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Review

A Review on Contaminants of Emerging Concern in the Environment: A Focus on Active Chemicals in Sub-Saharan Africa

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Abstract: Active chemicals are among the contaminants of emerging concern that are rarely covered in regulatory documents in sub-Saharan Africa. These substances are neither in the list of routinely monitored substances nor in the guidelines for routine environmental monitoring activities. This has been of concern to public health officials, toxicologists, communities, and governments, hence the need for risk assessment and regulation of these substances. In this review article, the presence of active chemicals in the sub-Saharan African environment was investigated. The results indicate the availability of few studies in some countries, while in other countries no reports of active chemicals were found, hence the need for further research targeting such countries. It was further observed that mixtures of active chemicals from different therapeutic categories—such as antibiotics and analgesics—were reported. The natural environment is increasingly at risk due to the presence of these substances, their metabolites, and their transformation byproducts. These substances are characterized by persistence as a result of their non-biodegradable nature; hence, they circulate from one environmental compartment to another through the food chain, causing harm along the way. Most studies that evaluated the toxicity of these substances considered the effects of a single drug, but observations indicated the presence of drug mixtures, hence the need for further evaluation of the effects of drug–drug interactions—including synergistic and additive effects—for environmental sustainability. The presence of ACs in several environmental compartments at quantifiable quantities was discovered in this investigation, indicating the potential for ecosystem injury as a result of bioaccumulation, bioconcentration, and biomagnification through the food chain. This necessitates further research on the subject in order to ensure a healthier environment.

Keywords: wastewater; pharmaceutical load; environmental toxicology; sub-Saharan Africa; active chemicals; contaminants; drug–drug interactions; mixtures

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1. Introduction

The presence of active chemicals (ACs) in the environment is an alarming global issue. These substances have been identified in different environmental compartments all over the world [1–3], causing concern to public health officials, and raising the question of environmental safety and health. These substances are used for the treatment of various medical conditions in humans, wild animals, livestock, and plants, finding their way into rivers, lakes, and drinking water systems. In these environmental conditions, ACs can have undesirable effects on both aquatic and human health. Active chemicals such as tranquilizers, psychiatric drugs, diuretics, and antibiotics are among the contaminants of emerging concern that have received little attention from researchers in sub-Saharan Africa. Among the environmental concerns posed by these substances is the development of antimicrobial resistance (AMR) as a result of discharge of antibiotics and other chemicals into the natural environment [4–7]. In the treatment of medical conditions, antibiotics play a vital role, but AMR has been declared a major threat to public health by the World Health Organization (WHO) [8,9]. It is projected that, by 2020, ~10 million lives per year will be lost due to AMR [4]. Increased demand for water as a result of a growing population and urbanization lead to the reuse of wastewater as a means to cater for water scarcity; this is practiced more in arid and semi-arid regions, where vegetables and other crops are irrigated using effluents from wastewater treatment plants [10,11]. Most wastewater treatment systems in sub-Saharan Africa are not designed for the removal of organic micropollutants such as active chemicals, and the existing environmental monitoring guidelines exclude organic pollutants in the routine analysis. Moreover, adequate treatment to meet discharge standards is rarely observed. It should, however, be noted that the reuse of wastewater before or after treatment for irrigation purposes is a common practice all over the world [10,11]. This is an inevitable result of the dwindling freshwater resources given the increase in urbanization and population.

Apart from the reuse of wastewater for the irrigation of vegetables and other crops, water safety issues have been raised, with legitimate concerns about contamination of the irrigated crops with pathogenic microorganisms. This, therefore, raises the question of whether water reuse could be a route through which some resistant pathogens can enter the food chain and harm organisms in its upper parts. In most developing countries, sewage systems are not well developed—normally, their wastewater treatment systems do not incorporate a disinfection step. Moreover, in some of these countries, the removal of contaminants of emerging concern such as ACs causes an increased load of these substances in the environment. Therefore, it is important to conduct more research in sub-Saharan African countries in order to investigate the presence and levels of active chemicals in the local environments. As active chemicals are usually present as mixtures of different categories of drugs, further studies are needed in order to investigate the toxicity as a result of interactions between these substances and their mixtures for ecological sustainability.

2. Materials and Methods

The scope of this literature review was the sub-Saharan African countries. The countries included were selected based on the availability of data on the presence of active chemicals and/or their transformation byproducts in the environmental matrices. The environmental matrices considered included, but were not limited to, wastewater, sediments, water, hospital waste, and soil. This review includes studies from 2000 to 2021, and a growing trend in published articles was observed from 2012. The search keywords included active chemicals, transformation byproducts or metabolites, environmental contaminants, and each country of sub-Saharan Africa. Web of Science, Scopus, Google Scholar, Wiley Online Library, ScienceDirect, Taylor & Francis online, Sage Publishing, Scopus, and PubMed were the search engines used for selecting scientific journal articles. The literature review was performed on papers obtained for the data related to environmental occurrence and ecotoxicity; this resulted in a database consisting of data that were extracted from studies of all sub-Saharan African countries. Figure 1 presents map of sub-Saharan Africa indicating the countries and active chemicals reported.

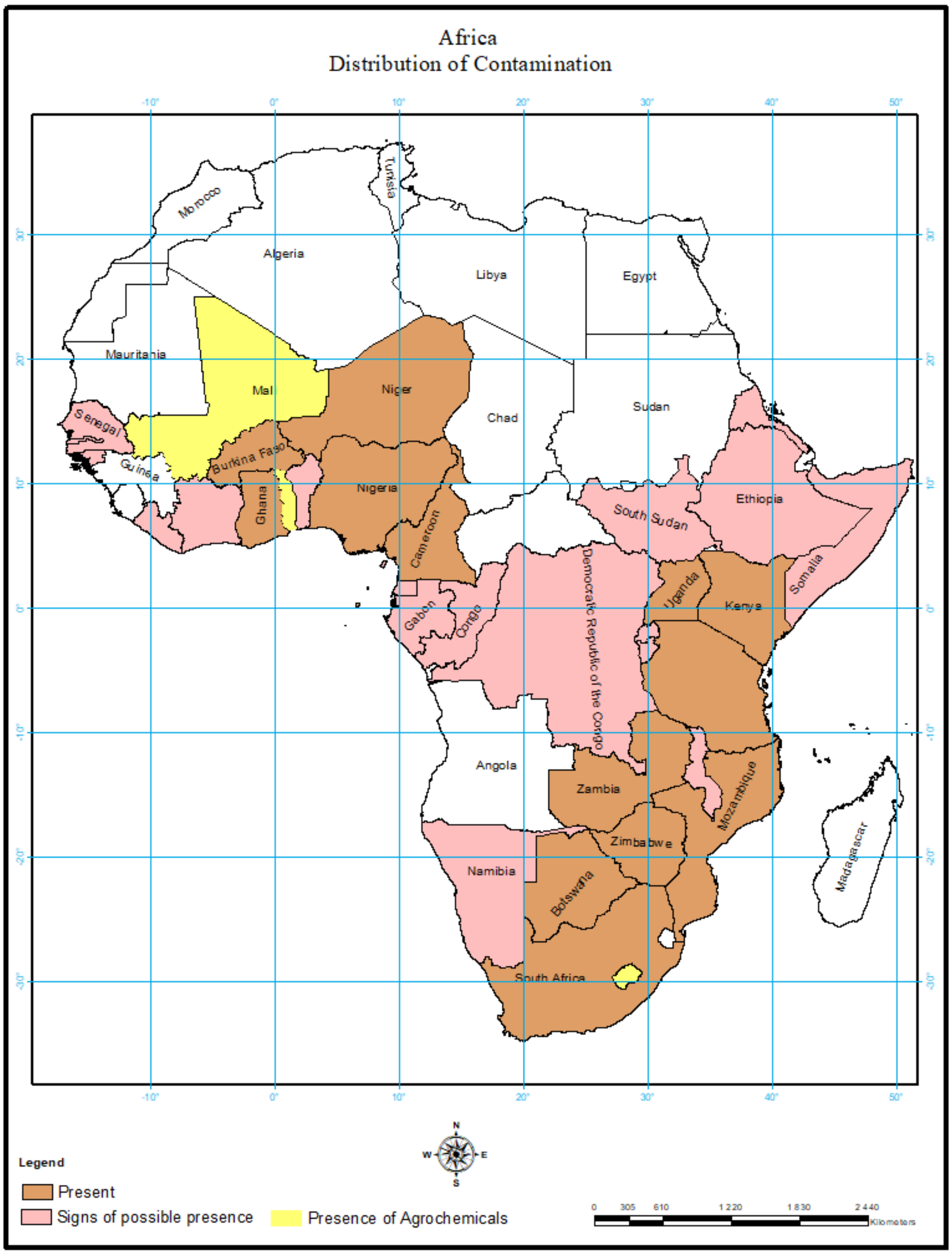

Figure 1. Map of sub-Saharan Africa indicating the countries and active chemicals reported.

