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Assessing the Impact of Pharmaceutical Contamination in Malaysian Groundwater: Risks, Modelling, and Remediation Strategies

Michael Lie[1], Rubiyatno[2]*, Faisal Saud Binhudayb[3], Nguyen Thi Thanh Thao[4], Risky Ayu Kristanti[5]

[1]Envirotech Engineering, Kuala Lumpur, 59200 Malaysia
[2]Graduate Faculty of Interdisciplinary Research, University of Yamanashi, 4-3-11 Takeda, Kofu, Yamanashi 400-8511, Japan
[3]Department of Chemistry, College of Science, King Saud University, P.O. Box 22452, Riyadh 11495, Saudi Arabia
[4]Institute of Environmental Science, Engineering and Management, Industrial University of Ho Chi Minh City, Ho Chi Minh City, Vietnam
[5]Research Center for Oceanography, National Research and Innovation Agency (BRIN), Pasir Putih I, Ancol, Jakarta, 14430 Indonesia

*Correspondence: yrubi@yamanashi.ac.jp

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ABSTRACT: Pharmaceuticals in Malaysia's groundwater are a growing concern as they can potentially affect the environment and human health negatively. Pharmaceuticals are found in abundance in groundwater from sources such as septic tanks, leachates from landfills, wastewater effluents from pharmaceutical-related industries, medical institutions, wastewater treatment plants, and households, agriculture runoff and leakage of effluent wastes in Malaysia. Pharmaceutical contaminant usually travels through advection and dispersion from waterways or soil into the groundwater. The mathematical model of the advection-dispersion equation and enzyme-linked immunosorbent assay (ELISA) are analysed for the prediction of movement and concentration of pharmaceuticals. Furthermore, the evolution of pharmaceuticals in the environment, living organisms and human health is assessed. Pharmaceuticals have found their way into the food chain and exhibit toxicity and hazard to aquatic ecosystems. However, the toxicity of pharmaceuticals to humans is still not yet much to be researched although strong evidence of possible negative consequences. Moreover, remediation technologies such as activated carbon adsorption, activated sludge, anaerobic treatment and advanced oxidation process are discussed for the mitigation of pharmaceuticals contamination.

KEYWORDS: Groundwater movement; Malaysia, pharmaceuticals; pollutant distribution and evolution; remediation

1. Introduction

Pharmaceuticals are drugs or medications that are used to treat, prevent, and diagnose illnesses in humans or animals. Normally, pharmaceuticals are manufactured in the form of tablets, capsules, creams, inhalers, and injections. The invention of pharmaceutical sciences has been a success story throughout history as they play a significant role in the maintenance of global health and supporting modern living styles [1]. With the rising demand for pharmaceuticals globally, the manufacturing and consumption of pharmaceuticals have rapidly increased every year, especially in the year 2020 when the Covid-19 pandemic outbreak [2]. Studies from the IMS institute predicted that about 4.5 trillion doses of pharmaceuticals were consumed globally where half of the global population consumes one or more doses per person per day of pharmaceuticals [3]. There is also no exception for Malaysia, with factors like population growth and the rising burden of chronic diseases, the use of pharmaceuticals in Malaysia has been steadily elevating. The statistic on pharmaceutical utilization in Malaysia from 2011 to 2016 is shown in Figure 1 [4, 5].

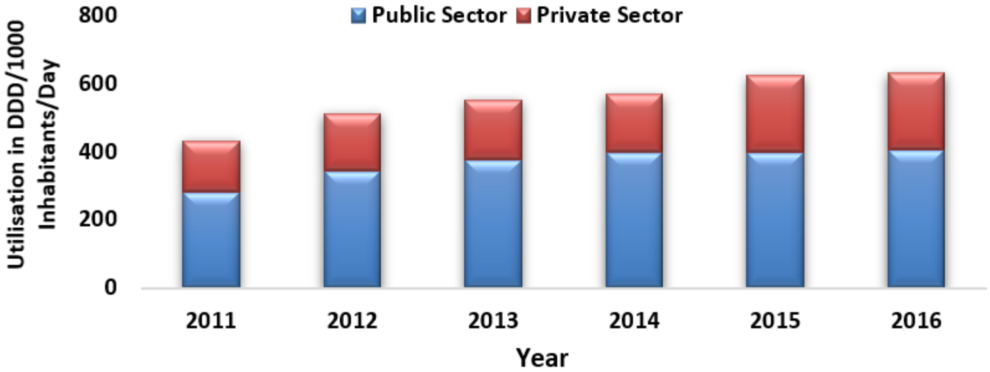

Figure 1. Graph of total estimation of medicine usage in Malaysia.

