the environment. Various methods to remove antibiotics from urine, such as membrane bioreactors combined with complex chemicals and physicochemical processes, were also examined. These methods, including activated powdered carbon, nano-filtration, ozone, and ozone/UV, target specific antibiotics and their metabolites to ensure the safety of urine-derived fertilizers.

Key words: Urine, Pharmaceuticals, Fertilizer, Nutrients, Microplastics, Heavy metal

INTRODUCTION

The present population in the world is estimated to be around 8.5 billion people, with 8.9% of the population still suffering from inadequate food supply (FOA, 2021). Therefore, transforming human urine into liquid fertilizer is critical for sustainable agriculture and improving global food security, particularly in low and middle-income countries. The application of human urine as fertilizer in crop production would help to minimize production costs compared to the use of chemical fertilizers, which can be more expensive (Simha *et al.,* 2017). Human urine contains about 75-90% nitrogen as urea, 71% potassium, and 47% phosphorus. The daily production of urine by an individual is approximately 1.2 liters, depending on various factors such as food type and water intake (Martin *et al.,* 2020). However, urine also contains micropollutants that can be associated with short and long-term toxicity, endocrine-disrupting effects, and antimicrobial resistance (Sundberg *et al.,* 2013). Eco-sanitation is an effective way to convert waste into useful resources and prevent the accumulation of harmful substances in the environment. It helps to close the loop between sanitation and agriculture by transforming waste into useful products. Although human urine constitutes most of the necessary nutrients for crop production, its application as fertilizer has numerous challenges in terms of safety, psychological perception, and societal acceptance (Shaw, 2010).

Furthermore, elimination of human waste products like urine from the body is an important process during excretion, and these wastes contain numerous substances that are harmful to humans and the environment. However, urine, which is considered animal waste, is made up of a large concentration of the major primary and other nutrients like nitrogen (N), phosphorus (P), potassium (K), calcium (Ca), magnesium (Mg), and iron (Fe) etc. which can be absorbed directly by plants (Sharma *et al.,* 2021). Urine as fertilizer has an appreciable amount of plant macro, micronutrients, and other substances necessary for plant growth. However, urine concentration varies for different people in different countries depending on many factors including the economic status of the individuals, environmental and climatic conditions, amount of fluid intake, and the type of food eaten (Shaw, 2010). Although human urine constitutes most of the necessary nutrients for crop production, its application as fertilizer has numerous challenges in terms of its safety, psychological perception of farmers and community people to use it as fertilizer, and to eat the crops grown from it is also a serious concern.

Research on the use of human urine as fertilizer has confirmed the presence of disease-causing pathogens and pharmaceuticals, which is a serious concern for consumers, farmers, and researchers. Various studies have focused on the treatment and removal of micropollutants from urine, such as the use of powdered activated carbon and chemical and biological extraction methods (Baumgarten *et al.,* 2007; Beaune, 2018).

Furthermore, there is a limited attempt made to provide a comprehensive summary of the occurrence of microbial resistance and removal of micropollutants like antibiotics in human urine by using an activated carbon filter. The main aim of this review is to investigate the literature of various authors on the conversion, perception, impact, and use of urine as liquid fertilizer and to examine the various pharmaceuticals, metabolites, and ways of removing them.

URINE COLLECTION, STORAGE, AND TRANSPORTATION

Urine collected as liquid fertilizer should be devoid of the presence of the pathogenic organism and should also be prevented from volatilization and toxicity of crops (Shaw, 2010). According to CDC, the pathogen in the urine mainly includes schistosomes and other microorganisms can be spread from host to host through urine. Therefore, urine must be kept in a closed container for four hours to terminate the parasite's life cycle, which alternatively kills the pathogen. However, prolonged storage of liquid urine at a temperature of 4 to 20 °C is approximately between one to six months which provides the platform for treating and killing diseases causing organisms and is the cheapest and most common strategy used by farmers in low-income countries, small-scale farming, vertical farming, and container garden (Quang, 2020). Similarly, this method is based on the risk and cross-contamination by users, and it also depends on the type of crop to be cultivated. Extended storage of urine for greater than six months makes the urine almost absolutely sanitized from pathogens (Tilley *et al.,* 2008). Notwithstanding, collection materials for urine must include low-cost and easily used materials such as 20 liters gallon containers, rubber buckets, jerry cans, and PVC storage tanks (Tilley *et al.,* 2008). Concentrated urine as liquid fertilizer can be obtained by different means which include a waterless urinal and by using a urine diversion toilet (Etter & Udert, 2015).