3. Sources of Active Chemicals

Reports indicate that active chemicals enter the environment via different pathways; the largest contribution is from medical applications, through which active chemicals can gain access to the human body and, eventually, enter the environment. Other pathways by which active chemicals are introduced into the environment include improper disposal of leftover and expired drugs—such as disposal in the sink, in water streams, or down the toilet—chemical waste from manufacturing facilities, and municipal landfill leachates [12,13]. Wastewater effluent reuse is among the risk factors that may lead to increased active chemical load in the environment [14]. Therefore, there is a need to devise a method for the proper management of active chemicals for a healthier ecosystem.

4. Environmental Effects of Active Chemicals

The existence of different categories of active chemicals in the environmental matrices has been reported in some sub-Saharan African countries. These reports indicate the presence of the active chemicals, and point to a possibility of the ACs causing harm not only to human health, but also to the natural environment. Most drugs reported were anti-inflammatories, antibiotics, antiretroviral drugs, analgesics, psychiatric treatment drugs, steroid hormones, diabetes treatment drugs, or hypertension drugs. Loads of active chemicals released into the environment after human, animal, and agricultural usage have been linked to both human and environmental health degradation. Although active chemicals are considered to be contaminants of emerging concern, they are currently neither monitored nor included in the environmental guidelines.

Chemicals that are environmentally persistent and have a tendency to bioaccumulate pose a great potential for environmental risk, especially when such chemicals come into contact with drinking water supplies and the food chain [15–17]. Various scholars have reported the effects of these substances and their potential for harm, including the development of AMR [4,5,7,18], as well as effects on the sex of aquatic organisms [19–25]. The early years of research in the area of the effects of ACs placed more emphasis on the assessment of the acute effects as a result of individual substances, largely ignoring the effects that may be caused by combinations of these substances. Recently, however, there has been a shift in focus to chronic exposure and the assessment of the effects of drug mixtures [23,25–27]. It is important to study drug mixtures—commonly described as a 'cocktail effect'—including drug–drug interactions leading to adverse effects. Usually, human subjects receive a prescription with instructions on how to properly use drug mixtures. For instance, patients should not mix ibuprofen with beta blockers, or opioids with alcohol. However, other organisms in the ecosystem do not receive instructions from medical doctors. As a result, a fish reeling in an effluent containing a mixture of drugs and other contaminants in a polluted river will simply succumb to the adverse effects thereof.

5. Environmental Load of Active Chemicals

Active chemicals are now some of the main environmental pollutants, and are abundant in water, soils, and other environmental media. Environmental risk assessment and routine environmental monitoring regulations do not include active chemicals, simply because acute risk assessments show insignificant human health hazards. However, the drawbacks of active chemicals extend beyond acute effects to delayed effects from bioaccumulation, amplified effects from drug–drug interactions, aggravation of drug resistance, and reduction in aquatic and terrestrial food production; this merits serious measures for public health protection [28]. Reports on the presence of active chemicals in the sub-Saharan African environment are still scarce, with only a few countries reporting [29,30], indicating a need for more research. Therefore, this review will aid in providing data that are necessary to indicate the presence and possible harm of active chemicals in the sub-Saharan African environment, and to inform current and future policymaking processes.

Occurrences of Active Chemicals in Other Parts of Africa

Apart from sub-Saharan African countries, South Africa is among the African countries with greater awareness and practice with regard to environmental protection [29,31–34]. In most developed countries, the use of active chemicals is higher; thus, the load to the environment may also be higher. Occurrences of active chemicals in the South African environmental compartments are presented in Table 1. Additionally, research [35], has reported that pollutants arise not only from waste products, but also from pharmaceutical products that have not been properly disposed of. The continuous exposure to unspecified sub-therapeutic doses of antibiotics presents a risk to humans and other animals.

Table 1. Occurrences of ACs in the South African environmental compartments.

Matrix	Substance (s)	Concentration (ng/L)	References
Wastewater	Clarithromycin Erythromycin Sulfadimidine Sulfamethoxazole Sulfapyridine Chlortetracycline Oxytetracycline Trimethoprim	5–30 10–100 0–10 5–1000 5–110 90 100 5–10,000	[34]
Seawater	Ibuprofen Naproxen	160 160	[31]
Wastewater	Nevirapine and efavirenz	2100 ng/L 17,400 ng/L	[36]
Wastewater Surface water Sediments	Ibuprofen	117,000 84,600 65,900	[37]
Water	Concentrations were efavirenz > nevirapine > carbamazepine > methocarbamol > bromacil > venlafaxine.	164–593	[38]
Surface water	Antiretrovirals (ARVs)	26.5–430	[39]

6. Active Chemicals in the Sub-Saharan African Context

Information on the occurrence of quantifiable levels of active chemicals in the sub-Saharan African environment is lacking. It is known that therapeutic consumption of active chemicals to promote human health is usually followed by excretion of these drugs via urine or fecal matter, due to their slight alteration of the human metabolism. The detection of several active chemical classes—including nonsteroidal anti-inflammatories, antibiotics, antiretrovirals, anti-epileptics, steroid hormones, and anti-malarial drugs—has been reported in water resources, influents, and effluents in some countries in sub-Saharan Africa [29,31,40,41]. Moreover, general investigation and monitoring of active chemicals in different sub-Saharan African countries are required, and the necessary instrumentation for their trace quantification in environmental samples should be made available. Occurrences of active chemicals in sub-Saharan Africa are presented in Tables 2 to 18.

6.1. Kenya

Reports of the presence of active chemicals in the Kenyan environment are available [42–44]. Some exclusive data on the concentrations and loads of chemicals such as antibiotics, antivirals, analgesics, anti-inflammatories, and psychiatric drugs are presented in Table 2.

6.2. Uganda

The presence of quantifiable levels of active chemicals was investigated in Uganda's environmental compartments [45–47]. The results indicate the presence of active chemicals belonging to multiple therapeutic categories, as presented in Table 3.

6.3. Tanzania

In Tanzania, as in other sub-Saharan countries, wastewater treatment plants are not designed for the removal of emerging contaminants such as active chemicals. Wastewater stabilization ponds are utilized to partially treat the effluents from industries, residential areas, and hospitals. Therefore, when effluents are released into the ecosystem, the chemical load is increased [48–54]. Occurrences of the active chemicals in the Tanzanian environment are presented in Table 4.

Table 2. Occurrences of ACs in the Kenyan environmental compartments.

Substances	Effluents	Surface Water (ng/L)	Sediments (ng/Kg)	References
Norfloxacin	4.2	1.6 to 4.9	248 to 776	[44]
Trimethoprim	15.8	3.8 to 4.4	11 to 90	
Ciprofloxacin	5.3	2.5 to 2.8	4125 to 1225	
Sulfamethoxazole	956.4	96.9 to 142.6	542 to 896	
Lamivudine	847.1	219.6 to 228.3	107 to 491	
Zidovudine	1.4	1.1 to 21	118 to 510	
Clavulanic acid	10–110			[34]
Erythromycin	100–150			
Sulfadimidine	0–5			
Sulfamerazine	2–20			
Minocycline	0			
Tetracycline	10–180			
Trimethoprim	5–100			
Lincomycin	5–80			

Table 3. Occurrences of ACs in the Ugandan environmental compartments.