With the widespread consumption and disposal of pharmaceuticals, their residues may infiltrate into the groundwater by a variety of channels, including wastewater, surface runoff and leachates from landfills. This raised concerns among Malaysians as 90% of the country's water supply depends on the groundwater in Malaysia. Many states such as Kelantan, Terengganu, Pahang, Sabah and Sarawak strongly rely on groundwater as their primary source of freshwater [6]. This report aims to present an overview of pharmaceuticals in Malaysia's groundwater, including sources, distributions, and movement of pharmaceuticals. It also studies the applications of the mathematical model in the groundwater system. This report also discusses the impacts of pharmaceuticals in groundwater associated with the environment, living organisms and human health, with some suggestions on remediation technologies to mitigate and treat pharmaceuticals in groundwater.

2. Source, Distribution, Contaminant Movement

Pharmaceuticals can derive from various channels and flow into Malaysia’s groundwater. They can be grouped mainly into two categories, which are point sources and non-point sources. Point sources normally refer to identifiable discrete locations or facilities where pharmaceuticals are released directly into the groundwater in a spatially explicit manner. Non-point sources are usually diffuse sources of pharmaceuticals that are difficult to track back to their specific location or facility and occur over broad geographical scales [7]. Point sources of pharmaceutical contamination include septic tanks, leachates from landfills, wastewater effluent from pharmaceutical-related industries, medical institutions, and wastewater treatment plants (WTPs) [8]. Household, industrial, and hospital sewage normally carry substantial amounts of medicines from unused or expired drugs, urine, and faeces that are disposed improperly into pit latrines, toilets, and drains. The effluent will eventually flow to wastewater treatment plants and the environment [9]. A survey of the household residents in Selangor shows that only 25.2% of people would return their household pharmaceutical waste to healthcare institutions, the rest of the people would dispose of their pharmaceuticals waste by throwing it into the bin, flushing it down to the toilet or drain, burying, and burning [10]. Besides that, although clinical waste handling is available in Malaysia's medical institutions, there are still challenges in handling pharmaceutical waste. For example, lack of awareness of the public on proper procedures for clinical waste disposal, storing of waste outside the fences, and improper disposal of clinical wastes such as needles [11]. These ways of improper disposal of pharmaceuticals from households and medical institutions would increase the risk of pharmaceuticals emission into the landfill, WTPs and the environment [12].

When pharmaceutical wastes are not disposed and treated in proper procedure, the solid pharmaceutical wastes normally will be deposited along with domestic waste and end up in landfills [9]. Leachates are normally formed due to the rainwater and the water content of municipal waste in landfills. Among the 166 operating landfill in Malaysia, only 8 of them are sanitary landfill whereas the rest are non-sanitary landfill [13]. These non-sanitary landfills mostly could not handle hazardous waste as they do not have a proper lining, drainage system, or leachate treatment plant. The leaching of pharmaceuticals can mobilize into the surface water and groundwater which is illustrated in Figure 2 [14]. In contrast to non-sanitary landfill, sanitary landfill might have all the facilities to capture and treat the leachates, but researchers found that the majority of the pharmaceuticals could not be eliminated effectively by leachate treatment plants [15]. Therefore, pharmaceuticals will eventually flow into the groundwater after being discharged from the plant.

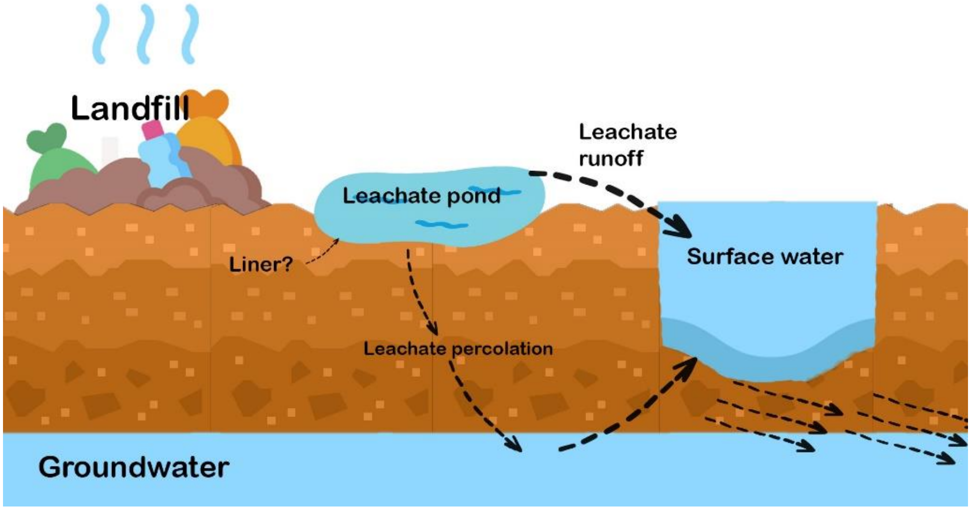

Figure 2. Process of leaching of pharmaceuticals into the groundwater.