PERCEPTION OF PEOPLE ON THE USE OF URINE AS FERTILIZER

The practice and tradition of community farmers during the green revolution should still be observed concerning the use of urine as fertilizer, but not be used as a complete obstacle to the use of urine as liquid nutrients. However, to a large extent, the application of urine as fertilizer has been a common practice in some cultures for low-income centuries. In other cultures, it may be viewed as unhygienic, unpleasant, and taboo. The social and cultural perception of using urine as fertilizer can have several effects in terms of:

- Acceptance: In cultures where the application of urine as fertilizer is widely accepted, people may view it as a valuable resource for enhancing soil fertility and plant growth. They may even take measures to collect and use urine effectively.
- Stigmatization: In cultures where urine has been seen as unclean or taboo, people may avoid using it as fertilizer, even if it could improve soil quality and plant growth. This can result in a negative impact on eco-sanitation practices on the environment and agricultural activities. As such, alternative applications of chemical fertilizers may be more expensive.
- Education: Educating people about the benefits of using urine as fertilizer and how to use it safely can help to change social and cultural perceptions. This can lead to increased acceptance. The use of urine as fertilizer can have positive effects on the environment and also the agricultural industry.
- Public health: There may be concerns about the safety of using urine as fertilizer, especially if not handled properly. In cultures where stigma is associated with urine, people may be less likely to seek information on how to use it safely. Education and outreach efforts can help to address these concerns and promote safe practices.

Overall, the social and cultural perception of using urine as fertilizer can have significant impacts on its use and effectiveness. Promoting acceptance and safe use of urine as fertilizer can help to improve soil quality, plant growth, overall sustainability, and cost-effectiveness.

Findings show that using urine in agricultural production is drastically influenced by social and cultural restrictions in a way that fails to see farming as an economic activity. Collaborative action, in which groups of community farmers jointly generate new procedures and adapt practices, serves as a very vital tool for social change and negotiation of cultural norms, skills, and taboos that will not negate the use of urine as fertilizer which can otherwise limit the acceptance and spread of urine as an alternative to chemical fertilizer (Devkota *et al.,* 2020). A perception survey conducted by Devkota *et al.* (2020) in a Nepal community school shows that only a few teachers agreed to use urine as fertilizer in their school garden. However, acceptance of eco-sanitation food products can be increased by using various methods of communication (Cohen *et al.,* 2020).

Another perception survey indicated that 59% and 46% of farmers show positive opinions on the recycling of urine and Feces as fertilizer respectively (Simha *et al.,* 2017), and the data were analyzed using a chi-square test. The one-way analysis variance (ANOVA) was applied to predict the structure of the population. Similarly, in research conducted by Mugivhisa and Olowoyo (2015), 85% of total respondents said they do not have any knowledge of the use of urine as fertilizer. 82.7% and 81.1% said they would not eat spinach and maize cultivated by urine respectively. However, 38.3% acknowledged the willingness to eat food cultivated by using urine. However, 69.9% of the total sample of the population said they are willing to eat food produced from urine if they are adequately sensitized. Similarly, another perception survey indicated that 55% of participants agreed that urine should be used as fertilizer, 44% agreed to eat crops cultivated by using urine as fertilizer, 65% said using urine as fertilizer is associated with potential health risks, and 80% believed that the risk can be mitigated (Simha *et al.,* 2018). Demographic results were evaluated using the chi-square test and one-way analysis of variance (ANOVA) (Simha *et al.,* 2018).

APPLICATION OF URINE AS FERTILIZER

In utilizing urine as liquid fertilizer, it is crucial to regulate its application properly and have knowledge of the hazards of volatilization, which can result in the release of ammonia gas and contribute to the greenhouse effect. This can lead to the precipitation of soluble salts, changes in the soil's alkalinity and acidity, and sometimes poor crop productivity (Simha & Ganesapillai, 2017). Nonetheless, the method of urine application depends on crop type and arrangement in the field (Hatfield & Hatfield, 2018). When crops are in a row, urine is applied around the crops' base using the ring method, close to the soil, with water added to minimize ammonia gas volatilization and evaporation. For family application, concentrated urine can be applied directly to crops, provided it is used one month after the last fertilization and before harvesting (Spuhler & Rath, 2017).

However, various organisations and authors have different urine dilution methods. The Regional Centre for Potable Water and Sanitation (CREPA) recommends a 1:1 ratio of undiluted urine to water. Morgan (2003) suggests a dilution factor of 1:3 to 1:5, depending on crop type and age. Esrey *et al.* (2001) recommend a dilution factor of 1:5 to 1:10. The use of human waste, such as urine, has significantly helped to reduce the high demand for chemical fertilizers globally. Germany and Sweden have reduced the cost of chemical fertiliser by up to 10-20% and 20-30%, respectively, by using urine (Winker *et al.,* 2009). Human urine and faeces can improve soil structure and quality, reducing the need for inorganic fertilisers, which can increase the total cost of crop production (Simha *et al.,* 2017). Concentrated urine contains almost the same amount of nutrients as mineral fertiliser, with the nitrogen concentration resulting from the presence of urea in urine (Martin *et al.,* 2020). Various types of crops have been cultivated using urine as fertiliser, and nutrient utilisation efficiency can be calculated to determine its effectiveness. Nutrient utilisation efficiency (NUE) is described as the ratio of the additional nutrients absorbed by the crop to the nutrients input by the fertiliser, compared to the nutrients absorbed by the controlled experimental crop without any added nutrients (Martin *et al.,* 2020). Nutrient utilisation efficiency can also be computed by comparing the increase in production yield in fertilised crops to the production yield of the controlled experimental crop without fertiliser (Martin *et al.,* 2020).