Matrix	Substance	Concentration (ng/ L)	References
Lake Victoria water	Sulfamethoxazole	1–5600	[46]
	Trimethoprim	1–89 L	
	Tetracycline	3–70	
	Sulfacetamide	1–13	
	Erythromycin	10–66	
	Sulfamethazine	2–50	
	Carbamazepine	5–72	
	Ibuprofen	6–780	
	Diclofenac	2–160	
	Sulfamethoxazole	1–5600	

Table 4. Occurrences of ACs in the Tanzanian environmental compartments.

Matrix	Substance	Concentration	References
Wastewater	Metronidazole	0.065–0.104 ppm	[51]
Msimbazi River waters	Metronidazole	0.0024 ppm	[53]
	Paracetamol	0.0060 ppm	
	Cetirizine	0.0073 ppm	
	Ibuprofen	0.0016 ppm	
Wastewater effluents	Ampicillin	bdl to 0.367 ppm	[48]
	Ciprofloxacin	bdl to 0.037 ppm	
AMR Lake Victoria water	Sulfamethoxazole/trimethoprim	100%	[52]
	Ampicillin/cloxacillin	100%	
	Erythromycin	72.7%	
	Tetracycline	90.9%	
	Nalidixic acid	63.6%	

6.4. Zambia

According to the available information, Zambia's environmental compartments were mostly affected by the presence of active chemicals from the classes of antibiotics and antivirals, as presented in Table 5. Although the industrial release of these contaminants is possible, a report indicated only the presence of metalloid toxicants [55]. As there were only a few studies, there is a need to further investigate the presence of active chemicals and other emerging contaminants in the Zambian environment.

Table 5. Occurrences of ACs in the Zambian environmental matrices.

Matrix	Substance	Concentration	References
Urine	Sulfamethoxazole	7740 μg/L	[56]
	Trimethoprim	12,800 μg/L	
	Lamivudine	10,010 μg/L	
Surface water	Antibiotics	11,800 ng/L	
	Antivirals	49,700 ng/L	
Effluents	Antibiotics	100–300,400 ng/L	
	Antivirals	680–55,760 ng/L	

6.5. Zimbabwe

Previous studies indicated that there was contamination as a result of the use of wastewater for irrigation, showing a possibility of exposure to other emerging contaminants, including active chemicals [57–59]. In some sub-Saharan countries, such as Zimbabwe, the funeral industry is well advanced; therefore, there is a possible high use of organic chemicals for the preservation of dead bodies [60]. The available information on this matter indicates that the funeral industry applies a range of toxic contaminants during thanatopraxy, post-mortem, along with cemetery processes. Hotspot pools of contaminants in the funeral industry were identified as human cadavers, solid waste, wastewaters, airborne particulates, and aerosols. In addition to the industry being both a source and a pool of contaminants, it could also pose an occupational exposure risk, which may occur during autopsy, thanatopraxy, cemetery activities, and crematoria via ingestion, inhalation of airborne particulates and aerosols, or dermal intake via cuts and wounds; therefore, there is a need to regulate and monitor this industry for a safer ecosystem [60]. A study of large randomized controlled trials conducted in Bangladesh, Kenya, and Zimbabwe revealed that the traditional household WASH interventions are unlikely to reduce diarrhea or improve linear growth in infants and children. The observed results may be attributable to the fact that traditional WASH interventions control microbial pathogens, but do not remove chemical toxicants such as contaminants of emerging concern. Exposure to toxicants is associated with diarrheal symptoms and other health risks [61]. This indicates a possibility for water to be contaminated by active chemicals. Therefore, regulatory authorities in sub-Saharan Africa need to include routine monitoring and analysis of these contaminants in their guidelines. The aquatic life in Zimbabwe has been reported to display various toxic effects as a result of industrial and municipal effluents [62] (Table 6). Industrial processes and domestic products have diverse natures; therefore, urban effluents are often contaminated with various anthropogenic endocrine-disrupting chemicals that may interfere with the reproductive physiology of the aquatic fauna.

Table 6. Occurrences of ACs in the Zimbabwean environmental compartments.

Activity in (ng/L)	Effluents from				References
	STPs	Ugumza	Matsheumhlope	Kihami	
17β-estradiol equivalent (EEq)	33	237	9	2	[62]
Dihydrotestosterone equivalent (TEq)	55	-	-	-	
Androgenic	93	-	-	-	

6.6. Mozambique

Reports of occurrences of active chemicals in the Mozambican environmental compartments are available [63]. The active chemicals identified are presented in Table 7. Remnants of these substances, their metabolites, and their transformation products have detrimental effects on ecosystems.

Table 7. Occurrences of ACs in the Mozambican environmental compartments.

Matrix	Substance	Concentration (ng/L)	References
Surface water	Azithromycin	8	[34]
	Clavulanic acid	5–20	
	Erythromycin	20–1000	
	Sulfapyridine	800–1300	
	Sulfamethoxazole	12	
	Oxytetracycline	1000	
	Trimethoprim	800	

Most studies have reported the presence of active chemicals in the environment. Therefore, there is a possibility of the occurrence of toxic metabolites and transformation products, which may harm humans and render adverse impacts on the natural environment. Moreover, because these substances are available in proximity to one another in the receiving environment, there is a possibility of drug interaction and consequent effects due to the combined concentrations of drugs acting either synergistically or antagonistically.

6.7. Ethiopia

Despite the absence of studies in Ethiopia, different surveys have been carried out to evaluate knowledge, attitudes, and practices with regard to the disposal of unused and/or expired active chemicals among the eastern and northern communities and retail outlets [64–66]. The majority of the respondents in Ethiopia had unused medicine stored at home, and the most common types of medicines kept in households were analgesics (~70%), followed by antibiotics. Preferred methods of disposal of both unused and expired medicines included throwing them away in household garbage, while two-thirds of the respondents disposed of the active chemicals in their original packaging and dosage form [64–66]. This drug handling and use pattern may lead to the presence of these drugs and/or their metabolites in the environmental compartments. Therefore, intervention is required for the proper planning and management of active-chemical waste to protect both human and environmental health. Reports relating to the identification of pesticides in plant leaves are available in Ethiopia [30]. The recent identification of pharmaceuticals in the Ethiopian environment is presented in Table 8.

Table 8. Active chemicals identified in the Ethiopian environmental compartments, and their respective amounts.

Matrix	Substance	Concentration (ng/L)	References
Wastewater	Trimethoprim	500	[67]
	Ciprofloxacin	10–300	
Water	Trimethoprim	7800	
	Caffeine	3200	
	Albendazole	2100	
Hospital water	Caffeine	320	
	Trimethoprim	780	
	Albendazole	210	

6.8. Malawi

The presence of contaminants such as active chemicals in the environment is a result of several risk factors, despite the lack of studies. Previous research has highlighted the significant risk to humans and the ecosystem as a result of the presence of pesticides in environmental compartments [68]; the authors further explained that Malawi's regulatory authority on pesticides—the Pesticides Control Board (PCB)—faces several challenges, including a lack of facilities for analyzing pesticides, and possibly a similar challenge hindering reports on active chemicals in the environments [68]. Research indicates that the management of healthcare waste in low- and middle-income countries presents many challenges. The findings in the reviewed literature indicate a need for waste management training suitable for rural settings, so as to prevent possible harm and environmental contamination [69].

6.9. Eritrea

Eritrea lacks information on the presence of active chemicals, although practices that could constitute risk factors—such as the reuse of wastewater—have been reported. Assessment of the health impacts of the utilization of raw domestic sewage for vegetable cultivation was conducted in the suburbs of the capital city of Asmara; the results showed high contamination of vegetables by fecal coliforms, as well as with *Giardia* cysts. The reuse of wastewater may be a route through which active chemicals and other contaminants are introduced into the Eritrean environment [70,71]. Groundwater quality investigation was conducted in Asmara, around Mai-Bela—an area with a long history of wastewater irrigation. Groundwater suitability for domestic and irrigation purposes was compared with the World Health Organization (WHO) and Food and Agriculture Organization (FAO) standards. Most of the parameters were found to be above the permissible limit. The results indicated that groundwater in most of the study sites was not suitable for drinking and irrigation purposes [72].