WTPs and septic tanks are the key point source of pharmaceutical pollution in groundwater. Commonly, WTPs and septic tanks will collect large amounts of wastewater that consist of a wide range of pharmaceuticals that were excreted into the water. The effluents normally are released into local waterways and enter the groundwater. Research on the Langat River from Selangor which contains the effluents from the public and sewage treatment plants found nineteen human pharmaceuticals' occurrence and three of them (salicylic acid, glibenclamide, and mefenamic acid) were discovered in all of the samples taken [16]. The highest concentration of pharmaceuticals detected in the effluents was 34228 ng/l of metformin [16]. Despite wastewater treatment facilities being built to remove contaminants, they occasionally struggle to do the same for pharmaceuticals, which leads to exposure of pharmaceuticals to the surface water and then to the groundwater.

Non-point sources of pharmaceutical contamination include agricultural runoff and leakage of effluent wastes [8]. Farmers often utilize veterinary medicines, hormones, and growth stimulants for their livestock production [9]. Then, the manures of the livestock are frequently used by the farmers as fertiliser for their crops along with pesticides and herbicides. Pharmaceuticals can enter the soil through urine, faeces, pesticides, and herbicides, accumulate in the soil, and seep through the soil into the groundwater [17]. For example, a study founds the presence of veterinary antibiotics and progesterone in agriculture soil and broiler manure in Selangor, Melaka and Negeri Sembilan [18]. Doxycycline (781516 µg/kg) in manure samples and flumequine (1331 µg/kg) was the highest concentration detected [18]. Besides that, contamination of groundwater can occur when unnoticed or unreported leakage of effluent wastes from sewage systems or spillage of pesticides and herbicides [17].

The illustration of pharmaceuticals' evolution from sources to groundwater is shown in Figure 2. Black arrows represent the pathway of pharmaceuticals from sources to groundwater while red arrows represent the potential impact pathway of pharmaceuticals back to sources.

