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Review

Aptasensors for the Detection of Environmental Contaminants of High Concern in Water Bodies: A Systematic Review

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Abstract: With the advancement of technology and increasing industrial activity, anthropogenic contaminants are currently detected where there is no record of their presence or insufficient information about their toxicological impact. Consequently, there are not sufficiently robust local or global regulations, the ecotoxicological and human health risks are critical, and they may not be routinely monitored despite being ubiquitous. The interest in studying environmental contaminants, including micropollutants and emerging contaminants, in complex environmental water samples has grown in the last decade. Due to the concentrations in which they are typically found in the environment and the rapid global dispersion, the detection procedures for these substances must be capable of measuring very low concentrations. Many efforts have been made to improve remediation procedures or develop novel analytical methods for their determination. Although there are several robust and reliable standard analytical techniques for their monitoring, pollutant contamination requires simple and inexpensive methods for massive, in situ monitoring campaigns. In this regard, biosensors have emerged as devices with high selectivity, sensitivity, easy operation, and short analysis times. Aptasensors are biosensors based on a nucleic acid recognition element (aptamer). Due to their synthetic nature, stability, and easy production, aptamers are frequently employed to develop bioassays. This work presents a systematic review of the trends in using aptasensors for detecting environmental contaminants present in environmental water samples, as well as the estimation of the potential technological contribution these devices might give to environmental monitoring.

Keywords: aptasensors; pollutants; emerging contaminants; nanomaterials; water contamination

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1. Global Problem of Contaminants in Water

The growing requirements of consumers for new products for everyday use have generated the appearance of many contaminants in the environment, mainly in aquifer systems. These substances, known as emerging contaminants (ECs), are found in trace concentrations in water bodies. ECs are currently of high environmental interest because they are recalcitrant compounds, ubiquitous throughout the ecosystems and, in many cases, have unknown toxicological effects [1,2].

The sources of environmental contaminants are mainly due to industrial practices or anthropogenic activities [2,3]. As shown in Figure 1, several contaminants are transferred by different routes to water systems. Wastewater treatment plants (WWTPs) constitute one of the main factors for the spread of contaminants. When contaminant degradation or removal processes are not appropriate, these substances are released into water bodies

in high amounts due to an enrichment and accumulation effect [3–6]. After release from WWTPs to water systems, contaminants can bioaccumulate in aquatic species [7–9] and be transported to different water bodies (groundwater, river water, lakes) where risk exists to reach water for human consumption (tap water, bottled water) [2,10–13].

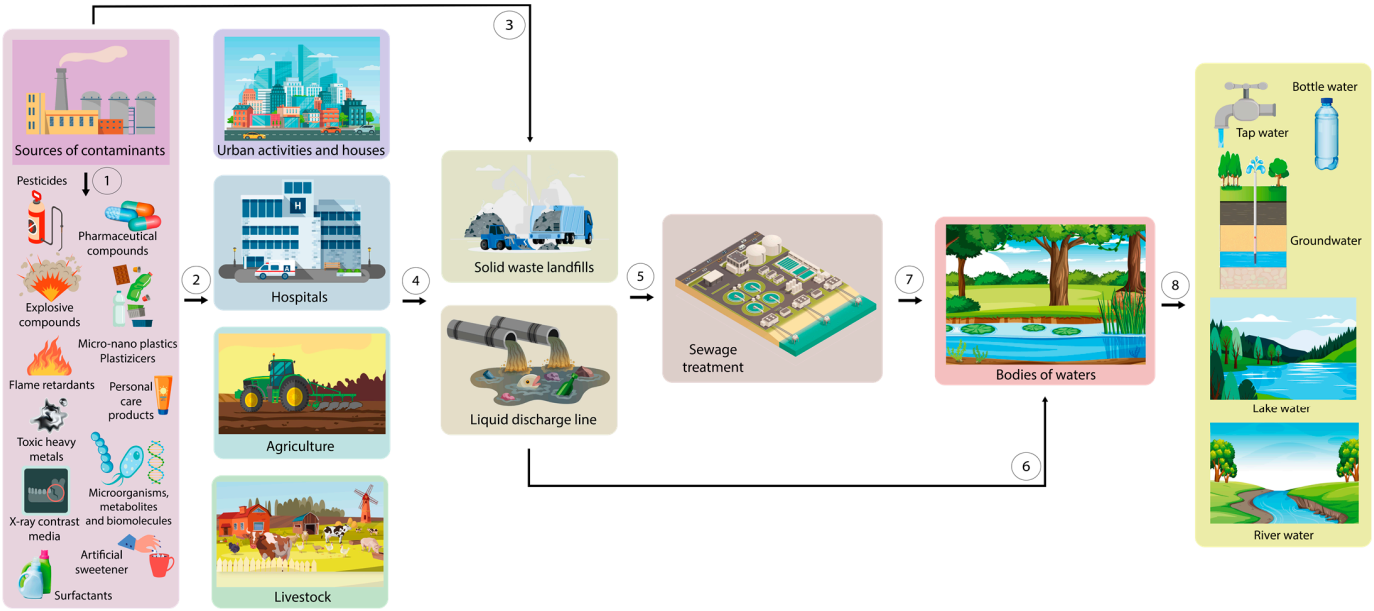

Figure 1. (1) Environmental contaminants from a synthetic origin are produced by different kinds of industrial activities for several applications. (2) Industrial, urban, and rural activities release contaminants in waste landfills and liquid discharge lines (3 and 4). These liquid waste dumps must be treated (5) before being released into natural water bodies (7). However, in various regions of the world, they are disposed of directly without prior treatment (6). Even when treated, in most cases it is not possible to eliminate or degrade contaminants. Thus, they will be then released into natural waters and eventually used for (8) industrial, urban, and rural activities.

Regarding the risks for the ecosystems and human health due to the presence of environmental contaminants in the hydric system, the World Health Organization (WHO) and the governments of different regions have established minimum concentration levels of some of these substances in water [14–18]. The concentrations allowed in water bodies, depending on the type of compound, are, generally, in the order of pico- to micro-molar in heavy metals [18–20], pesticides (insecticides, fungicides, herbicides) [21–23], pharmaceutical substances (anti-inflammatories, analgesics, antibiotics, hormones, diuretics, anxiolytics) [24–26], plasticizers and micro- and nano-plastics [27,28].

Traditional methods for their monitoring are based on chromatography coupled to mass spectrometry (GC-MS and LC-MS) and direct detection methods based on luminescence (absorption and fluorescence). GC-MS and LC-MS are frequently based on complex analytical procedures, requiring well-trained personnel and laborious sample treatments with associated high costs and low throughput. These techniques are undoubtedly suitable as a confirmatory method. By contrast, the development of screening analytical methods to be performed directly in the field is mandatory for monitoring programs. Screening methods allow the use of confirmatory methods only on positive findings, thus decreasing the number of samples to be analyzed and reducing the cost of the whole analysis. In this context, methods based on biosensors [29] are of particular interest. Indeed, any screening method must meet the Affordable, Sensitive, Specific, User-friendly, Rapid and Robust, Equipment-free, and Deliverable to End-users (ASSURED) criteria established by the WHO [18,30]. Recently, aptasensors have emerged as interesting tools in the detection of environmental contaminants due to their high selectivity in binding to the target and

their synthetic nature, compared to other biorecognition elements, such as antibodies or enzymes [31–33].

Aptamers are single-stranded oligonucleotides with high-affinity binding to a given target analyte, produced by in vitro selection. They fold into complex three-dimensional structures upon association with their target, providing multiple molecular interactions of different types (electrostatic, hydrogen bonding, etc.) that govern selective recognition. Aptamers are produced by chemical synthesis, avoiding biological raw materials, or living animals. Aptamers are selected by a universal approach that does not depend on a particular analyte with the possibility to use toxins as well as molecules that do not elicit a good immune response [34–36].

Moreover, aptamers have other interesting features such as high thermal stability and the opportunities for further chemical modifications that provide the immobilization of aptamers onto solid support with mild alteration of selectivity. Due to these features, aptamers are frequently used in biosensor assembly and are frequently combined with a wide variety of nanomaterials, improving the sensing performance [35,37–40].

Considering the above-mentioned advantages, this work aims to systematically review the use of aptasensors for detecting environmental contaminants in water bodies to evaluate the current trend, sensitivity projections, assembly materials, and the ability to reuse the devices. Although there has been a noticeable increase in the number of review papers related to aptasensors for detecting contaminants in environmental water samples in the last five years (see Figure 2), the vast majority are focused on describing only the original research on the development and functionality of aptamers, in a specific type of transducer (optical or electrochemical) [38,41–48], the effectiveness of certain materials (metallic nanoparticles, metal–organic framework, quantum dots, single- and multi-walled carbon nanotubes) [49–52], or type of contaminants (heavy metals, pharmaceutical compounds, pesticides, endocrine disruptors) [53–62]. Nevertheless, a systematic analysis that includes these aspects, emphasizing the analysis of water samples of environmental origin or that had undergone purification treatment, has not yet been published.

