



## Review

## Public health implications of endocrine disrupting chemicals in drinking water and aquatic food resources in Nigeria: A state-of-the-science review



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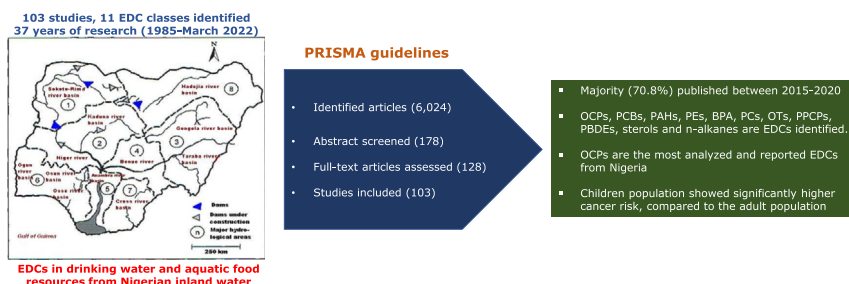
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## HIGHLIGHTS

- A total of 103 studies on EDCs occurrence in drinking water and aquatic food resources from Nigerian inland waters.
- OCPs are the dominant EDC in drinking water and aquatic food resources in Nigeria.
- Carcinogenicity, mutagenicity, and teratogenicity represent the most identified effects.
- Children population showed the highest Targeted Hazard Quotient (THQ) and Cancer Risk (CR).
- Among all EDCs, phthalates ester (PEs) in drinking water showed the highest THQ and CR (1.2) in the children population.

## GRAPHICAL ABSTRACT



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## ABSTRACT

This state-of-the-science review is aimed at identifying the sources, occurrence, and concentrations of EDCs, including potential public health risks associated with drinking water and aquatic food resources from Nigerian inland waters. A total of 6024 articles from scientific databases (PubMed, Scopus, Web of science, ScienceDirect, Google Scholar, and African Journals Online) were identified, out of which, 103 eligible articles were selected for this study. Eleven (11) classes of EDCs (OCPs, PCBs, PBDEs, PAHs, BPA, OTs, PEs, PCs, PPCPs, sterols and n-alkanes) were identified from drinking waters, river sediments and aquatic food species from Nigerian rivers, showing that OCPs were the most studied and reported EDCs. Analytical methods used were HPLC, LC-MS/MS, GC-FID, GC-ECD and GC-MS with all EDCs identified to originate from anthropogenic sources. Carcinogenic, mutagenic, and teratogenic effects were the highest (54.4 %) toxicological effects identified, while reproductive/endocrine disruptive effects (15.2 %) and obesogenic effects (4.3 %) were the least identified toxicological effects. The targeted hazard quotient (THQ) and cancer risk (CR) were generally highest in children, compared to the adult populations, indicating age-specific toxicity. PEs produced the highest THQ (330.3) and CR (1.2) for all the EDCs in drinking water for the children population, suggesting enhanced vulnerability of this population group, compared to the adult population. Due to associated public health, wildlife and environmental risk of EDCs and their increasing concentrations in drinking water and food fish species

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from Nigerian inland waters, there is an urgent need for focused and strategic interventions, sensitization and policy formulation/implementation towards public health and aquatic food safety in Nigeria.

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## 1. Introduction

The release of contaminants of anthropogenic origin into the environment represents serious public health concerns. Endocrine disrupting chemicals (EDCs) are a group of environmental pollutants that interfere with hormone synthesis, metabolism, excretion and functions in exposed organisms (Arukwe and Goksøyr, 2003; Bahamonde et al., 2015). These interactions eventually produce deleterious consequences on reproduction, development, metabolism, physiology, neurobehavioral disorders, other health and disease effects (Colborn et al., 1993; Colborn, 2006). For example, EDCs have been shown to produce effects related to cancers, diabetes, thyroid dysfunction, birth defects, infertility, early onset of puberty in girls, early menopause in women, mortality and morbidity in exposed individuals (Crisp et al., 1998; Hauser and Calafat, 2005; Heindel, 2019; Desvergne et al., 2009; Grün and Blumberg, 2009; Hines et al., 2009).