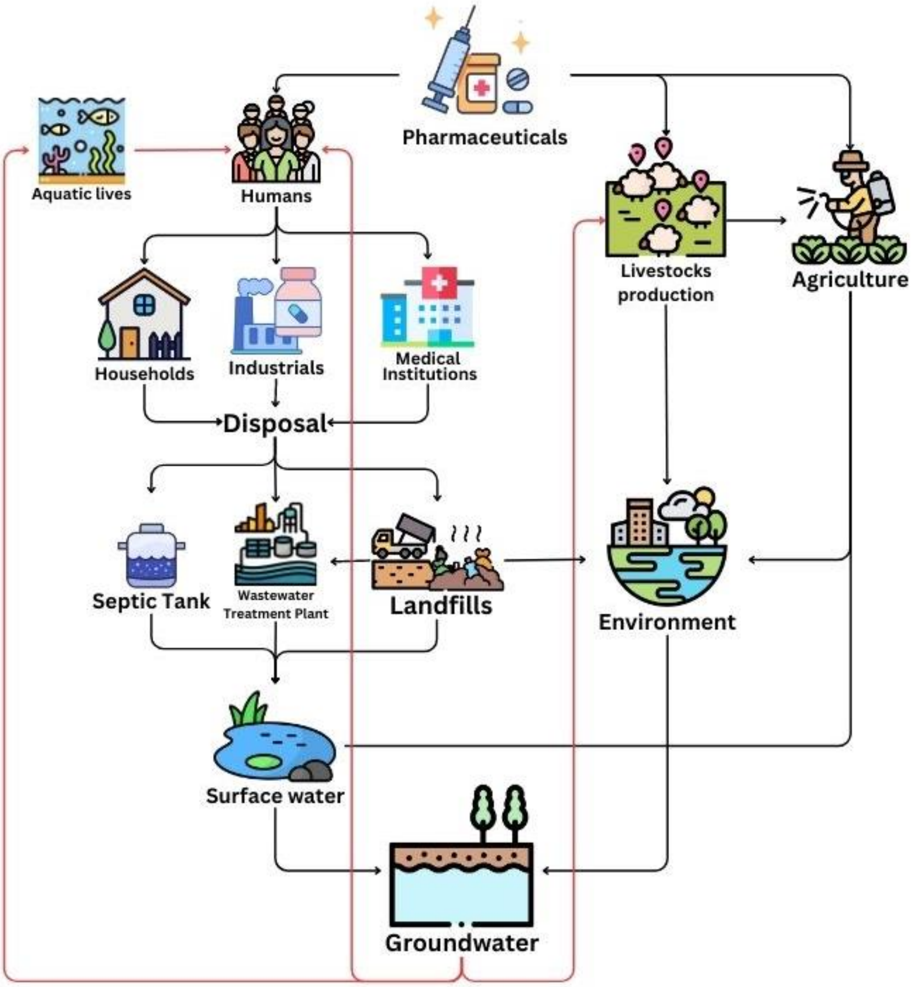

Figure 3. Summary of pharmaceuticals sources.

In Malaysia, pharmaceuticals can be found in surface water, riverbanks, drinking water, sewage treatment plant (STP) effluent, and hospital effluents. In Table 1, the highest concentration of pharmaceuticals found in different locations in Malaysia are listed. Most of the data below are extracted from Selangor and Negeri Sembilan due to insufficient studies on finding pharmaceuticals in other states in Malaysia. The most common pharmaceuticals that were found in these water samples are amoxicillin, atenolol, acetaminophen, caffeine, dexamethasone, chloramphenicol, metoprolol, ciprofloxacin, sulfamethoxazole, diclofenac, theophylline, and triclosan. Ciprofloxacin and caffeine are found to have the highest concentration compared to other pharmaceuticals in all the studied locations. Ciprofloxacin is frequently used by humans as an antibiotic to cure bacterial infections like pneumonia and urinary tract infections [19]. The frequent detection of caffeine is also not surprising as it is broadly available in food, medications, coffee, soft drinks, tobacco, and condiments [20].

Table 1. Highest concentration of pharmaceuticals found in different locations in Malaysia.

Location	Source	Pharmaceutical	Concentration (ng/l)	References
Lui River, Selangor	River	Ciprofloxacin	112.40	[21]
Gombak River, Selangor	River	Ciprofloxacin	267.20	[21]
Selangor River, Selangor	River	Ciprofloxacin	198.91	[21]
Putrajaya, Selangor	Drinking water	Ciprofloxacin	0.32	[22]
Kajang. Selangor	Drinking water	Ciprofloxacin	0.667	[23]
Sungai Langat (Sungai Semenyih, Sungai Beranang, Sungai Labu), Selangor	River	Furosemide	109	[24]
Langat basin, Selangor	STPs effluents	Norethindrone	7135	[24]
Sungai Langat, Selangor	Tap water	Ethinyl estradiol	130	[24]
Klang River, Selangor	River	Caffeine	20.62	[25]
Nilai & Seremban, Negeri Sembilan	Surface water	Caffeine	821	[26]
Nilai & Seremban, Negeri Sembilan	STP effluent	Caffeine	1190	[26]
Nilai & Seremban, Negeri Sembilan	Hospital effluent	Theophylline	3314	[26]

The average concentration of detected pharmaceuticals is detailed in Table 2 where the water sample is taken from rivers, STPs effluents, and tap water in Sungat Langat, Selangor. Sungai Langat is one of the four vital river systems that have three tributaries which are Sungai Semenyik, Sungai Labu, and Sungai Beranang [24]. The study showed that the concentration of pharmaceuticals in STPs effluents is the highest. This proves that STPs are the point source of pharmaceutical contamination in Selangor. Besides that, small amounts of pharmaceuticals are found in the tap water even though it had been treated. It is proved that WTPs are still not capable to remove pharmaceutical pollutants. Therefore, new treatment technologies are required for STPs and WTPs to ensure that treated water is pharmaceutical-free [16]. After pharmaceutical residues are released into the waterways (e.g., lakes, streams, surface water), there are two ways where they can enter the groundwater. First, when the groundwater level is below the water level of the contaminated waterways, pharmaceuticals can move downwards together with water through the hydraulic link by gravity [28]. Another alternative route to groundwater is through irrigation or artificial groundwater recharge system that employ sewage effluents or septic tank leach fields [28].