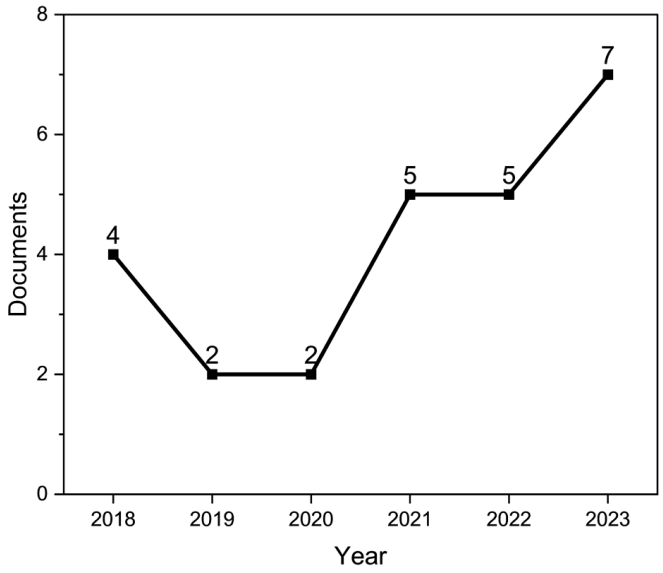

Figure 2. History of the number of review papers on the detection of contaminants in environmental water samples using aptasensors. Data extracted from Scopus on 20 March 2024.

2. Materials and Methods

This review followed the preferred reporting items for the systematic review and meta-analysis statement (PRISMA). The literature search focused on reports published in peer-reviewed journals indexed in Web of Science and Scopus databases and available in English.

The search for studies concerning aptasensors was performed by evaluating keywords, titles, and abstracts. Studies that did not assess the applicability of aptasensors in detecting contaminants in environmental water (river, lake, groundwater, wastewater) were excluded. Only articles published from the past five years were considered (2019–2023).

Focus questions were prepared based on the problem, intervention, comparison, and outcome (PICO) method: (P) what water contaminants are usually detected using aptasensors? (I) What configurations are frequently applied for aptasensors elaboration for contaminant detection? (C) Are aptasensors sensitive enough for environmental contaminant detection at ultra-low concentrations in complex environmental water samples? (O) What aptasensor exhibits the higher performance stability for analyzing real water samples?

The search was performed using the following components for every database:

Search component 1 (SC1), including the key terms: Aptasensor OR Aptamer AND Water; Search component 2 (SC2), including the key terms: Aptasensor OR Aptamer AND water OR wastewater OR groundwater OR river OR Sewage OR Environment.

The following data were extracted and captured in an Excel spreadsheet featuring the following information: article title, year, analyte, analyte classification, transducer type, detection principle, sensitivity, water sample type, test on real samples, aptasensor selectivity/specificity, reproducibility/repeatability, stability, and reusability. Table 1 shows the concept and description of the data searched.

Table 1. Description of the primary data sought in the systematic review.

Concept	Description
Analyte	Name of environmental contaminant.
Analyte classification	The environmental contaminants were classified according to their chemical family: metals, pesticides, toxins, industrial chemicals, and pharmaceutical compounds.
Transducer type	Electrochemical, optical, photoelectrochemical/electroluminescence (opto-electrochemical) transducers.
Sensitivity	Sensitivity according to the LOD [1] using the following ranges as a basis: low (LOD > 0.1 mg/L), medium (0.1 mg/L > LOD ≥ 1 µg/L), high (1 µg/L > LOD > 0.1 ng/L), and ultra-high (LOD < 0.1 ng/L).
Water sample type	Water used from a complex matrix: river water, lake water, wastewater, or seawater.
Test on real sample	Refers to whether the target analytes were found in real water samples, or the compounds were spiked to the water samples.
Selectivity/specificity	Presence of interferents in the complex matrix and whether the assay was performed: (1) with the target in the presence of the interferents in the same sample (mixed with interferents); (2) whether the target and interferents were analyzed separately (individual); (3) if the target was analyzed with one of the interferents (individual interferents with the target); and 4) if this test was not reported (NR).
Reproducibility/repeatability	Reported RSD [2].
Stability	To evaluate the behavior of the aptasensor over time.
Reusability	Determines if the same device can be used in different periods.

[1] Limit of detection; [2] relative standard deviation.

This review considered only original research articles in English directly related to detecting or quantifying water environmental contaminants using aptamers as recognizing elements. The exclusion criteria for full-text articles were articles written in a language dif-

ferent from English, aptasensors applied for the detection of other chemicals not considered environmental contaminants, abstract-only papers as proceeding papers, and conference, editorial, and author response theses and books. Finally, aptasensor applications in model water samples (distilled, buffer, or synthetic environmental water samples) or uncomplex water samples, such as those from drinking or tap water, were excluded as they were not useful to answer the research questions.

3. Results and Discussion

A total of 250 studies were found in the Scopus database and 286 in the Web of Science database, totaling 536 from 2019 until 2023. After duplicate exclusions, 151 studies that met the inclusion criteria remained. In addition, 42 reviews on aptasensors for contaminants application were identified in the same search period; of these, 13 reviews related to the detection of water contaminants were selected to identify some other original publications not collected in the initial search. The rest of the reviews were not selected because they focused on the development of aptasensors for a particular contaminant or a family of them (arsenic, bisphenol, pesticides, mycotoxins, metals, viruses, microorganisms, antibiotics) in another type of compartment (food, biological fluids, or plants); some other reviews focused on the detection of biomolecules in biological fluids, for the diagnosis of diseases (Alzheimer, cancer), molecular monitoring of metabolites or drugs in the body; and other reviews focused on the transduction system (electrochemical, optical). None of the 42 reviews were of the systematic type but rather were of the narrative type. In the eligibility step, the rest of the 13 reviews were excluded and no additional papers evaluated were chosen. The consultation of the full texts of the articles to determine the inclusion and exclusion criteria led to the exclusion of 36 articles, mainly because the articles excluded in this step applied the aptasensor in simple water samples such as buffer or distilled water and those applied in food samples, although the abstract mentioned that it could be applied in environmental samples or environmental monitoring. In total, 73 studies that fully met the inclusion criteria were subsequently analyzed to answer the research questions. The PRISMA flow diagram template used in this systematic review is shown in Figure 3. Table S1 of the Supporting Information details the 73 studies with the concepts developed in Table 1.

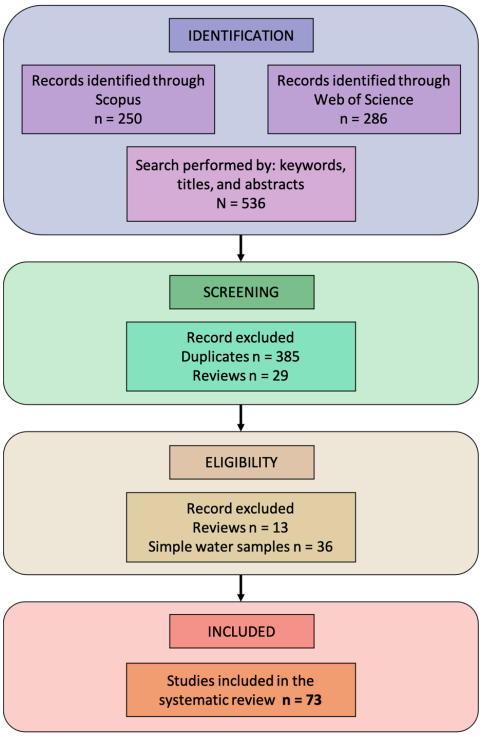

Figure 3. Exclusion and inclusion results of the systematic review in 2019–2023.