6.10. Mauritius

Mauritius is an African island found in the Indian Ocean, known for its beautiful beaches, reefs, and lagoons. Reports were found on the presence of active chemical waste generation as a result of anthropogenic sources that may lead to pollution—such as domestic effluents, agricultural runoff, offshore oil and gas exploration, active chemical industries, and mine drainage [73–75].

6.11. Madagascar

In a study conducted to investigate the parameters that modulate the contamination of environmental systems, 16 years of microbial quality data for water supplied to 32 urban areas of Madagascar were revisited. It was observed that contamination increased over the 16 years, reaching alarming levels—perhaps due to increased population and anthropogenic activities [76]. Reports of the presence of quantifiable levels of persistent halogenated compounds—such as pentabromotoluene and hexachlorobenzene—are available [77,78], indicating pollution.

6.12. Rwanda

The contribution of anthropogenic activities such as industrial activities to pollution is rarely investigated in Rwanda. Air pollution was observed around the Chimerwa area, but how the industries managed wastewater was not discussed, and the tailings may be a route towards the discharge of contaminants and, hence, pollution [79,80]. The performance of the Kacyiru Sewage Treatment Plant, and the impact of its effluents on the receiving wetlands, was investigated. Influent and effluent wastewaters, as well as receiving wetland water quality, were investigated from April to September 2019 at Kacyiru estate. The quality of discharged effluents was revealed to be poor due to the poor maintenance and treatment operations of the sewage treatment plant; this is why the removal efficiency for some key parameters was low, and may possibly be a source of emerging pollutants [81]. The activities leading to increased load and circulation of active chemicals in the Rwandan environment included the reuse of wastewater for irrigation, and the use of sludge as fertilizer—including untreated sludge, which is among the risk factors [45]. It was noted that there were some weaknesses in the execution of the environmental impact assessment (EIA) recommendations among the major industrial sectors of Rwanda, which may lead to the degradation of the natural environment [82]. Practices of reuse of wastewater for irrigation and the use of sludge as fertilizer are reported to exist, and are also the main routes through which active chemicals are introduced in the environmental compartments [83].

6.13. South Sudan

Reports on the presence of emerging contaminants, such as active chemicals, are lacking in South Sudan. Exploratory drilling for crude oil had been performed since 1974 in the southern areas of Sudan, and large deposits were discovered between 1979 and 1982. In addition to income generation, it was observed that the salinity of drinking water was increasing, coupled with human use incompatibilities and a rise in livestock mortality. Later, it was found that the region was contaminated with lead (Pb), and the concentration of Pb increased steadily with the decreasing distance from the oil fields, while the groundwater was polluted by harmful deposition of toxic industrial waste, hence the need for further investigation of the presence of other contaminants of emerging concern [84–88]. Equally important would be an investigation of the population at risk of being exposed to these contaminants. South Sudan, like other developing countries, suffers from issues of sewerage and solid waste management, hence the possibility of contaminating the environment [89]. Workers were found to work under unsafe conditions; therefore, they faced a possibility of contaminating themselves and the environment [90].

6.14. Burundi

Reports on the presence of contaminants such as active chemicals in the Burundian environmental compartments are lacking, but there is information on the presence of practices that may lead to contamination. As with other developing countries, Burundi faces challenges such as improper disposal of solid waste, including hospital waste, hence the possibility of contamination to humans and the ecosystem at large [91–93]. Contaminants of emerging concern, including active chemicals, find their way back and circulate in the ecosystem while they bioaccumulate, bioconcentrate, and magnify via the food chain, causing harm. In Burundi, there is a practice of preparing briquettes from solid waste as a substitute for charcoal, to aid in protecting forest reserves [94]. On the other hand, some types of solid waste may be the cause of contamination concerns that require intervention. Conventional wastewater treatments, such as the waste stabilization ponds used in most of sub-Saharan Africa, are not designed for the removal of organic contaminants; therefore, the effluents discharged may contain contaminants.

6.15. Seychelles

The presence of contaminants in the Seychelles' environmental compartments has been reported [95,96], indicating a possibility of ecosystem exposure. Table 9 presents reports of contamination in Seychelles.

Table 9. Contaminants identified in fish muscles from the Seychelles coast.

Matrix	Substance (s)	Concentration (pg g^{-1} ww)	References
Muscle	Organochlorine pesticides (OCPs)	5637	[97]
	Polychlorinated biphenyls (PCBs)	491	
	Perfluoroalkyl substances (PFASs)	331	

6.16. Somalia

In Somalia, there are active chemical industries, despite the initiatives by authorities to regulate and monitor the implementation of good manufacturing practices [98,99]. Groundwater is a major drinking water resource in the arid coastal regions of Somalia. Bosaso city's groundwater quality has experienced degradation due to rapid urbanization and industrialization. In terms of irrigation uses, a small portion of the country may be at risk of alkalinity or sodium hazards. However, not all groundwater supply points are suitable for irrigation, due to salinization. Somalia's groundwater sources can only be used to irrigate highly salt-tolerant crops. Salinity may be due to seawater intrusion as a result of over-pumping of water resources [100]. Somali communities have been facing many challenges regarding solid waste management. The Karan district community is known for its good level of education and positive attitude; however, the community's practices with regard to solid waste management are not eco-friendly, and may lead to contamination of soil, air, and water sources.

6.17. Nigeria

Similar to other sub-Saharan African countries, Nigeria releases wastewater from hospitals, agriculture, industrial production, and aquaculture into urban waste stabilization ponds. Most wastewater treatment schemes in Nigeria are not designed for the removal of organic contaminants such as active chemical compounds [101–104]. Occurrences of emerging organic pollutants (EOPs) have been reported, including active chemicals [105,106] (Table 10). Therefore, urban wastewater is the main source of chemical load.

Table 10. Occurrences of ACs in the Nigerian environmental compartments.

Matrix	Substance	Concentration	References
River water	Phenazone	<to 0.01 µ/L	[103]
	Trimethoprim	<to 0.01 µ/L	
	Estrone	<to 0.01 µ/L	
	Estriol	<to 0.01 µ/L	
	Acetylsalicylic acid	<to 0.02 µ/L	
	Carbamazepine	<to 0.02 µ/L	
	Diclofenac	<to 0.02 µ/L	
	Roxithromycin	<to 0.02 µ/L	
	Indomethacin	<to 0.02 µ/L	
	Erythromycin	<to 0.06 µ/L	
	Clofibric acid	<to 0.02 µ/L	
Borehole	Diclofenac	0.39 mg/L	[101]
	Artemether	0.62 mg/L	
Treated tape	Diclofenac	0.17 mg/L	
	Artemether	0.04 mg/L	
Well water	Diclofenac	8.84–1100 µg/L	
	Ofloxacin	0.73, 0.24 and 0.08 ng/L	
Sewage	Chemical load	10–10,000 ng/L	[104]
Chemical effluent	Chemical load	2–15,000 ng/L	
Urban river	Chemical load	10–10,000 ng/L	
Hospital wastewater and landfill leachate	Bisphenol A	2.3–59.2 ng/L	[106]
	Acetamidophenol	Bdl–30.1 ng/L	
	Oxybenzone	1.0–1.1 ng/L	
	Triclocarban	39.3–47.2 ng/L	
	Triclosan	55–63.6 ng/L	

Bdl: below detection limit.

Undocumented evidence has indicated the presence of inorganic and organic chemical substances, microorganisms, and/or radionuclides in most oil-producing communities, such as the Niger Delta [107]. Few reports on groundwater and surface water contaminated by petroleum hydrocarbons are available [107].

6.18. Ghana

Reports on Ghana indicate the presence of active chemicals in the environment that may adversely affect human and environmental health. The status of environmental occurrences of active chemicals in Ghana is presented in Table 11. Anthropogenic activities contribute to the presence of these substances in the environment. In some areas of Ghana, antibiotics, analgesics, drugs for diabetes, anti-malarial drugs, cardiovascular drugs, and anthelmintics are widely used, and may increase the chemical load in the environment [108].