Accumulating scientific and public health evidence has indicated the occurrence of environmental EDCs as phthalate esters (PEs) (Edjere et al., 2016; Adeogun et al., 2015a; Adeogun et al., 2015b), bisphenol-A (BPA) (Inam et al., 2015; Inam et al., 2019; Makinwa and Uadia, 2017), perfluoroalkyl substances (PFASs) (Sindikú et al., 2013), polychlorinated biphenyls (PCBs) (Ibor et al., 2016; Adeogun et al., 2016a; Adeogun et al., 2016b; Adeogun et al., 2016c; Adewuyi and Adeleye, 2013; Archibong et al., 2017; Unyimadu et al., 2018a; Unyimadu et al., 2018b; Ezemonye, 2005; Iwegbue et al., 2020; Ilechukwu et al., 2018; Bamidele et al., 2020; Irehievie et al., 2020; Benson et al., 2020), polycyclic aromatic hydrocarbons (PAHs) (Benson et al., 2020; Adeogun et al., 2016d; Ibor et al., 2019; Sogbanmu et al., 2020; Sogbanmu et al., 2019; Obiakor et al., 2014; Obanya et al., 2019; Aderinola et al., 2018; Okpashi et al., 2017; Asagbra et al., 2015; Ekere et al., 2019; Olayinka et al., 2018; Inam et al., 2018; Nduka and Orisakwe, 2010; Nwaichi et al., 2020), phenolic compounds (Inam et al., 2015; Inam et al., 2019; Ibor et al., 2016; Adeogun et al., 2016c; Adeogun et al., 2016d; Okpashi et al., 2020; Adebola A and Taiwo K, 2013; Adeogun et al., 2019), organotins (Adeogun et al., 2016c; Adeogun et al., 2019), organochlorine (OCs), organophosphate ester (OPE) pesticides (OPs) (Ibor et al., 2016; Adeogun et al., 2016a; Archibong et al., 2017; Adeogun et al., 2016d; Adeogun

et al., 2019; Ize-Iyamu et al., 2007; Tongo et al., 2019; Ezemonye et al., 2015; Ogbeide et al., 2016a; Ogbeide et al., 2018; Ogbeide et al., 2019; Ogbeide et al., 2016b; Atuma and Eigbe, 1985), pharmaceuticals and personal care products (PPCPs) (Inam et al., 2015; Ebele et al., 2020) in aquatic food resources and inland waters (rivers, lakes, streams) and sediments as a global environmental and health problem, including in Nigeria. However, knowledge gaps exist on the alarming rate of endocrine-related diseases/dysfunction including reproductive problems (birth defects, infertility, low sperm count and motility, early onset of puberty in girls, early menopause in women), developmental disorders (thyroid dysfunction), metabolic problems (obesity and diabetes), hormonal imbalance and cancer burden in many countries, including Nigeria. The remote/apparent cause of increases in endocrine-related diseases in Nigeria have been related to both genetic and environmental factors (Ekanem and Parkin, 2016; Jedy-Agba et al., 2012; Morounke et al., 2017). While genetic contribution has remained relatively unchanged over several decades, the emerging focus is on understanding the extent and role of environmental factors (including contaminants in drinking water and aquatic food resources) on the increasing endocrine-related disease.

For Nigeria as a developing country with limited supply of potable municipal water, majority of the local populations largely depend on potentially contaminated inland water sources for drinking and domestic water supply. These inland and potentially contaminated waters are also significant sources of aquatic food resources (fish, shrimps, prawns, crabs, periwinkles, and oysters) representing significant food safety concerns and public health risk. This is because in many developing countries, including Nigeria, environmental policies and laws are poorly enforced and rapid anthropogenic activities have resulted in the discharge of a wide range of environmental contaminants into inland rivers (Adeogun et al., 2015a; Ibor et al., 2016; Adeogun et al., 2016a). Irrespective of their fate, source or original intended application in consumer products, a high volume of these contaminants ends up in the aquatic environment, bioaccumulate, transport through successive links in the food chain exerting toxicological and physiological effects on humans and wildlife that depend on these water sources for drinking, food resources and sustaining livelihood. Interestingly, this surge may be related to the increasing rate of morbidity and

mortality linked to water-borne contaminants and infectious diseases in Nigeria (Ukpong and Okon, 2013; Udoessien, 2003). Also, there is an overwhelming significant increase in human health problems and burden of diseases in Nigeria (Ekanem and Parkin, 2016; Jedy-Agba et al., 2012; Morouнке et al., 2017); with recent biomonitoring reports indicating that human exposure to EDCs may be significantly higher in Asia and Africa, compared with other parts of the world suggesting that these regions are more vulnerable to health risks (Fång et al., 2015; Stuetz, 2006).