The characteristics and movement of pharmaceuticals in groundwater are dependent on the local geology, groundwater flow regime, density and solubility of pharmaceuticals. Some pharmaceuticals have lipophilic characteristics while some have moderate solubility and most of them have molecular masses lesser than 500 g/mol. Most pharmaceuticals are persistent in nature and able to remain active biologically [29]. Therefore, some pharmaceuticals can dissolve in water and seep through the pore spaces of the vadose zone to reach the groundwater rapidly by advection and dispersion [30]. In contrast, some pharmaceuticals may adsorb to soil particles and degrade by natural processes such as redox reaction, biological degradation, and biotransformation [31]. The movement of pharmaceuticals in groundwater is controlled by two fundamental processes which are advection and dispersion. Pharmaceuticals can travel through advection where the flow of groundwater carries the dissolved pharmaceuticals. However, when travelling through porous media, dispersion may occur due to mechanical mixing and molecular diffusion within the porous medium [32]. Dispersion can cause pharmaceuticals to spread over a large volume of the aquifer than estimated in an analysis of groundwater [32]. The study of the dispersion of pharmaceuticals is significant in predicting the point sources and non-point sources.

Table 2. Average concentration (ng/l) of detected pharmaceuticals in Sungai Langat [16, 24, 27].

Pharmaceutical	Sewage Treatment Plant Effluent	Tap Water	River
Amlodipine	3	ND	1
Atenolol	771	ND	39
Chlorothiazide	136	4.5	23
Chlorphenamine	ND	ND	ND
Cyproterone	103	ND	27
Diclofenac	32	ND	105
Ethinyl estradiol	77	130	ND
Furosemide	545	ND	109
Glibenclamide	44	0.3	1
Gliclazide	55	ND	4
Loratadine	14	1	3
Lovastatin	187	ND	ND
Mefenamic acid	147	ND	37
Metformin	4080	ND	55
Metoprolol	854	39	62
Nifedipine	ND	ND	3
Norethindrone	7135	ND	ND
Norgestrel	ND	30	67
Paracetamol	405	3.4	38
Perindopril	19	ND	3
Salbutamol	12	ND	1
Salicylic acid	110	ND	71
Simvastatin	ND	ND	ND

3. Application of Mathematical Model.

The application of mathematical models is an essential technique in the investigation of pharmaceuticals in groundwater systems. Mathematical models can analyse the interaction with the environment and the migration of pharmaceuticals through groundwater. With this, the fate and the movement of pharmaceuticals can be predicted and assessed for potential environmental impacts and remediation design.

2.1. Advection–dispersion equation.

Advection of pharmaceuticals refers to the movement of pharmaceuticals at the same velocity as the groundwater's average linear velocity of (v), where

$$v = \frac{KI}{n} \tag{1}$$

Where K denotes hydraulic conductivity; I denotes head gradient; n denotes effective porosity.

The transportation of pharmaceuticals through the soil can be described using the advection-dispersion equation. The equation is derived by the combination of Darcy's law and the equation of continuity [33].

$$\frac{\partial}{\partial t}c(x,t) - D\frac{\partial^2}{\partial x^2}c(x,t) - v\frac{\partial}{\partial x}c(x,t) - \lambda c(x,t) \tag{2}$$

Where t denotes the time, x denotes the horizontal distance measured positively to the right from the centre of the soil; $c(x,t)$ denotes the solute concentration at the time, t and distance x; D denotes the diffusivity of the soil-water; v denotes the average velocity; and λ denotes the decay coefficient (1/ t).

The pollution in groundwater can be determined by employing equation (1). The behaviour of pollutants in a saturated zone with zero initial concentration is considered,

$$c(x,0) = 0, x > 0, \tag{3}$$

and at x = 0 a periodic inflation rate is prescribed as:

$$c(0,t) = c0(1 + sin\,\omega t), \qquad t > 0, \tag{4}$$

where c_0 denotes the constant concentration at the entrance of the medium (x = 0) prescribed from t = 0.

2.2. Enzyme-linked immunosorbent assay (ELISA)

Enzyme-linked immunosorbent assay (ELISA) is a potent immunoassay that can detect chemicals, drug residues, and other microbial toxins qualitatively and quantitatively. Most of the data in Table 2 is obtained from studies that use ELISA analysis. The absorbance of the water sample is correlated to the quantity of the complex of the antibody and the enzyme-conjugated antigen after reacting with a chromogen substrate solution [34]. The calibration curve of competitive ELISA (absorbance vs. analyte concentration plot) will be a reverse sigmoid curve as the complex concentration declines, the analyte concentration in the sample increases.