Table 11. Occurrences of active chemicals in the Ghanaian environmental compartments.

Matrix	Substance	Concentration (ng/L)	References
Surface water	Oxytetracycline	0–350	[34]
	Sulfadimidine	0–50	
	Minocycline	2–14	
	Chlortetracycline	2–14	
	Streptozotocin	500	
	Lincomycin	2–10	
	Tetracycline	10–300	
	Trimethoprim	10–200	
	Clavulanic acid	5–14	
	Azithromycin	2–12	
	Erythromycin	10–110	
	Metronidazole	247–420	
Hospital wastewater effluent/influent, river water, and in vegetables	Ciprofloxacin	11,352–15,733	[109]
	Erythromycin	7944–10,613	
	Trimethoprim	94–4826	
	Tetracycline	58–116	
	Oxytetracycline	75–252	
	Chlortetracycline	16–24	
	Amoxicillin	2–6	
	Ampicillin	107–324	
	Cephalexin	1052–1557	
	Sulfasalazine	2315–3590	

6.19. Togo

It has been reported that the Togolese environment is highly contaminated, with more than 2 million tons of alluvial phosphorite mine tailings being discarded yearly in the coastal waters of Togo, without any pretreatment, causing serious pollution problems in the region [110]. The investigation of the pesticide-use practices of market gardeners in Lomé indicated the usage of insecticides, herbicides, and fungicides that were often not approved by the Togolese state, and the farmers often did not have a good knowledge of pesticides, and generally did not comply with manufacturers' recommendations, such as the wearing of protective clothing. These results indicate the potential risk of exposure of market gardeners, vegetable consumers, and the whole ecosystem to pesticides [111]. Selected potentially exposed agro-ecological areas in Togo were investigated for the presence of pesticides in the environment, where drinking water, cowpeas, and maize grains were sampled. The results indicated higher pesticide residue than the World Health Organization (WHO)'s maximum limit in drinking water (0.04–0.40 µg/L), while population exposure levels to dieldrin and heptachlor epoxide were higher than the FAO/WHO standards. This reiterates the need for monitoring these substances in the Togolese environment [112]. According to Table 12, higher concentrations were observed in crops than in water, indicating a possibility of bioaccumulation, bioconcentration, and biomagnification through the food chain.

Table 12. Organochlorine pesticide residues found in grains (maize and cowpeas, in μg/kg) and drinking water (in μg/L) in Togo.

Substances	Cowpea	Maize	River water	References
Gamma-hexachlorocyclohexane	4.95	6.38	0.03 to 0.05	[112]
2,4-Dichlorodiphenyldichloroethane	14.57	2.18	0.00 to 0.02	
4,4-Dichlorodiphenyldichloroethane	15.76	5.29	0.00	
2,4-Dichlorodiphenyldichloroethylene	11.66	-	0.03 to 0.15	
4,4-Dichlorodiphenyldichloroethylene	4.71	-	0.07	
4,4-Dichlorodiphenyltrichloroethane	12.49	21.79	0.11	
Aldrin	6	0.52	-	
Dieldrin	39.50	18.09	0.04	
Heptachlor	3.92	1.72	0.24	
α-Endosulfan	88.51	34.74	0.32	
β-Endosulfan	98.80	65.71	0.25	
Heptachlor epoxide	44.88	17.65	0.17	

6.20. Burkina Faso

Investigation of contamination in Burkina Faso was carried out in different seasons in four sites of the cotton culture area, following up concerns about the contamination of water by organochlorine pesticides such as endosulfan and aldrin. Surface water and groundwater were sampled and investigated, and the results indicated the presence of these contaminants at higher concentrations in residues during the rainy season [113]. This may be due to the washing away and carrying up of pesticides by rainy water through water circulation and recharge, hence the higher concentrations compared to dry seasons. The identified contaminants in the Burkinabe environments are presented in Table 13.

Table 13. Organochlorine pesticide residues identified in surface water and groundwater (in μg/L).

Amount of Substances in (μg/L)	Ground Water	Surface Water	References
Endosulfan	0.05 to 0.16	0.05 to 0.25	[113]
Aldrin	0.01 to 0.07	0.01 to 0.15	

6.21. Liberia

Reports directly addressing the issues related to active chemicals in the environment of Liberia are lacking. However, the mining sector is currently the backbone of Liberia's economy, since the discovery of high-grade iron ore in Bomi Hills, Bong, and Nimba. Recently, the mining sector has played a role in infrastructure development, income generation, and employment in Liberia. However, the mining sector has significant environmental impacts, as it has been identified as causing pollution [114]. Investigation of the water quality in the local water environment in Liberia revealed that all parameters analyzed were above the WHO and Liberia Water Standard Class I guidelines for drinking water [115]. In addition to the contribution of mining to pollution, medical waste disposal and wastewater reuse may also contribute to increased chemical load in the environment.

6.22. Benin

For the small West African state of Benin, information on the presence of active chemicals in the environment is scarce. Assessment of wastewaters' characteristics in Benin was determined on the basis of domestic (greywater and blackwater) and industrial (hospital, pharmaceutical, and commercial laundry) wastewater in Cotonou, the capital city [116]. The pharmaceutical wastewater in the area was found to have the highest concentration of organic contaminants (COD = 5912 ± 1026 mg/L, Abs. UV 254 = 2.667 ± 0.327 cm^{-1}). Mohamed et al. (2021) recommended that consideration should be given to Abs. UV 254, as compounds that are absorbed at this wavelength may include emerging contaminants from pharmaceutical loads [116].

6.23. Ivory Coast

Similar to Benin, Eritrea, Somalia, etc., reports of active chemical contamination for Cote d'Ivoire are rare. Recently, a life cycle assessment (LCA) was conducted to evaluate the environmental impacts of the Afema Gold Mine in Ivory Coast across the mine's value chain. The analysis revealed that the offsite impacts—mainly induced by fuel consumption—represented the majority of the total impacts for two of the three areas of protection (human health and ecosystem quality). From a time-based perspective, the study revealed that of the phases, the operating phase had the most impact. Extraction activities—especially excavation, ore and waste rock transportation, blasting, ore processing, and tailing treatment—were the main causes of impacts [117,118]. Assessment of wastewater management in Korhogo—a city in the north of Ivory Coast—was conducted, and the results indicated that 23% of the residences discharge their wastewater either into rivers around the city, via pipes intended for stormwater drainage, or on the way for laundry, crockery, and/or bathwater (43%), whereas (34%) released their water through watertight and non-watertight facilities such as septic tanks and latrines, respectively. It was further observed that factories evacuated their wastewater directly into the environment, without any prior treatment, which could mean that the discharge of contaminants was directed to the immediate environment [119].

6.24. Mali

Investigation of water quality from different sources in Pelengana commune, Segou, Mali found that the water quality was within the permissible limits, but there were some indications of contamination. Among the reasons for increased contamination were agricultural practices in the area, which included irrigation by reuse of wastewater and the use of sludge as fertilizer [120,121]. Reports on the reuse of wastewater and the use of sludge in the Malian agricultural sector are available [122]. A survey of pit latrines, domestic wells, and improved water sources was carried out in a large rural village of southern Mali, and all households were evaluated for water, sanitation, and hygiene habits. It was revealed that two-thirds of the households used bleach for the purification of drinking water, and for protecting themselves from fecal contamination [123]. However, the use of bleach to disinfect water is not safe, as the bleaching agents may react with contaminants and lead to the production of more toxic transformation products. Investigation of persistent organic contaminants revealed quantifiable levels of multiple contaminants in air samples, including benzo(a)pyrene, PCB [124], and fluoranthene. Representatives of contaminants are presented in Table 14.

Table 14. Representatives of identified persistent agrochemicals in the environmental samples of Bamako, Mali.