3.1. Production of Aptamers as Recognizing Elements

The aptamer selection process, called Systematic Ligand Evolution by Exponential Enrichment (SELEX), is a technique developed almost simultaneously by Tuerk and Gold [63], and Ellington and Szostak [64] in the 1990s. The SELEX technique consists of the following steps: selection, partitioning, and amplification (Figure 4). To carry out the selection, it is necessary to synthesize a library of approximately 10^{13}–10^{18} random oligonucleotide sequences. Each oligonucleotide contains random bases (20–50 NTs) flanked by two conserved primer binding sites, which are used for PCR amplification. In the selection step, the oligonucleotide library is incubated with target molecules, which are immobilized on solid phase supports; after incubation, the unbound sequences are separated using different methods. The target-bound sequences are amplified by PCR (DNA SELEX) or reverse transcription PCR (RNA SELEX); the products are used for the next selection round, performing the same sequence and target molecule interaction process. After several rounds of selection, the enriched oligonucleotides are sequenced and evaluated for their binding capabilities [63–66]. However, there are some deficiencies to be overcome; one of them is stringency, as SELEX assumes that the most enriched sequences are the most specific binders, which is not always the case, and high-affinity binders can sometimes be overlooked due to insufficient stringency in selection conditions. The process can enrich for non-specific binders that bind to the matrix used rather than the target molecule, leading to false positive results; in addition, minimal mistakes in the initial library result in a biased library; another restriction is the limited scale. Moreover, SELEX can be limited in its ability to identify specific binders for targets with low binding specificity or for targets with highly structured regions [37,67–71]. Over time, different modified SELEX procedures have been developed and continue to be developed to improve the efficiency, specificity, or speed of the selection process, including variations in the separation stage. Some examples are shown in Table S2.

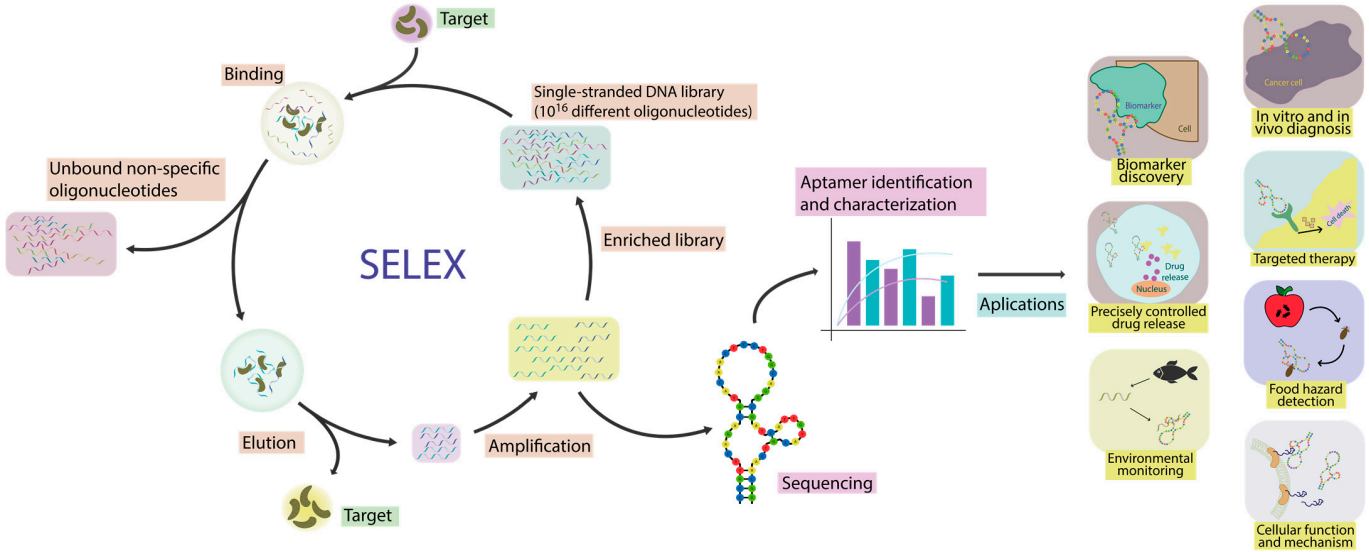

Figure 4. General scheme of SELEX and its main applications.

3.2. Overview of Data Collection

As can be seen in Figure 5 and Table S1, the 73 papers reported the detection of 30 aqueous contaminants: 5 metals, 6 pesticides, 4 industrial chemicals, 2 toxins, and 13 pharmaceutical compounds. In particular, the study of antibiotics stands out due to the promotion of bacterial resistance, an issue of global concern. Different environmental water matrices were analyzed: municipal and industrial wastewaters, lakes, rivers, ponds, and canal water. However, most of the assays were performed in spiked water samples, allowing for the study of the effects of natural interferents, but the concentrations used in these assays are usually much higher than the environmental ones. Most of the papers

studied the selectivity of aptasensors using chemically similar analytes, added to the assay individually or in a mixture of interferents, in significantly higher concentrations. However, very few addressed the study of the reusability of the aptasensor, a parameter of major importance in the environmental area, where a massive number of readouts are performed, which implies a high cost for an adequate determination of contamination in time and space.

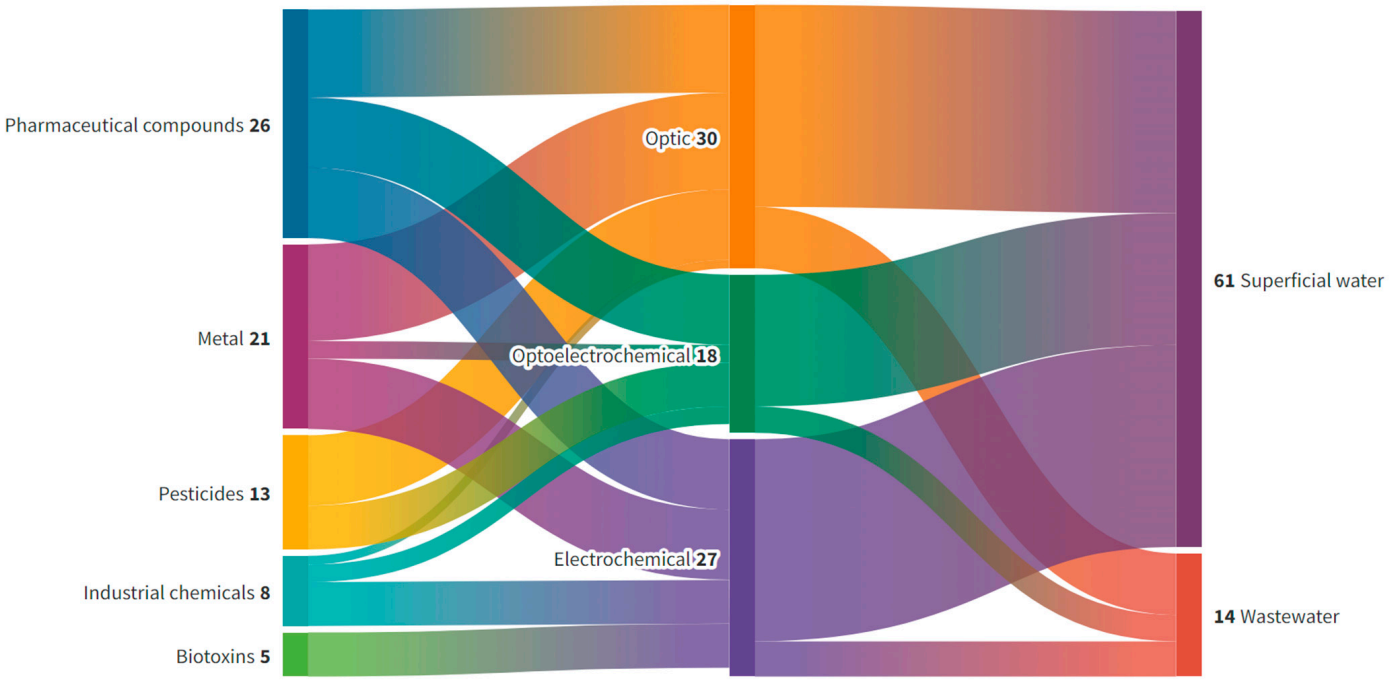

Figure 5. Applications of aptasensor in the environmental field from 2018 to 2023. The term optoelectrochemical includes photoelectrochemical and electroluminescent sensors. The numbers indicate the number of total papers. Created with flourish.studio.

3.3. Analysis of Categorizations

3.3.1. Environmental Contaminants

The systematic analysis of the literature on applying aptasensors in environmental water over the past five years shows that pharmaceuticals (PhCs) are the most studied, with 26 papers and 13 compounds reported (Table S1). In recent years, there has been a boom in the literature on monitoring PhCs as emerging contaminants [72,73]. Antibiotics are undoubtedly the most studied PhCs, and there are several reasons for this. First, they are the most widely used drugs worldwide for human, animal, and plant health; second, because of the above, they are expected to be discharged into the environmental compartments by various household, hospital, and industrial discharges. Thirdly, they are the cause of bacterial resistance, an issue of great concern worldwide, where the global action plans against antimicrobial resistance promote the monitoring of both resistant microorganisms and the antimicrobials commonly used as a reference [74]. In a recent work [2], it was found that, among the 53 compounds reported, those with the highest calculated relevance were PhCs, with antibiotics having the highest proportion.