The four-parameter logistic equation (2.0), which includes fitting parameters for a, b, c, and d, fits the analyte concentration and absorbance. A denotes the absorbance, and f(A) denotes the analyte concentration [34].

$$f(A) = \frac{a-d}{1+\left(\frac{A}{c}\right)^b} + d \tag{2.0}$$

According to Hayashi et al.'s model [35], the analysis (ρ_T) can be expressed as

$${\rho_T}^2 = \frac{A^2}{(A+G)^2}\left(\rho_A^2 + \rho_G^2\right) + \rho_B^2 + \rho_S^2 + \left(\frac{\sigma_w}{f(A)} \times 100\right)^2 \tag{2.1}$$

where G is the conjugated antigen concentration when the conjugated antigen binds to 50% of the antibody. ρ_A, ρ_G, ρ_B, and ρ_S, are the relative standard deviation (RSDs) of pipetted volumes of the analyte, the enzyme-conjugated antigen, the antibody, and the substrate, correspondingly. ρ_S is 2/3 of the RSD of the pipetted volumes of the chromogen substrate solution. σ_w is the absorbance inherent in the water sample.

4. Contaminant evolution

In recent decades, pharmaceutical evolution has become a growing concern as potential bioactive chemicals in the groundwater. Pharmaceuticals are continuously released into Malaysia's environment and are widespread at low concentrations which are proved in the studies in Table 2. These emerging contaminants can affect the environment (e.g., water quality, drinking water supplies, ecosystem), living organisms, and health impact on the community [36].

3.1. Environment.

Even though pharmaceuticals have been around in the environment for quite some time, the amount of pharmaceuticals in the environment has only recently been quantifiable and detectable as potentially hazardous to ecosystems [37]. The improvement of new analytical tools such as liquid chromatography–mass spectrometry (LC-MS) and tandem mass spectrometry has made possible observation of concentrations as low as nanograms per litre of pharmaceutical contaminants in complex matrixes in solid and liquid phase in surface water, wastewater, and groundwater [38, 39]. The evolution of pharmaceuticals contaminant after being released into the environment may include the processes of sorption, complexation, biodegradation, and photodegradation [29]. These processes have significant responsibility in eliminating pharmaceuticals before they further impact the environment. Some antibiotics such as tetracyclines have the propensity to bind to soil particles or form complexes with ions which causes antibacterial effectiveness to be lost [40]. For instance, tetracyclines form complexes with double cations (e.g., magnesium and calcium) in seawater. This discovery is not only intriguing from the standpoint of degradation, but it also highlights how hazardous it is to use potentially inactive antibiotics in aquaculture [41]. Furthermore, pharmaceuticals may experience a variety of reactions whilst entering the environment, such as partial or complete biotransformation, mineralization, or degradation [29]. Fungi and bacteria in soils, surface water, and groundwater are responsible for the biodegradation process for pharmaceutical pollutants [41]. However, more than twenty antibiotics comprising the most major antibiotic groups were discovered not to be readily biodegradable according to research [42]. If the pharmaceuticals contaminants did not degrade, it is very likely that contaminate the aquatic ecosystem, which is highly controlled and reliant on microorganisms few important processes (e.g., dinitrogen fixation), associations (e.g., nitrogen fixation), and services (e.g., breaking down of organic) [24]. The presence of pharmaceuticals in aquatic ecosystems can adversely alter the ecological function and negatively impact the different organisational levels of aquatic life [43]. Research assessing the ecological risk related to the occurrence of pharmaceuticals in groundwater at the landfill site in Putrajaya, Malaysia showed that 11 pharmaceuticals found have exceeded the predicted no-effect concentrations (PNECs) for some aquatic life, indicating potential detrimental impacts on the aquatic ecosystems [22].

3.2. Animals.

Pharmaceuticals are intended to target particular metabolic and molecular processes in both people and animals, but they also have adverse effects by influencing the processes in living organisms that have identical target biomolecules, cells, tissues, and organs [44]. As mentioned above, pharmaceuticals such as antibiotics and resistant bacteria could alter the biotic processes and interact with animals and aquatic environments [45]. Health effects have thus been identified in aquatic lives (e.g., benthos, zooplankton, fishes, amphibians), animals and humans. Studies have proven that long-term exposure to low concentrations of complex pharmacological compounds on stream biota can result in acute and chronic impairments, behavioural modifications, tissue accumulation, cell proliferation hindrance, and reproductive damage [46, 47]. In a Canadian whole-lake experiment, the population of Pimephales promelas collapsed at concentrations of 5 – 6 μg/l of 17α-ethinylestradiol (EE2) due to the feminization of male fish [48]. The exposure to synthetic estrogen in water sources has led to a decrease in egg fertilization and an imbalance in the sex ratio [48, 49].