Matrix	Substance (s)	Concentration (Pg/m^3)	References
Air	trans-Chlordane	44	[124]
	Sum chlordanes	48	
	Chlorpyrifos	9960	
	Dacthal	1.1	
	O; P-Dichlorodiphenyldichloroethane	152	
	P; P-Dichlorodiphenyldichloroethane	314	
	O; P-Dichlorodiphenyldichloroethylene	81	
	P; P-Dichlorodiphenyldichloroethylene	990	
	O; P-Dichlorodiphenyltrichloroethane	537	
	P; P-Dichlorodiphenyltrichloroethane	810	
	Diazinon	810	
	Dieldrin	1100	
	Endosulfan I	10,500	
	Endosulfan II	2510	

6.25. Cape Verde

For Cape Verde, pollution of the environment mainly results from anthropogenic sources, such as domestic use, solid waste sources, agriculture, industry, commerce, transportation, and power generation [125]. Investigation of air quality in Cape Verde revealed the presence of several persistent organic contaminants (POCs); some of the identified POCs are presented in Table 15. Despite the absence of immediate studies reporting occurrences of these substances in other matrices—such as water—the presence of these substances in air implies their presence in soil, effluents, and water.

Table 15. Representatives of identified persistent agrochemicals in the environment of Cape Verde.

Matrix	Substance (s)	Amount in pg/m^3	References
Air	trans-Chlordane	0.1	[124]
	trans-Nonachlor	0.2	
	Chlorpyrifos	1.0	
	Dacthal	0.1	
	O, P-Dichlorodiphenyldichloroethane	0.4	
	P, P-Dichlorodiphenyldichloroethane	0.8	
	O, P-Dichlorodiphenyldichloroethylene	0.3	
	P, P-Dichlorodiphenyldichloroethylene	0.2	
	O, P-Dichlorodiphenyltrichloroethane	0.6	
	P, P-Dichlorodiphenyltrichloroethane	0.5	
	Diazinon	0.7	
	Dieldrin	0.8	
	Endosulfan I	4.4	
	Endosulfan II	0.4	

6.26. Guinea-Bissau

A study was conducted to characterize groundwater-based water wells and to evaluate risks faced by the local population in Guinea-Bissau [126]. The results indicated that the water was contaminated with organic (methyl mercury) and inorganic (As and Pb) toxicants, indicating a lack of safety and a possibility of harm to the population and the environment. Therefore, the inhabitants in the study area may experience a chronic range of systemic effects, with children being more susceptible than adults this may be related to their physiology and interactions with the environment [127–129].

6.27. Gambia

In Gambia, there is a record of yearly floods in Ebo Town with polluted water from the uphill Kanifing Municipality, as a result of lack of proper infrastructure for sanitation and drainage [130]. Practices of reuse of wastewater for irrigation have also been recorded, which may be a major source of active chemicals in the environment.

6.28. Senegal

A study conducted by [131], reported a need for the presence of an efficient chain for biomedical waste (BMW) disposal (and solid waste management in general) in Dakar, Senegal. The evidence calls for significant investments for effective BMW management, in order to address environmental contamination, human exposure, and associated impacts on human health [131]. The results indicate a need for a proper means of disposal of active chemicals for the safety of the environment, or for the prevention of improper use of drugs. There were not many studies that covered the presence and threats of active chemicals in the Senegalese environment.

6.29. Equatorial Guinea

Currently, in Malabo—the capital of Equatorial Guinea—there is excessive deposition of air contaminants. This is based on the results of a study that evaluated air quality over a period of 50 years [132]. Similar to other countries mentioned above, the reports on the presence of active chemicals in Equatorial Guinea are lacking, apart from therapeutic and agronomic uses, reuse of wastewater, and the use of sludge as manure.

6.30. Cameroon

Reports of contamination of the Cameroonian environmental compartments are available; the risk factors leading to contamination have also been identified—for example, the practices that lead to pollution from anthropogenic activities, such as the disposal of municipal and agricultural waste [133–136]. Occurrences of active chemicals in hospital wastewater in Cameroon, along with polar pesticide contamination of urban and peri-urban tropical watersheds, are presented in Table 16.

Table 16. Occurrences of active chemicals in hospital wastewater and the watersheds of urban and peri-urban areas of Cameroon.

Matrix	Substances (s)	Concentration (μg/L)	References
Hospital wastewater	Paracetamol	211.93	[137]
	Ibuprofen	141	
	Tramadol	76	
	O-desmethyltramadol	141	
	Erythromycin anhydrate	7	
	Ciprofloxacin	24	
	Clarithromycin	0.088	
	Propranolol	0.3	
	Cimetidine	34	
	Hydroxy omeprazole	5	
	Diphenhydramine	0.38	
	Metformin	154	
	Sucralose	13.07	
	Azithromycin	0.39	
	Sulfamethoxazole	0.16	
	Trimethoprim	0.27	
	Caffeine	5.8	
	Carbamazepine	0.94	
	Atenolol	0.43	
	Acetochlor	4.1	[133]
	Atrazine	2.2	
	Chlortoluron	6.2	
	Diuron	1.5	
	Linuron	01	
	Flazasulfuron	1.0	

Reports on the presence of polar pesticide contaminants in both urban and peri-urban settings were found, and the concentrations were observed to increase during the rainy season, most likely due to surface runoff [133]. In another study that was carried out to assess the quality of most consumed foods of animal origin, it was revealed that animal-based diets contributed an average of 8.1% of the total diet of an individual in Cameroon. The results revealed that these food substances contained contaminants such as toxic metals, mycotoxins, veterinary drug residues, and pesticides, indicating a possibility of exposure to these contaminants [138]. For a safer natural environment, measures must be taken to identify the presence and levels of contaminants via routine analysis and monitoring activities.

6.31. Angola

Most of the countries in sub-Saharan Africa are in search for sanitation solutions [139], as a result of effluent disposal and reuse [140]. A high level of water-borne diseases in

Angola is associated with poor water quality [141], as effluents from sewage are discharged to water sources [140].

6.32. Gabon

The two main water bodies in Gabon—the Mpassa and Ogooué Rivers, which are subjected to anthropogenic pollution—are the main sources of irrigation water in Franceville. In an analysis that was conducted in the area, all water samples contained bacteria, and may therefore pose a health threat to the local population [142]. The results from another study [143], on the nucleotide sequences of the ESBL resistance genes indicated that all cefotaximase-Munichs (CTX-Ms) were CTX-M-15, and that all sulfhydryl variables (SHVs) were SHV-11: 41.67% CTX-M-15-producing *E. coli*, 16.67% CTX-M-15 + SHV-11-producing *E. coli*, 8.33% CTX-M-15-producing *K. pneumoniae*, 25% CTX-M-15 + SHV-11-producing *K. pneumoniae*, and 8.33% CTX-M-15-produced *E. cloacae* [143]. This study indicated for the first time the presence of multi-resistant ESBL-producing enterobacteria in fruit bats in Makokou [143].

6.33. Congo-Brazzaville

A direct report on the presence of active chemicals in the environment in Congo Brazzaville is missing. Also, inappropriate pesticide use may increase the risk of pest resistance for long-term use; this practice may also be a source of environmental pollution in Nkolo and its surroundings [144,145]. It was also reported that, wastewater in Brazzaville neighborhoods is characterized by organic and inorganic pollution [146]. This water is reused for other activities like irrigation, a possibility for contamination. The results from a study by [147], revealed the presence of antimicrobial resistance and antibiotics such as amoxicillin; amoxicillin + clavulanic acid; cloxacillin, and nalidixic acid.

6.34. Democratic Republic of Congo (DRC)

Current studies on environmental contamination in the DRC are rare; sensitization to environmental issues has not been adequately carried out. The wastewater mainly comes from industries, but may also come from residential areas and hospitals. This could be indicative of a possibility of the presence of contaminants such as active chemicals, and the adverse effects thereof [148,149]. The DRC is not free from contamination; in addition to reports of toxic metals in hospital effluents, one study [111], further highlighted the significantly high ($p < 0.05$) values of 16S rRNA, FIB, and ARG copy numbers in all sampling sites, including upstream (control site), at discharge points, and downstream of receiving rivers [111]. These findings reveal that several sources—including hospital and urban wastewaters—contribute to the spread of contaminants, including the biological emerging contaminants, in aquatic ecosystems.