Therefore, the chemical fertilizer efficiency (CFE) is given as:

$$\text{NUE} = \frac{\text{Nutrient absorbed by fertilized crop} - \text{Nutrient absorbed by control experimental crop}}{\text{Nutrient putin by fertilizer}} \text{X100}$$

$$\text{CFE} = \frac{\text{NUE of urine based fertilizer}}{\text{NUE of chemical fertilizer}} \text{X100}$$

According to Shaw (2010), the application rate of liquid urine fertilizer is not limited to the following methods.

- 2 Liters per square meter of field crop per week
- 4 Liters of garden crops per week
- 2 Liters of one tree crop per week.

NUTRIENT COMPOSITION

Human urine, when healthy, contains low levels of disease-causing pathogens and significant amounts of major plant micro and macronutrients such as nitrogen (N), phosphorus (P), potassium (K), calcium (Ca), iron (Fe), sulfur (S), and magnesium (Mg). Due to its high nutrient content and low pathogen levels, human urine is a potential and eco-friendly substitute for liquid fertilizer in crop production (Ranasinghe *et al.,* 2016). However, the mean concentrations of sodium, potassium, nitrogen, and phosphorus in human urine fertilizer depend on various factors such as climatic and environmental conditions, fluid intake, food type, and the kidney's ability and rate of osmoregulation in eliminating urine. Chemical analyses showed that the mean concentrations of nitrogen, sodium, phosphorus, and potassium in urine were 3.07±1.15 g\L, 1.17±0.12 g\L, 0.02±0.004 g\L, and 1.7±0.2 g\L (mean ±SE), respectively (Ranasinghe *et al.,* 2016). The mass concentration of urine depends on the family's income capacity. In high-income countries, urine has mass concentrations of 8.8-9.2 g\L of nitrogen, 0.74-2 g\L of phosphorus, and 2.2-2.7 g\L of potassium (Martin *et al.,* 2020). For example, in Thailand, the average daily urine production is around 0.6 to 1.2 liters, and in Finland, urine has a constituent composition of 2 g\L of potassium, 0.7 g\L of phosphorus, and 8.36 g\L of nitrogen at a pH of 9.2. In conclusion, urine concentrations vary depending on several factors, as discussed above (Hatfield & Hatfield, 2018) (Table 1).

According to Martin *et al.* (2020), around 60-70% of plant nutrients present in wastewater are derived from urine, which provides 79% nitrogen, 71% potassium, and 47% phosphorus as provided in Figure 1. Typically, a healthy adult excretes one to one and a half liters of urine daily under optimal conditions, as noted by Rose *et al.* (2015). Fresh, undiluted urine has a slightly acidic pH of 6.2. The main plant nutrients in human urine (Figure 1) include 80% nitrogen, 55% phosphorus, and 60% potassium, as reported by Schönning (2001).

However, the amount of nutrients excreted by individuals varies based on their diet and economic status, as different countries have different levels of protein consumption per capita, as shown in the protein consumption data provided by FOA (Shaw, 2010). The daily nutrient output in feces and urine can be predicted by using the following equations:

Nitrogen = 0.13 x Total protein in food --------------------- (1)

Table 1: Shows the quantity of NPK in urine at various PH by different authors

Reference	Nitrogen		Phosphorus		Potassium		pH
	Mg\L	g\L	Mg\L	g\L	Mg\L	g\L	
Udert and Wächter (2012)	2390	2.38	208	0.208	1410	1.14	8.69
Kocatürk and Baykal (2012)	5700	5.7	415	0.415	1200	1.2	6.0
Pradhan *et al.* (2007)	940	0.94	63	0.063	360	0.36	8.6
Akpan-Idiok *et al.* (2012)	4280-4970	4.28-4.97	420-280	0.42-0.28	760-940	0.76-0.49	8.9-9.2

Source:(Hatfield & Hatfield, 2018)

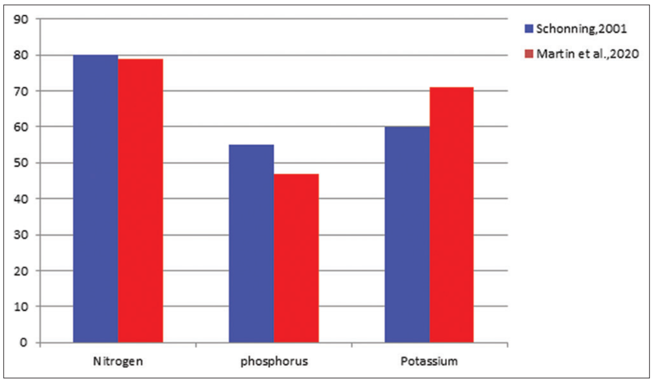


Figure 1: Percentages of three primary nutrients in human urine (NPK) from two different studies (Martin *et al.,* 2020; Schönning, 2001)

Phosphorus = 0.011 x Total protein in food + Food protein in plant--- (2)

EFFECT OF URINE AS FERTILIZER ON PLANTS, SOIL, AND HUMAN

The use of inorganic fertilizers in large-scale commercial and industrial agriculture has been common practice worldwide, resulting in increased productivity but also high capital costs (Andersson, 2015). However, farmers in low and middle-income countries often cannot afford the high cost of chemical fertilizers, leading to food insecurity and environmental degradation. Excessive use and mismanagement of chemical fertilizers can cause adverse environmental and climate change impacts, as well as health problems such as kidney disease and skin cancer (Filippelli *et al.,* 2012). To address this, researchers are exploring low-cost and sustainable alternatives to chemical fertilizers, including the use of natural fertilizers that are environmentally and farmer friendly (Ranasinghe *et al.,* 2016). Human urine is a readily available source of natural fertilizer, containing nitrogen, phosphorus, and potassium, which are essential for plant growth (Martin *et al.,* 2020). However, the use of urine as a fertilizer requires proper management to address concerns about safety and effectiveness. For example, urine from people with medical conditions should not be used as fertilizer due to the potential presence of pharmaceuticals and other micronutrients (Devkota *et al.,* 2020).