In second place was the detection of metals, with 21 works for detecting copper, mercury, lead, cadmium, and arsenic. Metals are pollutants with a broader concentration range, from mg/L to ng/L, because they are produced by intensive industrial activity from several sectors; in addition, they can be released into the environment from natural sources. They have been studied for many years, and their toxic effects and environmental impact are known. Hence, the search for accurate, sensitive, and stable methods or devices will promote the development of research and innovation in the field. Indeed, aptasensors have been widely applied to detect metals, as reported in recent literature reviews [32,53].

The other family of contaminants analyzed using aptasensors is pesticides. These compounds are widely discharged into aqueous compartments upon spraying over large areas, so they are prone to being partially deposited outside the target sites and carried into streams or reservoirs by runoff or filtration. Their presence as contaminants is documented, as is their effects on human and environmental health [75–77]. Although applied in large quantities, some undergo chemical and biological transformation reactions, leading to their detection at μg/L or ng/L concentrations. The most studied pesticides are diazinon, chlorpyrifos, atrazine, acetamiprid, quinclorac, and malathion, as reported in 13 papers.

Fewer papers have been devoted to the determination of industrial chemicals (8 papers, 4 chemicals) and toxins (5 papers, 2 toxins), as reported in Table S1. Studies performed within complex samples and in the presence of many interferents indicate that aptamers are robust molecules capable of maintaining their affinity towards the analyte of interest in environmental conditions.

3.3.2. Sensor Design and Sensitivity

Regarding the most used sensor configurations (Figure 6), 77% of the cases (56 articles) used the aptamer without further modification or a simple modification, such as functionalization with an amino group or thiol group to anchor at the surface of the transducer. On the transducer side, three types were documented. Electrochemical, optical, and opto-electrochemical techniques were used within these transducers. With the term opto-electrochemical, we include both electrochemiluminescent and photoelectrochemical systems.

To enhance aptasensor performance, nanomaterials have become a prevalent strategy. Their well-documented properties enable them to exert significant influence on several critical aspects, including controlling assembly density, regulating the accumulation of the aptamers, optimizing the orientation of these elements for target interaction, and facilitating the rate of electron transfer at the sensor interface [78]. In this review, 60% of the papers used composites of two or more materials of metallic or carbonaceous type, or their combination. Among those, noble metal nanoparticles, graphene and graphene oxide, carbon nanotubes, quantum dots, and metal–organic frameworks are the most widely employed. Particularly, 18 papers used electrochemical transducers modified with nanocomposites, while 18 papers used opto-electrochemical transducers with a surface composed of two or more materials, and only 9 were optical with nanocomposites. A total of 28 papers used a "simple" interface with only one or no nanomaterial, most using the optical transducer (colorimetric analysis). Figure 6a shows the number of papers classified based on the transducing principle. Figure 6b–d describe a simplified subdivision of the works in line with the heterostructure used, i.e., (i) simple: bare surface or one nanomaterial; (ii) composite: heterostructures of two nanomaterials; (iii) complex: more complex heterostructures. Moreover, a further classification according to sensitivity is also reported.

Regarding sensitivity, in the selected works, the reported LODs displayed a wide interval of values, from mg/L to ag/L. A total of 82% of LODs (60 papers) fall in the value here defined as high to ultrahigh sensitivity (LOD < 1 μg/L), 14% showed a medium sensitivity (0.1 mg/L > LOD > 1μg/L), and only three papers showed a low LOD (LOD > 0.1 mg/L) (Figure 6). It is well known that aptamers present dissociation constants like those shown by antibodies, with values of approximately 10^{-9} M, which helps to achieve high sensitivity. Regarding the type of transducer on the sensitivity parameter, 100% of the papers using opto-electrochemical transducers showed high and ultra-high sensitivity, followed by 90% of the electrochemical and 50% of the optical transducers (Figure 6).

The data presented in Tables 2 and S1 show that the high sensitivity of the aptasensors can be attributed to the coupling of specific aptamers with nanomaterials.

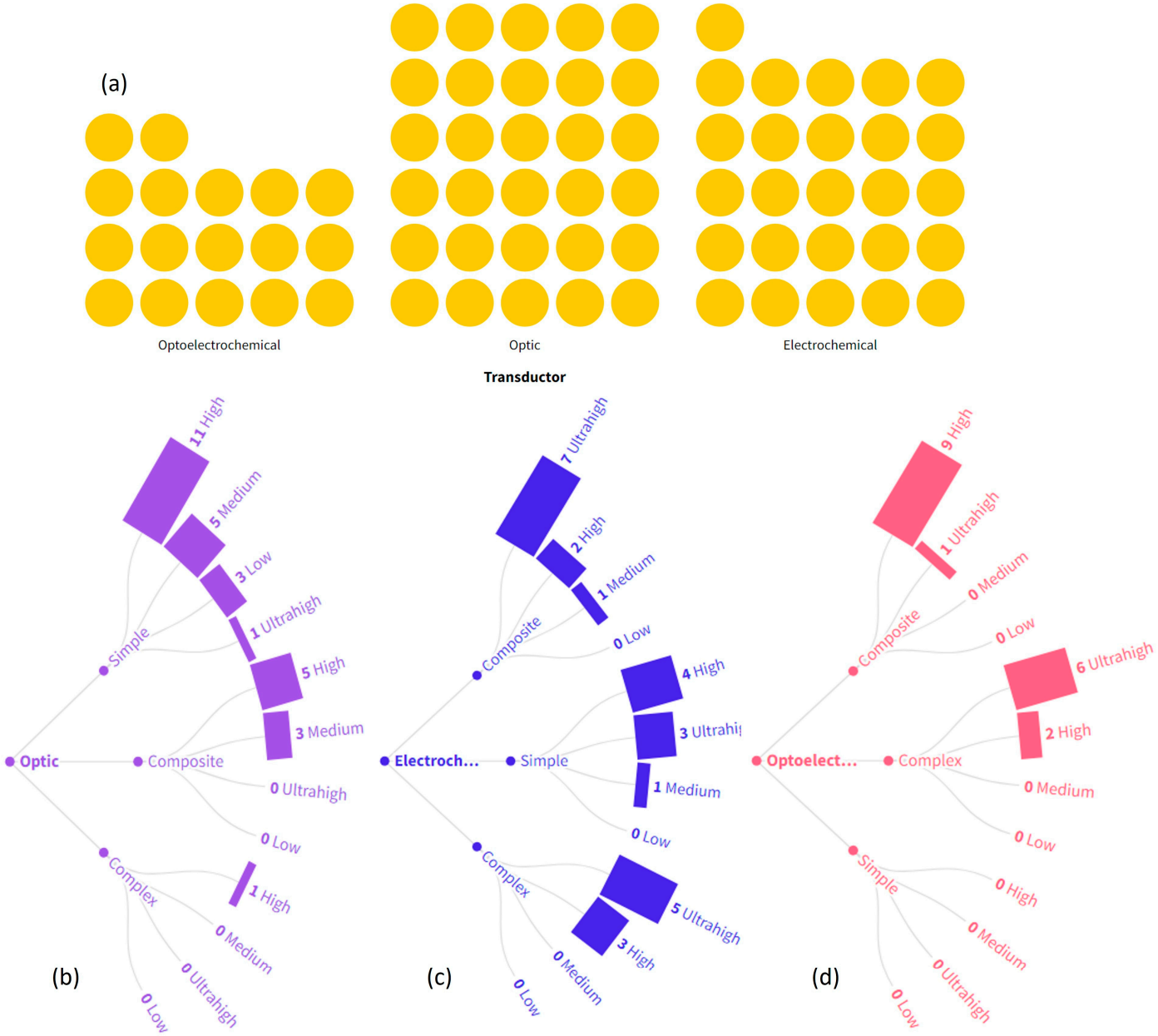

Figure 6. Configuration and sensitivity of aptasensor for contaminant detection in environmental water from 2015 to 2023. Upper part: total aptasensor according to transductor used (**a**). Type of interface and sensitivity for optical (**b**), electrochemical (**c**), and opto-electrochemical (**d**) transductor. Created with flourish.studio.

Table 2. Examples of aptasensors for environmental applications.