Besides that, many pharmaceuticals such as oxytetracycline, chloropromazine and trimethoprim antibiotics exhibit acute toxicity impacts towards Daphnia magna, the cyanobacteria Anabaena Flos-aqua and the green alga Pseudokirchnerialla subcapitata [50]. Studies found that the reproduction of Daphnia magna was diminished by 100% at high concentrations of pharmaceutical pollutants [41]. The rate of survival and fecundity of Daphnia magna critically reduce in 0.33 mg/l concentration of chlorpromazine and 0.128 mg/l concentration of propranolol [51]. When ibuprofen is released into the environment, it aids the growth of fungus, which significantly enhances toxicity [52]. Animals that are exposed to these toxins may be threatened with poisoning, gene expression, and reproductive damage [52]. For example, diclofenac induces severe visceral gout and renal failure, which increase mortality rates (5 to 86%) in adults and subadult oriental white-backed vultures in the Indian subcontinent. The vultures bioaccumulate diclofenac when they feed on dead cattle that have been given diclofenac, resulting 95% drop in the population of ventures [53, 54]. Furthermore, the weighted-average concentrations of diclofenac were above the PNEC (0.1μg/L) in surface water, diclofenac is believed to impair the inner organs of rainbow trout, suggesting an unacceptable danger according to the regulatory environmental risk assessment [55, 56]. Hence, all living organisms will be adverse ecotoxicological affected by the presence of pharmaceuticals in the aquatic ecosystem depending on the concentration of the contaminants and the tolerance of the living organisms [56].

3.3. Community.

As pharmaceuticals are abundant in the environment, pharmaceuticals contaminants have found their way into the food chain, and drinking water [28]. It is carcinogenic to humans if humans are in contact with them through eating, drinking, or breathing [52]. The toxicity of pharmaceuticals to humans is still not yet much to be investigated despite strong evidence of possible negative impacts [49]. The concentration level of pharmaceuticals reported in groundwater and drinking water is relatively low and it is usually in the ng/l range which is shown in Tables 1 and 2. Little is determined about the long-term consequences of consuming such water [57, 58]. Moreover, pharmaceuticals can be ingested through the intake of fish, meat, vegetables, and fruits [59]. The intake of these concentrations of pharmaceuticals in a lifetime only surpasses the limit of quantification which is lower than the recommended daily dosage level [60, 61]. Therefore, there are concerns about the cumulative effect of the consumption of pharmaceutical mixtures in drinking water and food.

According to the study on the total risk quotient (RQ_T) of Putrajaya residents, all age categories' RQ_T values exceeded one, indicating that the residents were exposed to health dangers posed by the bioavailable pharmaceuticals in drinking water [62]. Besides that, the residents between the ages of 61 and 75 experience the highest RQ_T (1.39) which can be associated with the ageing of residents and rising pharmaceutical consumption [62]. Despite the interaction and toxicity of pharmaceuticals that might arise against human health is still unknown, pharmaceuticals residues can potentially have caused an allergic reaction, bioaccumulation, and metabolic disruption in the human body [22, 62]. Therefore, the evaluation of specific pharmaceutical classes individually is required to further understand the hazards of pharmaceutical residues in Malaysia's groundwater. In Malaysia, the incineration of pharmaceutical residues is mainly used in treatment and waste management. Incineration of pharmaceutical waste can produce secondary pollutants if the incineration plant was not designed and operated properly [63]. The emission of pollutants is hazardous to both human and animal health as they could lead to cancer and liver failure [64].

4. Remediation Technologies

Most pharmaceuticals are persistent in the environment. Many pharmaceutical remediation technologies have been intensively studied and developed to remove pharmaceuticals from water to mitigate the contamination of groundwater. The remediation technologies are classified into four categories which are physical treatment, biological treatment and chemical treatment (Table 4).