Management practices for urine fertilizer use should also consider the amount of urine added, the constituents of the urine, soil properties, and nutrient requirements. Research has shown that excess urine application can lead to higher ion concentrations at the bottom of maize plants, indicating the need for optimal application rates (500 mL) to avoid adverse effects on plant growth (Kassa *et al.,* 2018). Soil pH, however, does not significantly affect urine fertilizer effectiveness.

Effect of urine on crop yield

Human urine is a liquid waste product that is produced by the kidneys of humans and other animals. It contains macronutrients such as Nitrogen, Phosphorus, and Potassium (NPK), which are essential nutrients for plant growth. Urine also contains micronutrients such as Calcium, Magnesium, Iron, and Sulphur, which are taken in by plants and have a similar composition to chemical fertilizer (Güereña *et al.,* 2016). The use of urine as a liquid fertilizer for plants is a low-cost and low-risk method that can significantly increase crop yield, contributing to food security and income generation, especially in low and middle-income countries (Andersson, 2015). Studies have shown that urine can have a positive effect on plant growth, yield, and nutrient content in various crops, including tomatoes, cucumbers, and maize (Güereña *et al.,* 2016; Miheso *et al.,* 2020a). This is due to the high nitrogen content of urine, which is essential for plant growth (Buckley *et al.,* 2010). One study found that the application of urine to tomato plants significantly increased their growth and yield compared to plants that received no fertilizer (Buckley *et al.,* 2010) (Table 2). Another study examined the effect of urine on maize growth and found that urine had the same effect on maize growth as mineral fertilizers (Eriksen *et al.,* 2010).

In one study, tropical horticulture plants were cultivated by using 50 L of diluted urine in a ratio of 1:3 and 2:3 rainwater was used as a control experiment for 36 days. The plants grown in diluted urine were greener with more leaves and increased height (Beaune, 2018). In another study, Bushita beans were cultivated using different samples of fertilizer, and the plot with 20% more urine showed positive growth and high productivity (Ranasinghe *et al.,* 2016). The application of urine as a liquid fertilizer has shown very good results in crop production compared to chemical fertilizers in various types of crops, including vegetables (Table 2). The liquid form of urine makes the nutrients more readily available to plants (Kassa *et al.,* 2018). For instance, the cultivation of maize seeds using liquid fertilizer in which the leaf size, length, height and width of each maize plant were analyzed. The root's dry mass

Table 2: Shows selected crops yield in metric tons per hectare by using urine and inorganic fertilizers

Crop	Control Experiment	Urine Fertilizer	Chemical fertilizer	Countries Tested
Corn	2.4	3.6	3.5	Benin
Tomato	2.1	5.2	5.8	Burkina Faso
Cassava	45.0	60.0	60.0	Ivery.Coast
Okra	1.7	2.3	2.6	Burkina Faso
Cabbage	19.1	32.0	31.0	Togo

Source:(Shaw, 2010)

was also measured after harvesting. The result showed that 500 mL of liquid urine was optimum for effective cultivation, and any extra addition of urine did not have a positive effect on growth (Kassa *et al.,* 2018).

In summary, the use of urine as a liquid fertilizer is a low-cost and low-risk method that can significantly increase crop yield (Table 2) and contribute to food security and income generation, especially in low and middle-income countries. Urine is a valuable source of nutrients for plants and can be used instead of traditional fertilizers because it is cheaper (Buckley *et al.,* 2010; Eriksen *et al.,* 2010; Andersson, 2015; Güereña *et al.,* 2016; Ranasinghe *et al.,* 2016; Beaune, 2018; Kassa *et al.,* 2018).

Effect of urine on soil health

The use of urine as a liquid fertilizer has been shown to have potential benefits for soil health. Miheso *et al.* (2020b) conducted a study which found that applying urine to soil can improve soil organic matter, soil microbial biomass, and soil enzyme activity. The researchers suggest that the high nitrogen content in urine may stimulate bacteria and accelerate the breakdown of organic matter. Another study by Kirchmann *et al.* (2015) investigated the effect of urine on soil nutrient levels. The researchers found that urine application significantly increased soil nitrogen and phosphorus availability compared to unfertilized soil. Furthermore, the study revealed that urine had a similar effect on nutrient availability as mineral fertilizers, indicating that urine can be a sustainable alternative to traditional fertilizers. However, excessive amounts of urine or high urine concentration levels can harm plant growth and development by causing a salt buildup in the soil (Miheso *et al.,* 2020b).