Sensitivity (LOD)	Transducer	Nanomaterials	Target Classification	Reference
7.11 ag/L	Opto-electrochemical	Graphitic carbon loaded by CoN nanoparticles (CoN/g-C_3N_4)	Pesticides	[79]
0.33 pg/L	Electrochemical	$CoMoS_4$ hollow nanospheres	Mycotoxins	[80]
2.07 pg/L	Electrochemical	Nanocomposite structure of AuNPs/PPy/$Ti_3C_2T_x$	Heavy metals	[81]

Table 2. *Cont.*

Sensitivity (LOD)	Transducer	Nanomaterials	Target Classification	Reference
0.601 pg/L	Opto-electrochemical	$Ru(bpy)_3^{2+}$-doped silica nanoparticle-nitrogen-doped graphene quantum dots ($Ru@SiO_2$-NGQDs)	Heavy metals	[82]
3.01 fg/L	Opto-electrochemical	(CoAl LDH/g-C_3N_4) two-dimensional/two-dimensional structure	Pharmaceutical compounds	[83]
0.742 pg/L	Electrochemical	Cu@carbon nanoneedles (Cu@CNNs)	Heavy metals	[84]
12.64 pg/L	Opto-electrochemical	NiFe layered double hydroxide (NiFe LDH)/graphitic carbon nitride (g-CN) heterojunction	Pharmaceutical compounds	[85]
97.8 pg/L	Electrochemical	Nanostructure composed of MoS2 nanosheets and conductive polypyrrole nanoparticles (PPyNPs)	Pharmaceutical compounds	[86]
3.6 fg/L	Electrochemical	Zeolitic Imidazolate Framework-8 (ZIF-8)-derived Ag@Au core–shell nanoparticles (Ag@Au/ZIF-8)	Heavy metals	[87]
22 fg/L	Optic	Magnetic beads and gold nanoparticles (AunNPs)	Heavy metals	[88]
15 pg/L	Optic	Not applicable	Pharmaceutical compounds	[89]
0.189 pg/L	Electrochemical	Gold-plated coplanar electrode array	Heavy metals	[90]
0.22 pg/L	Electrochemical	CoNi-based metal–organic framework (MOF), $CoxNi_{3-x}$,$(HITP)_2$,	Pharmaceutical Compounds	[91]
29.86 pg/L	Electrochemical	ZnO quantum dots decorated B, N co-doped graphene (BNG/ZnO)	Mycotoxins	[92]
29.86 pg/L	Electrochemical	3D cobalt-based oxide modified boron and nitrogen co-doped graphene hydrogel (3D BNG/Co)	Mycotoxins	[93]
75 fg/L	Opto-electrochemical	Metal–organic framework NH_2-MIL-125(Ti)	Pharmaceutical compounds	[94]
80 fg/L	Electrochemical	Thionine (Thi)-functionalized MoS_2-rGO nanocomposite	Industrial chemicals	[95]
0.20 pg/L	Electrochemical	Nanohybrid of Ag, Ag_2O, Ag_2S, and ultra-thin MoS_2 nanosheet ($Ag/Ag_2O/Ag_2S/MoS_{2(600)}$)	Industrial chemicals	[96]
15 pg/L	Opto-electrochemical	Cu(I) modified carbon nitride (Cu/g-C_3N_4)	Industrial chemicals	[97]
18 ag/L	Electrochemical	Multi-walled carbon nanotubes (MWCNT), amino-functionalized magnetite, and gold nanoparticles (NH_2-Fe_3O_4/Au NPs)	Industrial chemicals	[98]
99.86 pg/L	Opto-electrochemical	N-doped TiO_2 nanotubes (N-doped TiO_2 NTs)	Industrial chemicals	[99]

Table 2. *Cont.*

Sensitivity (LOD)	Transducer	Nanomaterials	Target Classification	Reference
0.22 pg/L	Electrochemical	Co-based metal–organic frameworks (Co-MOF) and terephthalonitrile-based covalent organic framework (TPN-COF) (Co-MOF@TPN-COF)	Pharmaceutical compounds	[100]
17.4 pg/L	Electrochemical	Nanohybrids of Covalent organic framework (COF) and Ce-based metal organic framework (Ce-MOF) (Ce-MOF@COF hybrid nanostructure)	Pharmaceutical compounds	[101]

As an example of an electrochemical transducer, Zhao et al. [98] recently reported an aptasensor for bisphenol A (BPA) detection (Figure 7). Their design employed a glassy carbon electrode (GCE) modified with a composite material consisting of multi-walled carbon nanotubes (MWCNTs), amino-functionalized magnetite (NH_2-Fe_3O_4), and gold nanoparticles (Au NPs). The combination of these elements resulted in a limit of detection (LOD) of 0.08 aM (18 ag/L) for BPA, along with a linear detection range spanning from 10^{-19} M to 10^{-14} M. The authors reported an advantage in using a dual-signal amplification effect based on (i) the synergic properties of the composite material and (ii) the conductivity of the SWCNTs. The specific aptamer also facilitated a "signal-on" sensing scheme, contributing to a simple and efficient protocol.

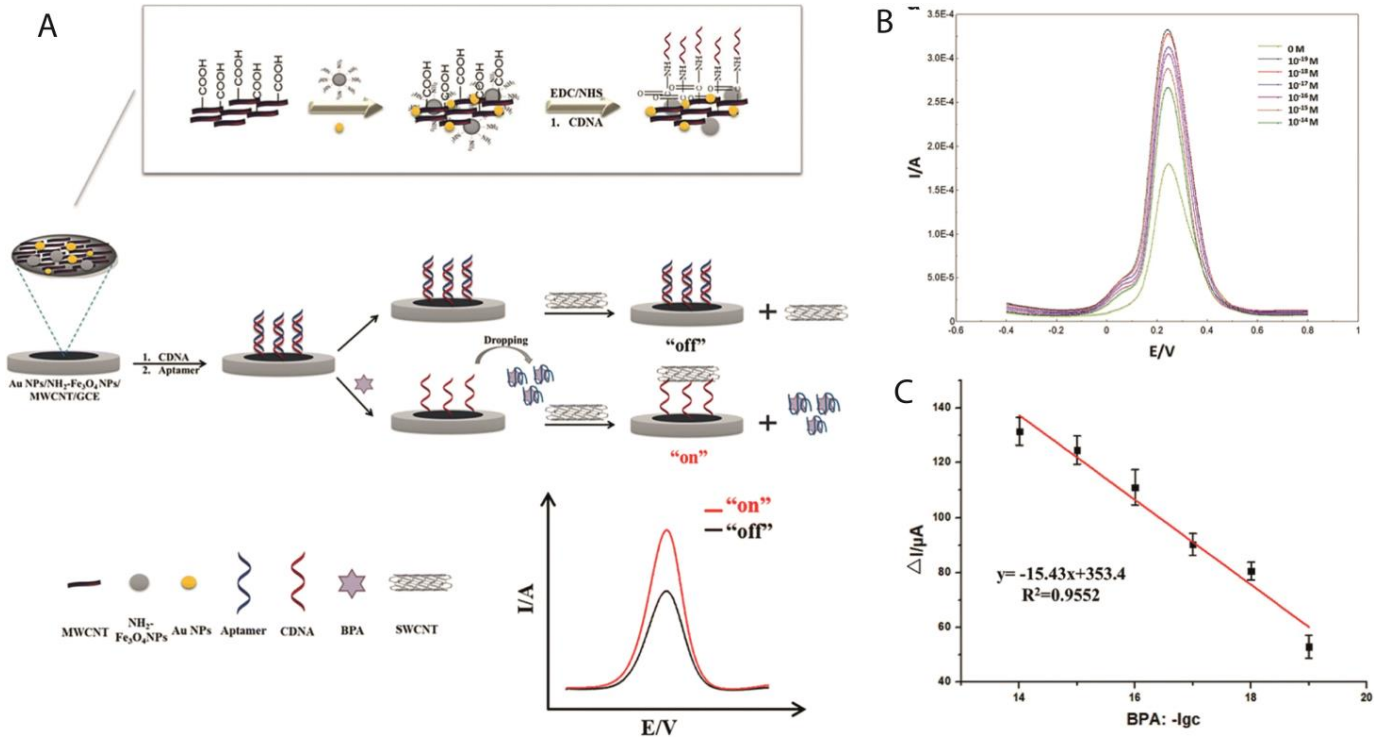

Figure 7. (**A**) Schematic diagram of the fabrication of a "signal-on" sensing model. (**B**) Differential pulse voltammetry responses at different concentrations of BPA (10^{-19} M, 10^{-18} M, 10^{-17} M, 10^{-16} M, 10^{-15} M, 10^{-14} M) in lake water. (**C**) BPA calibration curve in lake water. Reprinted from reference [98] with permission from Springer Nature.