6.35. Namibia

A report from Namibia indicated a deterioration of water quality at Goreangab Dam as a result of increased population and associated human activities [150]. Windhoek, Namibia's capital, has been augmenting its drinking water sources with reclaimed wastewater since 1968, and is widely regarded as a leader in water reclamation and reuse in sub-Saharan Africa [151]. Reports on the toxic effects of contaminants in aquatic ecosystems—such as reduced fertility, abnormal development of male and female secondary sexual characteristics, alterations in sex ratios, feminization of males, and alteration of behavior—as well as increased effluents owing to urbanization and ineffective wastewater treatment, resulting in contaminated effluents, are common [19,152]. This has resulted in a proposed application of sustainable treatment of used water in Namibia and Ethiopia [151].

6.36. Lesotho

For Lesotho, the results revealed low levels of contaminants; the presence of mercury (Hg), fly ash, and polycyclic aromatic hydrocarbons (PAHs) indicate a probability of industrial fossil-fuel combustion as a source of contamination [153]. Some of the identified active chemicals in the environment of Lesotho are presented in Table 17.

Table 17. Occurrences of ACs in environmental compartments of Lesotho.

Matrix	Substance (s)	Concentration (ng/g)	References
Lake water, sediments	Hexachlorobenzene	0.1–0.3	[153]
	Total polycyclic aromatic hydrocarbons	50–250	
	Total 16 USEPA polycyclic aromatic hydrocarbons	0–150	
	High-molecular-weight polycyclic aromatic hydrocarbons (4–6-rings)	0–10	
	Benzo(a)pyrene	0.5–1	
	Indeno (1, 2, 3, c, d)pyrene	1–3	
	Benzo (g, h, 2)pyrene	1–3	
	Total polychlorinated biphenyls	0.1–3	
	Total 7 polychlorinated biphenyls	0.1–2	

6.37. Botswana

In Botswana, active chemicals were found as a result of the accumulation of antibiotic resistance determinants in wastewater treatment facilities, and their subsequent release into the water ecosystems downstream [154]. In the environmental compartments of Botswana, high frequencies of potentially pathogenic microorganisms were observed. The antibiotics that were identified are presented in Table 18.

Table 18. Occurrences of ACs in Botswanan environmental compartments.

Matrix	Antimicrobial Resistant (AMR)	Percentage	References
Wastewater influent, effluent, and downstream environment	Ampicillin	54	[154]
	Penicillin	85	
	Erythromycin	76	
	Cephalosporin	69	
	Sulfamethoxazole	54	
	Trimethoprim	85	

7. Lack of AC Reports for Some Sub-Saharan African Countries

Reports of the prevalence of active chemicals in several sub-Saharan African countries are scarce, and those that are accessible are insufficient to play a role in advising the countries' policymaking processes. Medical and agronomic usage, wastewater reuse, and the presence of industrial activities that could be a source of these compounds have all been reported. Furthermore, for the results to be ascertained, some analysis would need to be conducted using state-of-the-art laboratory equipment, such as high-pressure liquid chromatography (HPLC) equipped with mass spectrometry detection. However, in most sub-Saharan African countries, there is still a lack of laboratory infrastructure for investigation of contaminants of emerging concern, such as active chemicals [28,32,62,71,154,155]. Despite the scarcity of information on the presence of active chemicals in sub-Saharan Africa, a study was conducted to investigate the relationship between exposure to contaminants and socioeconomic development among immigrants from 19 sub-Saharan countries who arrived in the Canary Islands (Spain). The results revealed higher serum concentrations of organochlorine pesticides and PCBs in the blood samples of the immigrants from Central and West African countries [156]. It was further observed that Africans from low-income countries had higher levels of organochlorine pesticides, indicating agricultural application of these substances, while those from high-income countries had higher levels of PCBs. People from West Africa had significantly higher levels of PCBs. PCBs are associated with westernized life, and the use of more industrial goods.

Currently, the management and treatment of hospital wastewaters in Asia, Africa, and Australia poses challenges. Hospital wastewaters are subjected to different treatment scenarios, such as specific treatment, co-treatment, and direct disposal into the environment. Waste treatment and effluent discharge have become some of the routes through which contaminants, including active chemicals, circulate within the environment [20].

8. Flow and Fate of Active Chemicals

Active chemicals used as curative agents by humans and animals end up in the soil, rivers, lakes, subterranean water and, eventually, drinking water, where they can have disastrous consequences for ecosystems. The fate and persistence of introduced active chemicals and/or metabolites in the environment are influenced by the physicochemical qualities of the environmental compartments with which they interact [157]. The primary processes that decide their fate in the environment are biodegradation rate, photodegradation rate, and sorption kinetics [157–159]. The movement of active chemicals in the different environmental compartments is depicted in Figure 2.

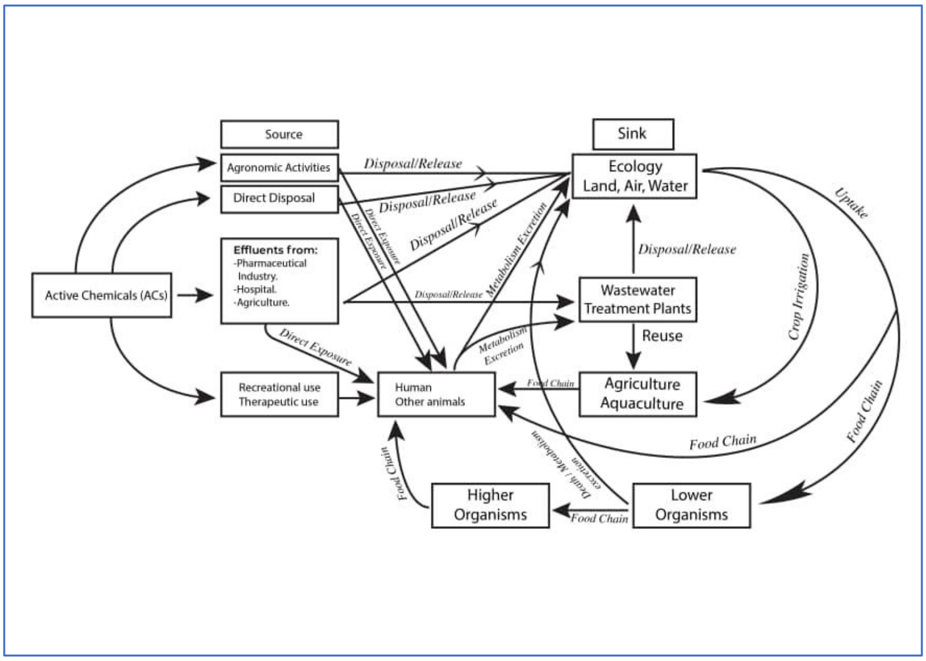

Figure 2. Flow of active chemicals in different environmental compartments. After the introduction pollutants to the environment, they circulate while being converted to secondary pollutants that can infect human beings. This indicates that human beings act as both sources and sinks of pollutants.

Humans may consume active substances for a variety of reasons, including medical or recreational uses, as shown in Figure 2. Medication can also be consumed by animals (e.g., veterinary drugs). Following ingestion, biotransformation occurs, with a portion of the drug's remains and metabolites expelled directly into the environment, such as water bodies or sewage systems. Active substances and their metabolites circulate in all of these situations. Active chemicals in sewage or water bodies can affect humans, large mammals, and other life forms. Sewage containing waste from residential regions mixes with sewage from industrial and clinical settings, adding to the chemical burden in waste stabilization ponds. Water is reused in agriculture and aquaculture, and sludge is applied as fertilizer; at this point, active chemicals are injected into the soil once more. Active chemicals enter the food chain via these methods, bioaccumulate in aquatic ecosystems after uptake by plants and algae, and cause bioconcentration and biomagnification through the food chain, according to previous studies [160,161]. After interacting with the ecosystem, active chemicals and biotransformation products are used by humans again through the food chain. Active chemicals and biotransformation products may affect the ecosystem at any of the steps described.