The presence of antimicrobial-resistant bacteria in urine can pose potential risks to human and plant health. The World Health Organization (WHO) states that the presence of antimicrobial-resistant bacteria in urine can lead to urinary tract infections that are difficult to treat (WHO, 2021). Moreover, Donovan *et al.* (2008) have found that using urine from individuals who have taken antibiotics or have a UTI can introduce antimicrobial-resistant bacteria into the soil and onto plants. Antimicrobial-resistant bacteria in soil can potentially transfer to plants and endanger human health if consumed. Additionally, using antimicrobial-resistant bacteria-contaminated urine as fertilizer can aid in the spread of resistant pathogens in the environment (Berendonk *et al.,* 2015). To prevent the spread of antimicrobial-resistant bacteria, it is crucial to use urine as a fertilizer only from individuals who have not recently taken antibiotics or have urinary tract infection (UTI) and to ensure that appropriate sanitation measures are taken during the collection and use of urine as a fertilizer. Further research is required to understand the potential risks of using urine from individuals who have antimicrobial-resistant bacteria on plant health and human health. In conclusion, using urine as a fertilizer can benefit plant growth and development, but it is essential to apply urine correctly and monitor soil conditions to avoid any negative effects.

Effect of heavy metals in human urine

Heavy metals, such as lead, cadmium, and mercury, can accumulate in the body over time, resulting in chronic toxicity and a variety of health problems, including neurological disorders, kidney damage, and cancer (ATSDR, 2019). These metals can enter the body through ingestion, inhalation, and dermal contact, among other routes. For individuals working in industries where heavy metal exposure is common, including mining, smelting, and battery manufacturing, urine may be a significant source of exposure (Rahman *et al.,* 2021). Furthermore, urine used as fertilizer can also expose individuals to heavy metals. If heavy metals are present in the urine used as fertilizer, they can accumulate in the soil and potentially enter the food chain (Gwenzi *et al.,* 2015). Therefore, it is crucial to monitor heavy metal exposure in at-risk individuals and implement appropriate measures to reduce exposure and mitigate the negative health effects associated with heavy metal toxicity.

Effect of microplastic in human urine

There has been limited research on the potential health impacts of microplastics found in urine (Prata *et al.,* 2020), but it is concerning that exposure to microplastics could have negative consequences. Microplastics, which are small plastic particles that are less than 5 millimeters in size, are present in many environments and can be consumed or inhaled by humans through food, water, and air (Koelmans *et al.,* 2019). Studies have demonstrated that microplastics can accumulate in the organs and tissues of animals and may have toxic effects (Rochman et al., 2013). While the presence of microplastics in human urine has been confirmed, the potential health consequences remain unclear (Schluter *et al.,* 2020). There are indications that microplastic exposure can lead to inflammation, oxidative stress, and damage to cellular and DNA structures (Wright & Kelly, 2017). Nevertheless, additional research is necessary to fully understand the effects of microplastics in urine on human health. Despite this, it is crucial to continue studying this subject and taking measures to decrease exposure to microplastics in the environment.

ANTIBIOTICS RESISTANCE BACTERIA IN HUMAN

Antimicrobial resistance is a multifaceted environmental problem resulting from the interaction of microbial populations that impact the well-being of animals, humans, and the ecosystem (McEwen & Collignon, 2018) (Figure 2). It has become an increasingly pressing public health issue worldwide, particularly among healthcare providers (Burnham *et al.,* 2017). The presence of antibiotic-resistant microorganisms in human waste is a natural occurrence due to the overuse and misuse of antibiotics. If left unaddressed, this could put millions of people at risk of infection, making it imperative to manage this issue both in the laboratory and through clinical diagnosis in hospitals. Several factors contribute to the dissemination of antibiotic-resistant bacteria and their genes, both within and beyond communities, including the movement of infected individuals between regions, inadequate infection management and control measures, and environmental contamination (McEwen & Collignon, 2018).

The most suitable genotypic approach for identifying antimicrobial resistance is the Polymerase Chain Reaction (PCR) and DNA sequencing method. This technique allows for the rapid detection of resistance genes present in a given sample (Patil, 2012). The PCR and DNA sequencing methods have proven effective in identifying resistance in organisms such as vancomycin-resistant enterococci, methicillin-resistant Staphylococci, and fluoroquinolone resistance mutations (Patil, 2012). However, as early as the 1950s, approximately 50% of Staphylococcus strains isolated by laboratory technicians demonstrated penicillin resistance due to beta-lactamase production (Leeson & Hsueh, 2015).

Different types of pharmaceutical drugs

Pharmaceuticals refer to different types of drugs administered by medical practitioners such as doctors and pharmacists to treat various human and animal illnesses. These drugs can be categorized based on their chemical structures, mechanism of specific biochemical reactions, and physiologic responses in humans and animals (https://www.verywellhealth.com/drug-classes-1123991)-Drugs-classes medication classification. However, the World Health Organization (WHO) has developed a multi-dimensional system of classification known as Anatomical Therapeutic Chemicals (ATC), which categorizes drugs into five levels. The first level focuses on the types of organs and systems that the drug treats, while the second level describes the drug's therapeutic effect. The third level provides a description of the mechanism or mode of action of the drug, and the fourth level focuses on its chemical properties. Finally, the fifth level describes the chemical components that make up the drug (WHO, 2021). Based on their usage, diagnoses, and the diseases or conditions they treat, drugs can be classified into 49 therapeutic classes (Drugs, n.d.).