Besides nanomaterials, an interesting signal enhancement mechanism that can be introduced when dealing with aptamers relies on nucleic acid amplification techniques. In

an optical aptasensor developed by Tian et al. [88], the detection of Hg^{2+} was accomplished through a dual recycling amplification strategy (Figure 8). The method utilizes a functional aptamer (DNA 1) harboring Hg^{2+} recognition sites and amplification regions. Additionally, hairpin DNA conjugated to magnetic nanoparticles and a SERS probe comprised of capture DNA and labeling DNA (Rox-DNA) immobilized on gold nanoparticles (AuNPs) were employed. Upon Hg^{2+} addition, the first amplification cycle generates numerous trigger DNA strands. These unfold the hairpin DNA so that a second amplification cycle can start through the capture of SERS probes by the unfolded hairpin DNA. This complex formation triggers the release of more trigger DNA strands through the sequential action of polymerase and endonuclease enzymes. These released strands initiate the formation of additional complexes with hairpin DNA and SERS probes. Magnetic separation of these complexes effectively eliminates background noise caused by excess SERS probes. In this way, a limit of detection (LOD) of 0.11 fM (22 fg/L) was obtained, with a linear detection range of 0.2–125 fM.

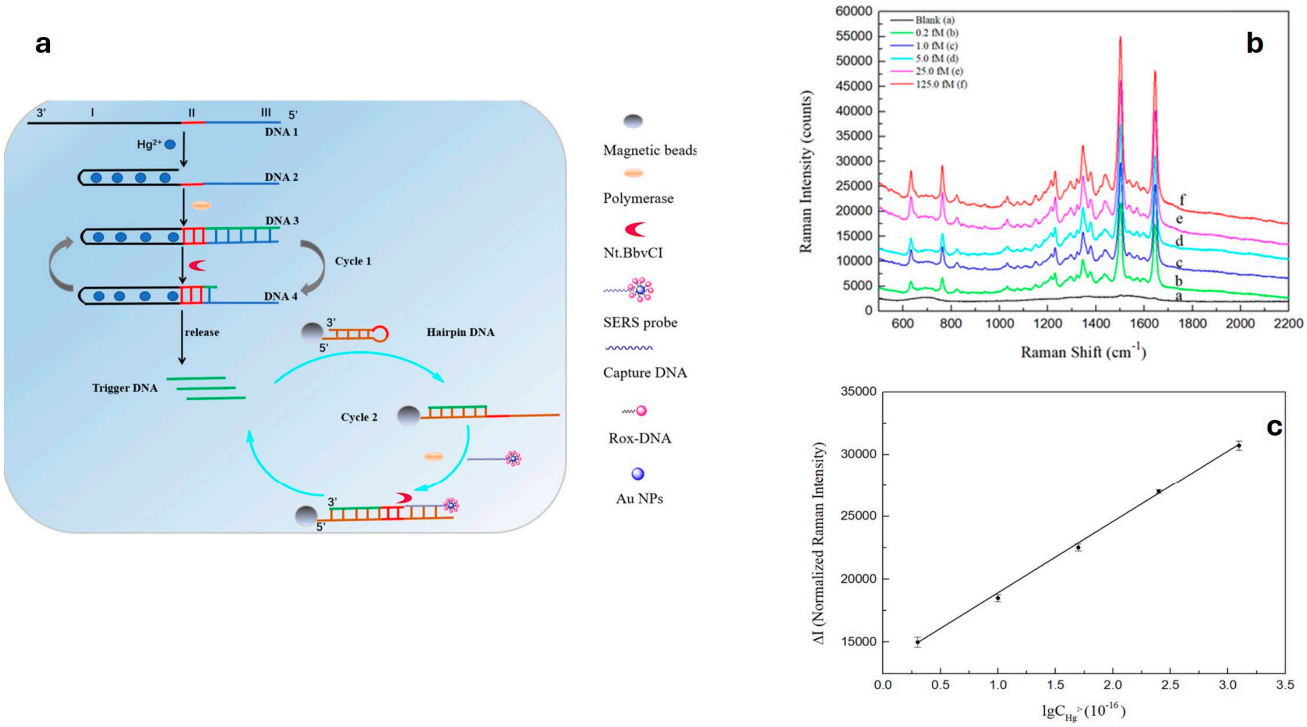

Figure 8. (**a**) Schematic diagram of SERS aptasensor based on dual recycling amplification for trace Hg^{2+} detection; (**b**) SERS spectra under different concentrations of Hg^{2+}; (**c**) linear relationship between Raman intensity and different mercury ion concentrations. Reprinted from reference [88] with permission from Elsevier.

As seen in the first quartiles of Figure 9, the aptasensor configurations can reach levels lower than 1 ng/L, which is sufficiently sensitive for detecting contaminants in real environmental samples. Nine works reported LODs below the ag/L level (Table S1). These ultralow values could be found in environmental water a certain time after the discharge event when the original concentrations had decreased significantly due to spontaneous transformations (biodegradation, adsorption, chemical oxidation, etc.). The highest LOD values reported were in the order of mg/L for metals (2–10 mg/L) (Table S1). These values seem unrealistic in environmental samples unless they can be found at sites of high industrial activity. At this point, it can be concluded that aptasensors could have enough sensitivity to detect contaminants in real environmental water samples. However, further testing on real, unfortified, contaminated samples is needed to determine their feasibility more accurately.

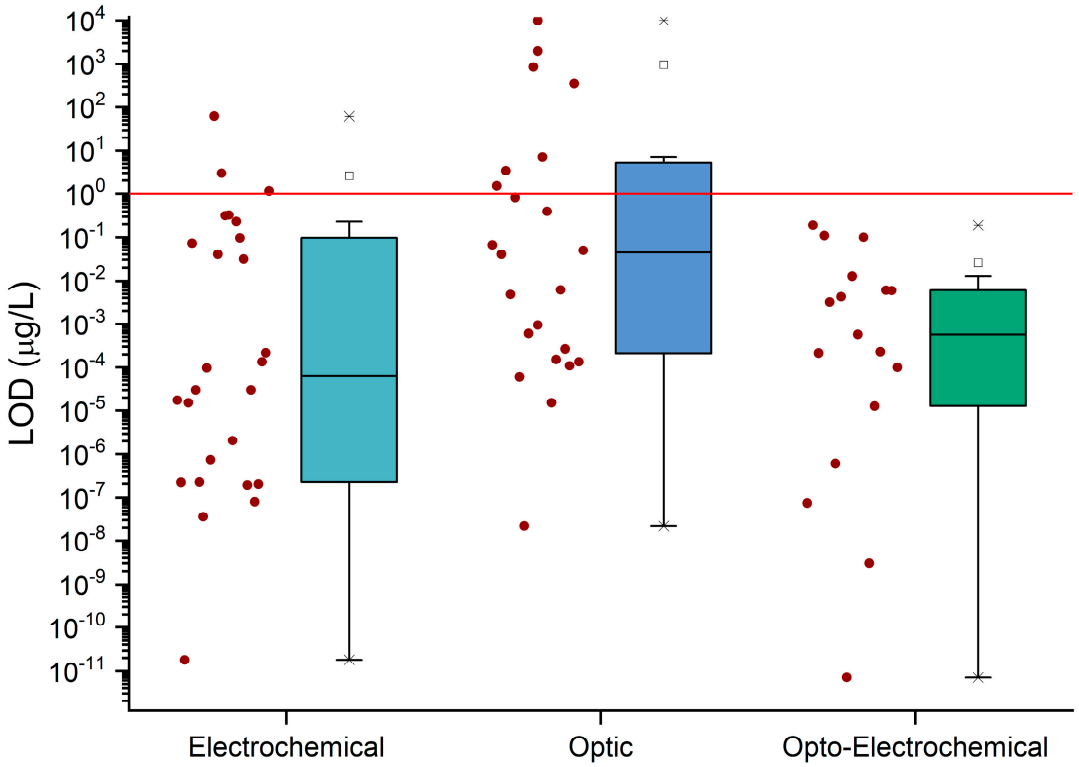

Figure 9. Limits of detection for the different configurations of aptasensors. The red line represents 1 µg/L. The points are the total papers according to the LOD of the aptasensor.

The limit of detection (LOD) analysis demonstrates the exceptional sensitivity of aptasensors for contaminant detection in real environmental water samples, reaching concentrations quite below 1 µg/L (Figure 9). Notably, the median LOD achieved with optical transducer systems was 0.045 µg/L. This sensitivity significantly improved for opto-electrochemical transducers, reaching a median LOD of 0.00056 µg/L. The most impressive performance was observed with electrochemical detection, achieving an ultra-low median LOD of 0.000064 µg/L. These remarkable sensitivities suggest the aptasensors' suitability for real-world environmental monitoring applications where contaminants are often present at trace levels.