4.1. Physical treatment.

One of the well-known physical pharmaceutical treatments is adsorption on activated carbon. The pros of utilising activated carbon are that it has a great capacity to adsorb and eliminate pharmaceuticals that do not produce a hazardous or pharmacologically active product [59, 60]. The main mechanism for the adsorption of pharmaceuticals onto carbon-based adsorbents is electrostatic interaction (e.g., the attraction of anion and cation), hydrophobic interaction, hydrogen bonds, π–π interactions, pore filling, partition into un-carbonized factions, and precipitation [67, 68]. Research on the maximum and minimum amount of pharmaceuticals eliminated from aqueous solution per mass of activated carbon adsorbent used has shown that removal rates could reach higher than 300 mg/g on the high end and higher than 100 mg/g at the low end of the range [69]. Other common physical treatments include reverse osmosis, nanofiltration, and electrodialysis [29]. The molecular weight cut-off of the membrane on reverse osmosis and nanofiltration is capable to clog and prevent more than 85% of pharmaceuticals from being emitted into the environment [70]. Moreover, electrodialysis can effectively eliminate a range of spiked pharmaceuticals such as ibuprofen, carbamazepine, propranolol, ethinylestradiol and diclofenac [71].

4.2. Biological treatment.

Biological treatments such as activated sludge and anaerobic treatment technology are normally in the treatment of wastewater [29]. The activated sludge system also can be known as a suspended-growth aerobic system which consists of aeration tanks and sedimentation tanks [72]. This process requires the establishment of degrading microorganisms such as bacteria, fungi, algae and biocatalysts and dissolved oxygen supply [73]. The degrading microorganisms will feed, grow and biodegrade oxidisable pharmaceutical pollutants [74]. Furthermore, anaerobic treatment is a process where pharmaceutical contaminants are broken down in the absence of oxygen [75]. It is crucial to immobilise and achieve well-balanced bacteria consortia to maintain high-rate anaerobic reactors [76]. Other biological treatments include aerated lagoons, trickling filters, phytoremediation, and stabilization pond [77]. The main advantages of biological treatments are low cost and stable treatment effect [78].

Table 3. Advantages and disadvantages of remediation methods.

Method	Type	Advantages	Disadvantage	Reference
Physical Treatment	Adsorption on activated carbon	• Selectivity, it can be engineered to adsorb specific pollutants • Cost-effective, many cheap adsorbents can be used as activated carbon	• Limited adsorption capacity, replacement is required over time • The handling and disposal of activated carbon requires special equipment and process as it will contain toxic pollutants	[59, 60, 67–69]
Biological Treatment	Activated sludge Anaerobic treatment technology	• Low-cost treatment process • Environmentally friendly and sustainable	• Complex process that requires specialized monitoring and maintenance for optimal performance	[72–76]
Chemical Treatment	Advanced oxidation process (AOPs)	• Effective removal of pharmaceuticals contaminant • Short treatment time, treat pollutants rapidly	• High energy consumption and high cost • Risk of hazardous byproducts such as hydrogen peroxide	[79]

4.3. Chemical treatment.

Even though physical and treatment plants can generally treat contaminated water, but sometimes these treatments could not degrade pharmaceuticals to the law-required level or be essential for other uses. This is where chemical treatment such as neutralization, calcination, exchanging ions, reduction and precipitation would be useful for extra effective removal of pharmaceuticals [29]. Advanced oxidation processes (AOPs) are usually recommended as it has high efficacy in removing pharmaceuticals-derived contaminants from water by oxidation through reactions with hydroxyl radicals (OH·). Some examples of types of AOPs are ozonation, radiation, oncolysis, electrochemical oxidation, Fenton, photo-Fenton, and photocatalysis. With AOPs installed and operated in drinking water plants, groundwater and surface water can be chemically oxidised to disinfect and eliminate possible harmful pharmaceutical pollutants [79]. The comparison of advantages and disadvantages of the three different types of treatments are shown in Table 3.

5. Conclusions

Pharmaceuticals in Malaysia’s groundwater are a growing concern as they detrimentally impact animals and aquatic life. The toxicity of pharmaceuticals in drinking water to humans is still a mystery to be researched. All in all, a comprehensive strategy that incorporates source reduction, pollution prevention, and remediation is necessary for the management of pharmaceuticals in groundwater. Governmental organisations can help to mitigate pharmaceutical pollution in groundwater by implementing legislation and management procedures. Public awareness of responsible usage and disposal of pharmaceuticals is also crucial to safeguard both human health and the environment. Further research is much needed to analyse the characteristics, interactions, movement and potential impact of pharmaceuticals in groundwater so that better strategies and remediation technologies can be developed to prevent and mitigate the contamination of pharmaceuticals. In conclusion, the occurrence of pharmaceuticals in groundwater is a complex issue that necessitates a multidisciplinary strategy combining regulatory, environmental, and public health organisations. Therefore, all authorities including the public are responsible for the prevention and mitigation of pharmaceutical pollution.

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Conflict of Interest

The authors declare no conflict of interest.

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