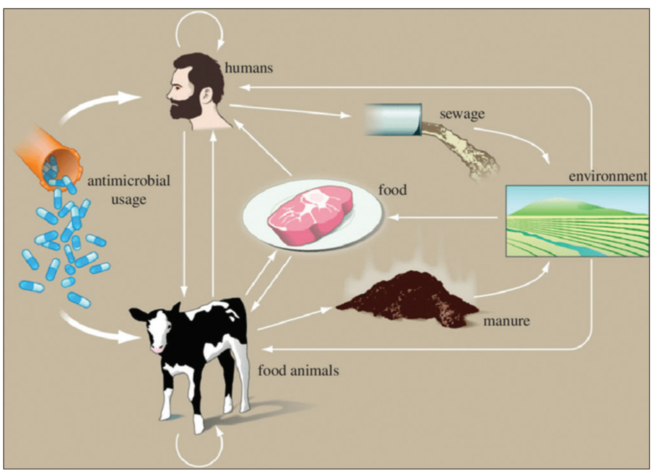


Figure 2: Diagrammatic representation of the routes of transmission of antimicrobial resistance (AMR) between domestic animals, the environment, and humans (Woolhouse *et al.,* 2015)

Antibiotics as a major type of pharmaceuticals

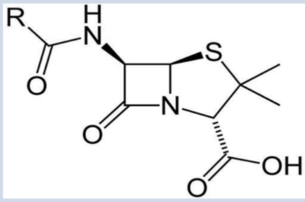
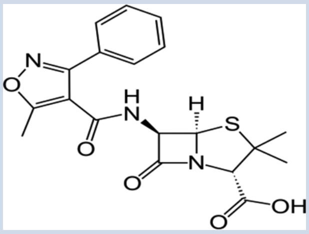
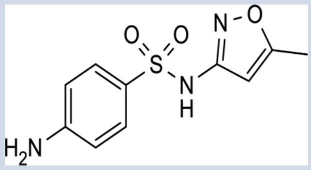
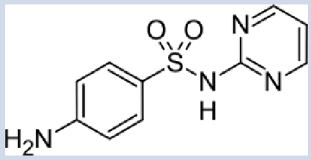
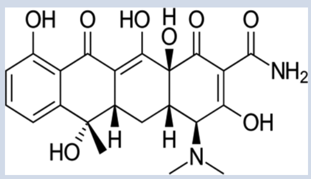
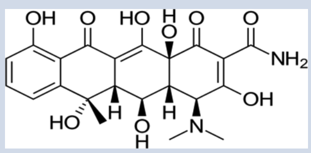
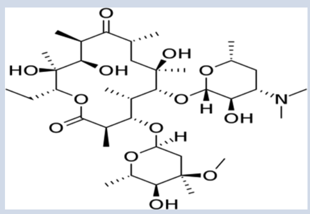
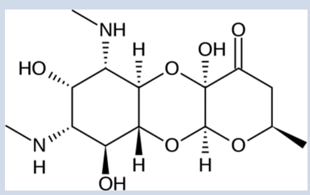
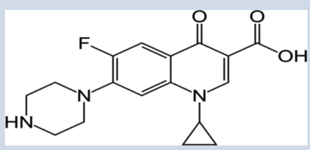
Different types of antibiotics are commonly used by medical practitioners to treat infectious diseases in our environment (Table 3), although many people are unaware that these infections are caused by pathogenic bacteria (Pauter *et al.,* 2020). Throughout history, various plant parts have been used to treat infections worldwide. However, it was not until the 19th century that German physician Paul Ehrlich discovered the principle that certain dyes can be used to selectively color bacterial cells. He concluded that it was possible to create chemical substances capable of killing specific cells without affecting others. Ehrlich was the first scientist to discover Arsphenamine as an antibiotic for the treatment of Syphilis, which he called 'chemotherapy'(https://microbiologysociety.org/members-outreach-resources/outreach-resources/antibiotics-unearthed/antibiotics-and-antibiotic-resistance/the-history-of-antibiotics.htm).

Antibiotics were initially derived from plants but with advances in technology, drug manufacturing industries have begun producing synthetic substances with similar chemical properties to antibiotics that are used to prevent or mitigate bacterial infection in humans and other domestic animals (Pauter *et al.,* 2020). From a chemical perspective, antibiotics form diverse groups of compounds with low molecular mass, chemical structures, and physicochemical properties. The most widely used group of antibiotics includes Beta-lactams, which are composed of penicillin and cephalosporin. Other important classes include tetracycline, aminoglycosides, and sulfonamides (Pauter *et al.,* 2020).