3.3.3. Accuracy and Precision

In terms of accuracy and precision, aptasensors showed real application potential when tested in different environmental water matrices, from surface water (river or lake) to effluents from municipal, hospital, and industrial treatment plants. Although in 92% of the cases, the tests were performed with spiked samples, in the remaining 8%, the aptasensors were applied in a real analyte concentration (Table S1). For the spiked samples, the accuracy was measured as recovery (comparison of the added to the measured concentration). In the cases where the natural concentration was measured, the accuracy was obtained by comparing the measured amount with the concentration measured with a reference standard technique, such as high-performance liquid chromatography coupled to mass spectrometry (HPLC-MS) [102,103], inductively coupled plasma (ICP) [104,105], atomic absorption spectroscopy [106] or enzyme-linked immunosorbent assay (ELISA) [107]). Both accuracy and precision were interesting, with recovery values in the 90–110% range, and precision, as measured by the coefficient of variation of the replicates made, was less than 10%.

As an example, Wang et al. [108] reported a detection method for microcystin-LR in spiked water samples from Jinshan Lake using a laser-induced graphene-based electrochemical aptasensor. The accuracy and precision were then compared with the HPLC-MS/MS

technique, observing a correlation between the two methodologies. A good agreement between the results achieved with a photoelectrochemical aptasensor and HPLC were also found by Zhang et al. [109] for atrazine detection in real environmental water samples.

3.3.4. Selectivity

In 71 of the 73 papers analyzed, the selectivity of the method or device was investigated. Selectivity was measured in different ways, for example, by quantifying the response in the presence of a similar chemical compound but in the absence of the analyte of interest; it can also be performed in the presence of the analyte and adding one interferent at the same time, or it can be performed in the presence of the analyte and a mixture of interferents. Many papers (50 out of 71) reported the addition of an interferent with a similar chemical structure to the pollutant tested; the remaining 21 works did the same but also studied the mixture of compounds. Usually, the interferents were added in concentrations up to 100 times higher than the analyte under study. Table 3 shows some examples of studies that examined the selectivity using structurally similar interferents, both in individual and mixed forms.

Table 3. Selectivity and interference assessment of some aptasensors: criteria (ultrahigh) and (individual and mixed with interferents) selectivity.

Aptasensor	Contaminant	Selectivity	% Interference	Reference
Sandwich-like AuNPs/PPy/Ti_3C_2Tx	Pb^{2+}	Individual and mixed interferents	The aptasensor was used to test the response towards eleven other ions; excluding Pb^{2+} and Mix, all other ions caused negligible response changes	[81]
Aptamer linked with AuNPs and Ru@SiO_2-NGQD	Hg^{2+}	Individual and mixed with interferents	Ten different interfering ions. The response caused by individual interfering ions or their mixtures was nearly negligible	[82]
Urchin-like Cu@carbon nanoneedles modified electrode	Hg^{2+}	Individual and mixed with interferents	Each of eight interferents with the concentration of 1 μM produced a negligible signal response compared to that generated by 1 nM Hg^{2+}	[84]
ZIF-8-derived Ag@Au core–shell nanoparticles (Ag@Au/ZIF-8)	Hg^{2+}	Individual interferents with the target	The presence of a 100-fold higher concentration of eight metal ions produced negligible effect on the current response of aptasensor	[87]
CoNi-based metal–organic framework (MOF), $CoxNi_{3-x}$,$(HITP)_2$	Enrofloxacin	Individual and mixed with interferents	No significant response was observed for each individual interferent (thirteen antibiotics, small biomolecules, and harmful ions). In addition, the response with a mix is comparable to that of a pure enrofloxacin solution (104.4%)	[91]
Metal–organic frameworks NH_2-MIL-125(Ti)	Diethylstilbestrol	Individual and mixed with interferents	There was no significant difference between the response of the sensor with diethylstilbestrol and the response of three different interferents or their mixture	[94]

Table 3. *Cont.*

Aptasensor	Contaminant	Selectivity	% Interference	Reference
Nanohybrid of Ag, Ag_2O, Ag_2S, and ultra-thin MoS_2 nanosheet	Bisphenol A	Individual and mixed with interferents	The response with nine interferents showed fluctuations of approximately 2.3–4.8%. When all the interferences were mixed with bisphenol A, the obtained value was 106.28% compared to that of pure bisphenol	[96]
Multi-walled carbon nanotubes (MWCNT), amino-functionalized magnetite, and gold nanoparticles (NH_2-Fe_3O_4/AuNPs)	Bisphenol A	Individual interferents with the target	In the presence of four interferents and bisphenol A, the response is close to that of the bisphenol A alone, with <3% difference in value	[98]
Nanohybrids of Covalent organic framework (COF) and Ce-based metal organic framework (Ce-MOF) (Ce-MOF@COF hybrid nanostructure)	Oxytetracycline	Individual and mixed with interferents	Negligible response variation in the presence of eleven interferents (some ions, biomolecules, and antibiotics), except for oxytetracycline	[101]
Graphene oxide (GO)	Tetracycline	Individual and mixed with interferents	The system responded only to tetracycline, whereas other analogs (eight antibiotics) did not produce significant signal changes	[110]

As reported in Table 3, Salandari-Jolge et al. [87] observed no effects (<5%) on the current response of the aptasensor for the detection of Hg^{2+} even in presence of a 100-fold higher concentration of other metal ions. Working with another aptasensor configuration, Xu et al. [100] developed a fluorescent aptasensor based on graphene oxide for tetracycline detection. The selectivity towards tetracycline was tested in the presence of other chemically related compounds, such as doxycycline, chlortetracycline, minocycline, demeclocycline, lymecycline, methacycline, sarecycline, and their mixture. Significant signals were only obtained when in the presence of tetracycline, except for a low response with oxytetracycline due to the dramatic homologue structures between the two molecules.

Lin et al. (2023) [89] developed a rapid lateral flow assay based on aptamers for the simultaneous detection of ampicillin (AMP) and kanamycin (KAN) utilizing G-quadruplex fragments as an internal standard to achieve high assay selectivity (Figure 10). The latter was demonstrated by testing it with various non-target antibiotics (streptomycin sulfate, oxytetracycline hydrochloride, etc.). In the presence of these antibiotics, there was no significant signal change on the AMP and KAM lines, confirming that the aptamers specifically bind only to the target antibiotics. The method proposed successfully detected antibiotics in water samples from diverse sources, including hospital wastewater, chicken farm wastewater, tap water, and aquaculture water.

The reported studies exhibited excellent selectivity in most cases, with interference values below 10%. Notably, the use of environmental water samples did not significantly impact analyte quantification, suggesting a tolerance for potential natural interferents. However, it is crucial to acknowledge that these findings may not translate directly to real-world scenarios. Environmental water matrices are inherently complex, often harboring mixtures of pollutants. Even minimal cross-reactivity with common ions, organic compounds, or a confluence of changing physicochemical and environmental conditions can lead to inaccurate readings or false positives. Therefore, while the current research suggests adequate selectivity, further optimization in this area remains paramount for reliable on-site water quality monitoring applications. Developing aptasensors with high

and unequivocal target selectivity is essential to ensure the accuracy and robustness of these analytical tools in complex environmental matrices.