8.1. Environmental and Human Health Effects

Hormonal disruption is one of the impacts of active chemicals in the environment, such as the hormone ethinylestradiol, which is the main active element in many contraceptive pills. At extremely low concentrations, ethinylestradiol has been observed to influence the sexual development of male fish in the laboratory, and intersex fish have been identified downstream of sewage facilities in rivers all over the world. A follow-up study in Canada indicated that persistent, low-level exposure to the drug harmed both male and female fish, and resulted in the study population's near-extinction, despite the fact that the concentration in the experiment was higher than that found in rivers [162]. In male fish, the active chemical metformin, which is used to treat diabetes, was shown to cause expression of a gene relevant to egg production, indicating hormonal alterations. As a result, metformin may have a feminizing effect on male fish, reducing their ability to procreate [163–165]. In this case, the veterinary anti-parasitic medicine ivermectin was found to reduce the number and variety of insects in cow dung, which might delay dung degradation and potentially lower the amount of food available to birds and bats [165]. Millions of vultures died in India between 1996 and 2007, as a result of exposure to the anti-inflammatory medication diclofenac, driving the birds to near-extinction [162]. These are just a few examples of the impacts of medications, and each of them is an example of a specific drug's effect. There is a chance of the interactions of medications, because these drugs occur as mixtures in the environment. As a result, more research is needed in order to assess the consequences of various mixtures.

8.2. Challenges Associated with ACs in the Environment

There have been decades of research on the existence of contaminants in the environment, as well as reports on the presence of active substances in the environment. The introduction and prevalence of ACs, as well as their fate in the environment, were and continue to be a source of worry. The presence of active chemicals in the environment has been widely proven, prompting a shift in the focus of study from compound analysis in various environmental matrices to field trials. The presence of medication combinations in the environment raises concerns about toxicity, drug–drug interactions, and combined concentration effects. Technical management strategies such as oxidative or photolytic effluent treatment, filtering techniques, and the use of charcoal have all been discussed. All of these approaches have flaws; consequently, more efforts concentrating on green pharmacy should be considered [16,166]. Example, in advanced treatment, methadone and tolylfluanid, as well as other nitrogen-containing active drugs, generate one hazardous transition product (nitrosodimethylamine (NDMA)) and the formation of possible unknown dangerous compounds. A rapid NDMA metabolism in experimental animals, resulting in hazardous and carcinogenic chemicals, has been reported. It was also shown that NDMA has moderate-to-high acute oral toxicity and high acute inhalation toxicity, with the liver being the primary target organ. NDMA can also be produced endogenously via the ingestion of nitrite and other nitrogenous chemicals [27,167–170]. Some of these active compounds, such as ciproxacilin's UV photolysis products, create several biotransformation intermediates with uncertain toxicity [27,170]. On the other hand, micronucleus tests, cell toxicity, and genotoxicity of CIP photoproducts show a wide range of genotoxicity [27,170,171]. It is necessary to examine the effects of hazardous exposure to active substances on humans, and on the ecosystem as a whole. Currently, environmental risk assessment guidelines do not include these compounds in routine monitoring. These chemicals have been found to be available and flowing in environmental compartments all over the world, including sub-Saharan Africa.

8.3. Limitations of Wastewater Treatment

Apart from the fact that most wastewater treatment plants in sub-Saharan Africa are not intended to remove active chemicals, reports suggest that even those that are do not completely remove them [167,168,172,173]. There is a possibility of unknown harmful compounds forming during advanced treatment, such as methadone and tolylfluanid transformation products, which are highly poisonous and have a limit of 7 ng/L in water [167,174–176]. In recent years, the global identification of active chemicals in the aquatic environment and drinking water has been a source of worry. The possibility of concurrent formation of nitrosamine DBPs (disinfection byproducts) during chloramine disinfection has become another significant concern in terms of drinking water quality, because of their potent carcinogenicity. During chloramine disinfection, roughly 20 active pharmaceuticals and personal care products (PPCPs) were found to be nitrosamine precursors, according to Shen and Andrew (2011) [173]. Eight active compounds have molar yields greater than 1%, with ranitidine having the greatest propensity to produce N-nitrosodimethylamine (NDMA). Furthermore, molar conversion increases as the Cl2:N mass ratio increases, suggesting that dichloramine is involved in the production of NDMA from these precursors—hence the potential for toxicity [173]. Toxicity could be caused not only by the presence of multiple parent compounds, but also by the presence of numerous unknown transformation products per parent molecule. Factors include a lack of understanding, too many compounds for targeted treatment, and inadequate mineralization products being generally unknown, making it difficult to monitor active chemicals in the environment.

8.4. Overcoming the Challenges Relating to ACs

The fundamental worry regarding active chemicals in the environment is their persistence, which may lead to toxic effects in the environment as a result of bioaccumulation, bioconcentration, and biomagnification through the food chain [15]. As a result, the best way to solve this difficulty is to start with drug design, taking into account product biodegradation. For existing medications, current active chemicals are being redesigned for environmental biodegradability—for example, 4-hydroxy propranolol is being developed to replace propranolol, despite the fact that it has a lower activity, as it is biodegradable, making it safer for the environment by reducing toxicity [81,177–180]. Figure 3 represents the structure of biodegradable drug (4-hydroxy propranolol) and a non-biodegradable drug (propranolol), as depicted by Rastogi et al. [81]. Similarly, application of green synthesis in manufacturing will aid in creating a sustainable ecosystem [166]. Therefore, it is necessary to utilize green approaches in agricultural activities, such as organic farming [181], and biological control [182]. A study by Hassanisaadi et al. (2021) [166], utilized plant water extract for biosynthesis of gold nanoparticles, which is environmentally friendly, as reported by other researchers [183–187]. It is further recommended to utilize alternative medicine or plant-based drugs for the treatment of medical conditions, as they are green and lead to sustainable ecosystems, which is very helpful in overcoming drug resistance [188–191].

On the other hand, it is necessary to review guidelines and include these substances in routine environmental assessment and monitoring activities. Utilization of novel techniques in monitoring—such as chemical and biochemical nanosensors—is necessary [16,192–196]. For areas facing environmental pollution, bioremediation techniques such as biosorption can be used for clean-up and, hence, restore the natural situation [197–201]. This can help to build functioning ecosystems and, hence, sustainability.

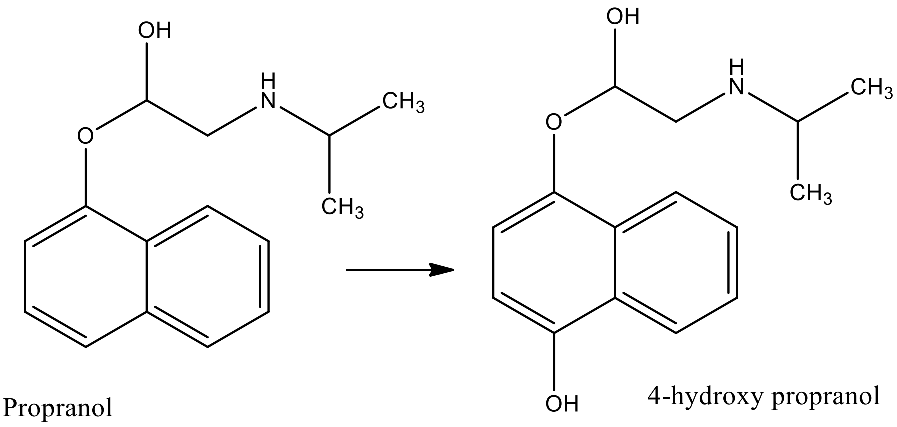

Figure 3. Structure of a biodegradable drug (4-hydroxy propranolol) and a non-biodegradable drug (propranolol), as depicted by Rastogi et al. [81].

9. Conclusions and Recommendations

Mixtures of active chemicals form multiple therapeutic categories, and their biotransformation products are present in sub-Saharan African environmental compartments; hence, the possibility of toxic exposure to humans and ecosystems. As a result, more research is needed in order to determine the existence and amounts of these active chemical compounds, as well as their potential toxicity when used individually or in combination. For the sustainability of ecosystems, policymakers and regulatory authorities should include these compounds in guidelines for routine monitoring activities, and ensure that the necessary facilities for their detection and analysis are available. Biodegradability should be considered in the design, importation, and prescription of active substances.

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