SOURCES OF PHARMACEUTICALS IN THE ENVIRONMENT

Medical practitioners and livestock veterinary doctors worldwide use thousands of pharmaceuticals, including different types of antibiotics, analgesics, anti-inflammatory

Table 3: Commonly used antibiotics and their molecular structure

Antibiotics	Chemical Formula	Molecular Structure
Penicillin	$C_{14}H_{21}N_3O_6S$	
Oxacillin	$C_{19}H_{19}N_3O_5S$	
Sulfamethoxazole	$C_{10}H_{11}N_3O_3S$	
Sulfadiazine	$C_{10}H_{10}N_4O_2S$	
Tetracycline	$C_{22}H_{24}N_2O_8$	
Ox tetracycline	$C_{22}H_{24}N_2O_9$	
Erythromycin	$C_{37}H_{64}NO_{13}$	
Spectinomycin	$C_{14}H_{24}N_2O_7$	
Ciprofloxacin	$C_{17}H_{18}FN_3O_3$	

drugs, and others (Becker *et al.,* 2020). However, most of these pharmaceuticals enter the environment through multiple pathways, including wastewater from hospitals, clinics, and emergency rooms, resulting from medical procedures carried out in these facilities (Becker *et al.,* 2020). Pharmaceuticals can also be found in partially metabolized feces and urine from humans and other domestic animals. However, 30–90% of the most frequently used pharmaceuticals are excreted in urine and feces as either parent drugs or active isomers (Xu *et al.,* 2022). In human feces and urine, 212 different drugs are typically present. The partial metabolization of pharmaceuticals in humans occurs through oxidation, reduction, and hydrolysis reactions that convert them into their metabolites, which allow the drugs to become bioactive.

IDENTIFICATION OF MICROBIAL CELL AND PHARMACEUTICALS

Pathogenic microorganisms are known to cause serious problems and infections in humans and other domestic animals. However, they also play an important role in industries, human life, and the environment. Early detection of infection is crucial for determining the biomarker that identifies specific characteristics of a particular individual. More accurate modern methods have been developed over the years to identify microorganisms, along with antibiotics drugs and their metabolites. Biochemical tests based on the biological properties of organisms, such as aminoglycosides in Enterococci, glycopeptides, and methicillin in staphylococci, have been developed to identify susceptibility and antibiotic resistance mechanisms (Pauter *et al.,* 2020). Molecular methods, including DNA hybridization and PCR-based methods, are also used for microorganism identification.

Various separation techniques, such as Liquid Chromatography (LC) and Gas Chromatography (GC), are available for identifying pharmaceuticals and their metabolites, combined with different detection systems like NMR and Mass spectrometry to identify constituents present in the raw sample. For this review, HPLC (High-performance liquid chromatography) is the chosen identification and detection technique for pharmaceuticals and their metabolites. HPLC-MS is vital in determining antibacterial drugs and other pharmaceuticals in humans and animals, including the analysis of pharmaceuticals and metabolites in fluids of living organisms such as blood plasma, serum, or animal urine (Mohamed *et al.,* 2020). The use of HPLC-MS enables the detection, identification, and quantification of a wide range of pharmaceuticals and their metabolites, even at low concentrations (Becker *et al.,* 2020). Advanced procedures of test sample preparation for analysis enable reproducible results, even in complex matrices or samples. UV, MS, and universal detectors are used for determination, and HPLC is equipped with columns that have a particle size of 5 µm or less. For instance, in an analysis of clarithromycin in urine and blood samples by HPLC-FL (fluorescence detector), liquid-liquid extraction of the antibiotics-dichloromethane was used. The HPLC column was 150 cm long and 4.6 mm with a particle size of 5 µm (Pauter *et al.,* 2020). In another analysis, a rapid HPLC assay with micro-extraction was used for the analysis of ciprofloxacin and levofloxacin in human fluid. Chromatographic separation was achieved using a Gemini C18 column of 250 mm × 4.6 mm with an internal diameter of 5 µm, a mobile phase phosphate buffer of 30 mM, pH 2.5, 1% triethylamine (TEA), and acetonitrile (1% TEA) (86:14, v: v) at 1.0 mL/min flow rate and the detection of peaks was reached by the photodiode array detector (PDA) at 295 nm for levofloxacin and 279 nm for ciprofloxacin (Pauter *et al.,* 2020).

REMOVAL OF ANTIBIOTICS AND PHARMACEUTICALS IN URINE

Pharmaceuticals and their intermediates are considered to be environmentally hazardous micro-contaminants that are predominantly found in human or animal waste that is discharged into land and water ecosystems (Luo *et al.,* 2014). The sorption of micro-contaminants primarily depends on the Octanol water partition coefficient (KOW) and their hydrophobicity. Rogers (1996) discovered that Log KOW can be used to predict or estimate the sorption of micro-pollutants in an organism. Log KOW greater than 2.5 signifies low sorption potential, Log KOW less than 4 means high sorption potential, and medium sorption potential indicates that Log KOW is greater than 4 or 2.5 is greater than Log KOW.

The application of liquid urine from unhealthy sources as fertilizer in many crop productions has been associated with the accumulation of primarily harmful substances and compounds such as pharmaceuticals, microplastics, and ionic salts, which may lead to an increase in soil conductivity. However, the high amount of salt, heavy metals, and hormones in untreated urine on crops can result in soil and underground water contamination, which may also lead to food contamination (Kassa *et al.,* 2018). These pollutants enter the environment through the use of antibiotics, contraceptives, and anti-depressive agents by human beings via human excreta, and they are non-decomposable with polar structures that persist in the environment. More pharmaceuticals are produced in urine in developed countries than in underdeveloped countries (Hatfield & Hatfield, 2018). These pollutants are not completely removed during the temporal treatment of human wastewater and are therefore discharged into the environment, contributing to contamination of water bodies and environmental health and sanitation challenges (Baumgarten *et al.,* 2007). Researchers have found out that pharmaceuticals and their derivatives can be removed by using a membrane bioreactor combined with complex chemicals and physicochemical processes that include activated powdered carbon, Nano-filtration, ozone, and ozone\UV, which are applied to the filtrate from the membrane bioreactor with specific targeted pharmaceutical compounds. The efficiency of the processes was generally tested using liquid chromatography combined with a mass spectrometer (LC-MS and MS-MS) (Baumgarten *et al.,* 2007).