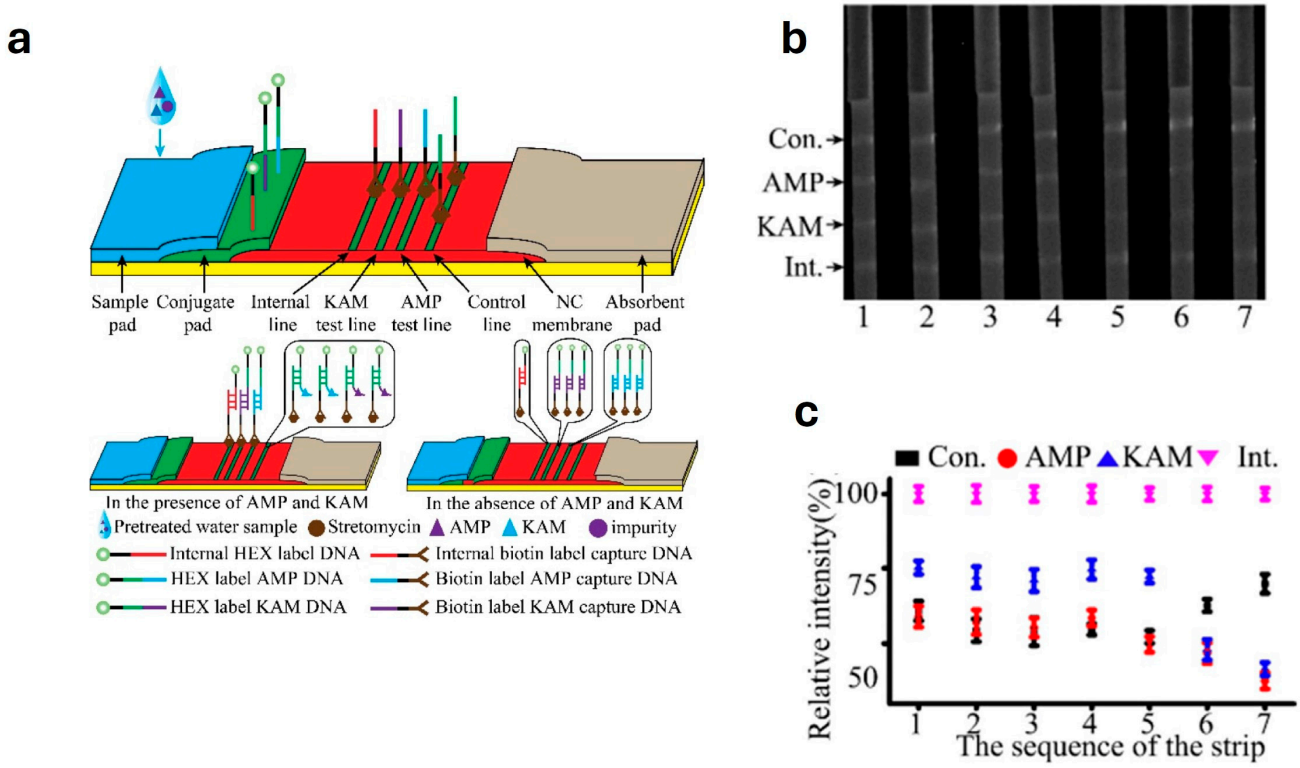

Figure 10. (**a**) Schematic of lateral flow assay for simulation detection of kanamycin and ampicillin. (**b**) Fluorescent images for selectivity analysis and (**c**) its corresponding intensities. The concentrations of KAM and AMP on strip 6 were 30 ng/L, and the concentrations of KAM and AMP on strip 7 were 80 ng/L, respectively. The concentrations of other interfering antibiotics (1, 2, 3, 4, and 5) were 80 ng/L. Con. and Int. represent the control line and internal line, respectively. Reprinted from ref. [89] under the terms and conditions of the Creative Commons Attribution license (http://creativecommons.org/licenses/by/4.0/) accessed on 10 March 2024.

3.3.5. Stability

An important performance criterion in environmental monitoring is the stability of the method or device. In 43 papers, stability studies were reported (Table S1). The stability reported was mainly storage stability, which is the ability of the device or method to give the same response after being stored in suitable laboratory conditions, such as 4 °C, neutral pH, etc. The results varied in testing time; the most prolonged time reported was 30 days, where the same response was maintained as on day 1 [84,104,111,112]. Some papers discussed other types of stability such as signal stability; in the case of opto-electrochemical aptasensors, the device's response to different cycles of light stimuli in the same test was registered. Reports showed that the photocurrent response almost remained stable after 20 cycles [79,94], 7 cycles [113], 12 cycles [83,85] and 50 scanning cycles [84] under light off-on irradiation. An additional type of stability is given by considering the reusability or regeneration of the device. Liu et al. [84] reported an electrochemical aptasensor for Hg^{2+} detection consisting of a gold electrode modified with Cu@carbon nanoneedles, in situ constructed through a controllable pyrolysis process of melamine and $CuCl_2$. The principle of detection involved an exonuclease-III-assisted cycling amplification strategy. To regenerate the aptasensor, the modified electrode was immersed in distilled water for 10 min at 80 °C to dissociate the DNA-based signal-reporting structure, rinsed with buffer and subjected to another reading cycle. The stability was measured through 30 cycles and the signal response remained almost unchanged.

In the work of Yildirim-Tirgil et al. [112], a biosensor-containing probe-DNA immobilized on functionalized SWCNTs for oxytetracycline (OTC) detection was developed. The protocol involved an initial incubation step where OTC was exposed to its specific aptamer for 3 min. Following the completion of this binding phase, the incubated mixture was injected across the surface of a gold chip. This facilitated the interaction of any remaining free aptamers with their complementary immobilized DNA counterparts on the semiconducting surface. The sensing surface could be regenerated for upwards of 20 cycles while maintaining minimal signal loss (less than 15%). This regeneration process was achieved through a simple washing step with a 0.5% SDS solution for 5 min, followed by a rinsing step with a buffer solution at pH 7.2. The reusability of this sensor was attributed to the precise control of assembly parameters during the aptasensor fabrication process, which ultimately led to the creation of a stable system.

In a separate study, Song et al. [96] developed electrochemical aptasensors using bimetallic AgMo heteronanostructures to detect bisphenol A (BPA). To demonstrate the reusability of the sensor, after each BPA measurement, the aptasensor was rinsed with 1 mM NaOH at room temperature for 5 min. This step disrupted the bond between the aptamer (recognition molecule) and BPA. The sensor was then rinsed with a large volume of phosphate buffer solution, allowing the aptamer to return to its original shape. Finally, the electrode was dipped into a fresh BPA solution for the next detection cycle. Notably, the sensor's response signal showed minimal variation even after seven cycles.

While aptasensors have shown promising stability in controlled environments, their suitability for commercial applications, particularly in pollution monitoring, requires further investigation. Environmental monitoring demands frequent and geographically dispersed measurements, making reusability crucial for cost-effective implementation. In-depth studies incorporating cost–benefit analyses are necessary to determine the optimal number of reuse cycles that balance sensor performance with economic viability. This will help establish whether aptasensors can offer a cost-competitive and sustainable solution for environmental monitoring.

3.3.6. Scalability

All the inherent advantages of aptasensors position them favorably for the design of user-friendly and portable devices for in-field analyses. Indeed, (micro)fluidic approaches have gained wide interest as a tool in the automation of sample collection and handling, allowing for on-line and continuous measurements [114,115]. New smartphone-assisted platforms or other compact analyzers based on colorimetric and electrochemical readouts have been introduced in recent years [116,117]. C. Xu and co-workers [118], for instance, replaced the common microplate reader used for optical readouts with the camera of a smartphone for the detection of acetamiprid. J. Wei et al. [80] developed a sunlight-driven self-powered portable system based on a digital multimeter and aptamers for the on-site detection of microcystin-arginine-arginine. Unfortunately, only very few works have exploited their advantages and scalability for real-time decentralized monitoring of contaminants; thus, the traditional laboratory-based procedure remains the most effective approach.

4. Conclusions

The detection of environmental contaminants in water bodies is becoming increasingly imperative. Thus, detection methodologies capable of rapidly detecting such contaminants for screening purposes have been studied and developed in the last decade. Among those, aptasensors, namely biosensors that rely on aptamers as biorecognition elements, have received great attention. This systematic review provides an in-depth analysis of the trends in the use of aptasensors for the detection of contaminants in environmental water samples. All scientific papers on this topic, published from 2019 to 2023, were identified, screened, and evaluated according to precise inclusion criteria. A total of 73 studies passed the phase of eligibility and were further analyzed and categorized based on the environmental contaminant(s) examined, transduction system employed,

sensitivity, accuracy and precision, selectivity, and stability achieved. A total of 29 aqueous contaminants were investigated, including pesticides, metals, industrial chemicals, toxins, and pharmaceutical compounds, with the latter being the most studied.

Most of the works focused on optical transducers; nevertheless, electrochemical transducers showed lower limits of detection overall. Aptasensors have demonstrated recoveries of 90–110% in the detection of environmental contaminants in spiked and real environmental water samples. Stability—considered either as the reusability of the device or the ability to provide comparable outputs upon long storage times—was evaluated by fewer works among those under analysis. Although promising, the results cannot ensure proper stability for commercial applications over long and continuous monitoring periods.

On balance, aptasensors have proven to be a valuable and cost-effective tool in the detection of environmental contaminants of high concern in water bodies. Indeed, thanks to their versatility and ease of synthesis, which overcome ethical problems linked to the more widely used antibodies, aptamers might encounter increasing demand in the future over their protein counterparts. Nonetheless, considering that most of the works herein reported analyzed the analytes in buffered solutions or spiked samples, further investigations focused on real contaminated samples over long-term monitoring are required to better assess their strengths and limits.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/chemosensors12040059/s1, Table S1: Studies included through systematic review. Table S2: SELEX variants and purposes employing different technologies. References [119–167] are cited in the supplementary materials.

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