According to Baumgarten *et al.* (2007), the effectiveness of powdered activated carbon of Carbotech (PAK) 800 in eliminating selected pharmaceuticals was studied. Results showed that 50 mg/L of PAK 800 for 15 minutes was an effective eliminator for Ofloxacin with a 60-70% removal rate, but poor for Fluoroquinolonic and Flufenamic acids with only a 26-40% removal rate (Figure 3a). However, increasing the concentration to 500 mg/L for 15 minutes made it more effective in removing almost all selected pharmaceuticals with a 60-70% removal rate (Figure 3c). In addition, Baumgarten *et al.* (2007) also found that Norit-SA UF powdered activated carbon was far more effective in eliminating selected antibiotics compared to PAK 800. Even at 50 mg/L for 15 minutes, it showed an 85-95% removal rate for Fluoroquinolonic and Flufenamic acids and a 65-95% removal rate for all selected Floxacins (Figure 3b). Furthermore, in Figure 3d, at 500 mg/L of SA UF powdered activated carbon, almost all selected pharmaceuticals were eliminated (80-100%).

RESEARCH GAPS ANALYSIS

Ecological sanitation has been gaining attraction worldwide. In order to address the challenges faced by environmental sanitation and agriculture, many studies have been conducted on the perception and use of urine as liquid fertilizer; however, few or none have been conducted in Sierra Leone to combat the challenges posed by improper sanitation. Similarly, there are various research studies related to the transformation of urine into liquid fertilizers in other to mitigate the problems caused by chemical fertilizers on soil and crop production. Nonetheless, based on the literature reviewed conducted during this study, further research is necessary to address the following knowledge gaps:

- Monitoring and evaluating the human toxicological risk assessment associated with microplastics in urine.
- Designing an appropriate and eco-friendly technique for the removal of pharmaceuticals and heavy metals and microplastics in urine.
- Identifying pharmaceuticals and their metabolites, as well as the effect of anti-microbial resistance organisms in plants cultivated with urine.

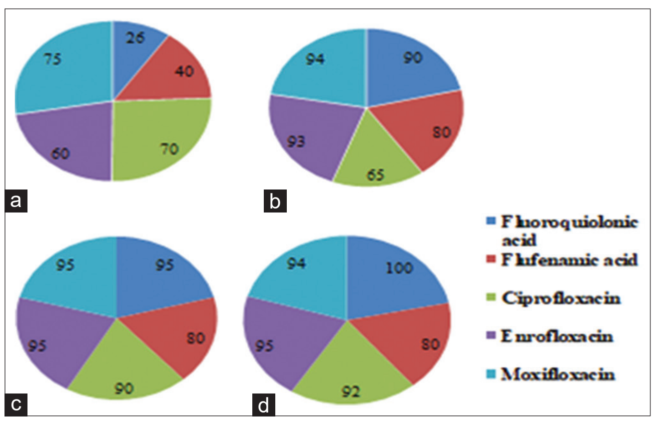


Figure 3: Elimination rate in % of powdered activated carbon after 15 minutes for selected pharmaceuticals (Baumgarten *et al.*, 2007)

- Conducting plant safety tests, including nutrient composition and pathogenic identification tests on plants cultivated with human urine.
- Identifying, quantifying, and chemically characterizing microplastics in human urine.

CONCLUSION

Urine is generally regarded as a highly effective bio-fertilizer that can be used as a soil amendment to improve crop production and mitigate the challenges caused by inorganic fertilizers. According to literature reviews, maize and other vegetables thrive when urine is used as a liquid fertilizer (Shaw, 2010; Hatfield & Hatfield, 2018). However, religious and cultural factors are major challenges faced by community members and farmers regarding the application of urine as fertilizer (Mugivhisa & Olowoyo, 2015). Heavy metals, microplastics, and pharmaceuticals in urine are serious concerns for consumers, especially for raw or unpeeled food such as leafy greens (e.g., lettuce, cabbage, and other vegetables). In addition, antimicrobial resistance poses a potential risk for disease transmission, including sexually transmitted and other diseases. Nevertheless, the pharmaceutical elimination techniques described by Baumgarten *et al.* (2007) are complex and not feasible for local community farmers due to their capital intensiveness and lack of sustainability as a closed-loop sanitation method. To effectively close the loop between sanitation and agriculture, especially by using urine as a fertilizer for crop production, more community sensitization is required, and the concept must be integrated as part of an agriculture extension program to promote and change the mindset of farmers. To improve the safety of crops cultivated using urine as a liquid fertilizer, a cost-effective eco-sanitation technique involving a column filter filled with solid activated charcoal can be fabricated to eliminate pharmaceuticals and other micropollutants in urine.

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