Regional and national concerns over reports on the occurrence of significantly high concentrations of EDCs in many drinking water sources and aquatic food resources have informed several research efforts into the public health risk implications associated with continuous exposure to this group of contaminants (Maigari et al., 2016; Odey et al., 2018). To address the paucity of information on public and environmental health risks resulting from EDCs exposure in developing countries, several efforts have been made to identify the unique challenges facing Africa with specific focus on EDCs exposure and related health effects (Bornman et al., 2017). Other studies on the occurrence, fate and transport of emerging pollutants (Egbuna et al., 2021) and chemical contaminants in marine and freshwater fish in Nigeria exist (Uzomah et al., 2021). However, a focused systematic review addressing effect-based studies including public health risks of EDCs in drinking water and aquatic food resources from Nigerian inland waters is non-existent. Therefore, this systematic review is an integrated effort aimed at critically analyzing published literatures to identify pollution with endocrine-active properties and their sources into drinking waters, potential public health risk associated with consuming contaminated drinking water and aquatic food resources from Nigerian inland waters. Based on these, we have highlighted four (4) research questions that guided our study - i) what are the sources and concentrations of EDCs in drinking water and aquatic food resources from Nigerian inland waters? ii) what are the highest concentrations of individual or group of EDCs in drinking water and aquatic food resources from Nigerian inland Rivers? iii) Does the concentrations of EDCs in drinking water and aquatic food resources constitute potential public health problems and potential disease burden risk to vulnerable populations? (iv) Are EDCs in drinking water and aquatic food resources from Nigerian inland waters implicated in the growing endocrine-related diseases/dysfunction including reproductive, endocrine, and metabolic problems, developmental disorders, hormonal imbalance, genotoxic and cancer burden in Nigeria? These questions are necessary to benchmark important scientific outcomes that will form a technical basis for informed and effective drinking water interventions, sensitization, and policy formulation/implementation towards public health safety in Nigeria based on the United Nations Sustainable Development Goals 14 (life below water).

## 2. Materials and methods

We performed this systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (Moher et al., 2009).

### 2.1. Data sources and search strategy

For this study, we examined only peer-reviewed publications without restriction on the year of publication. Different databases such as PubMed ([www.ncbi.nlm.nih.gov/pubmed](http://www.ncbi.nlm.nih.gov/pubmed)), Scopus ([www.scopus.com](http://www.scopus.com)), Web of science ([www.webofscience.com](http://www.webofscience.com)), ScienceDirect ([www.sciencedirect.com](http://www.sciencedirect.com)), Google Scholar ([www.google.com](http://www.google.com)), African Journals Online ([www.ajol.info](http://www.ajol.info)) were searched. Other relevant Nigerian gray literatures (local and online newspapers and publications) including inaugural lectures, undergraduate and postgraduate thesis, reports from organizations and national environmental agencies which are not published in traditional commercial channels and therefore not indexed in electronic databases were sourced for and important information extracted. Appropriate medical subject headings (MeSH) term and text words in title, abstract and keywords were used in a search that was carried out in two steps. Firstly, individual

MeSH term and text words were searched using the Boolean operators (AND, OR): ('endocrine disrupting chemicals' OR 'EDCs') AND ('water' OR 'aquatic' OR 'marine') AND ('diseases' OR 'health risk') AND ('Nigeria' OR 'Nigerians'). Secondly, the additional sort criteria were applied to obtain more relevant titles and further reading of abstracts and full texts. We further examined all reference lists of the main reviews on EDCs and Public health risks to identify additional papers that have been missed.

### 2.2. Eligibility criteria

Eligible studies focused on all forms of drinking water sources (treated, untreated water, wells, boreholes, rivers, streams, lakes, reservoirs, and river sediment). Further, all aquatic food resources including vertebrates and invertebrates (fin- and shellfish, shrimps, prawns, oysters, periwinkles, crabs, mussels, mollusc, benthos, etc.) from inland waters in Nigeria were considered for the review. The exposure factors included all environmental contaminants listed by WHO, USEPA, Endocrine Society, Food and Agricultural Organization (FAO), United Nations Environmental Program (UNEP), Organization for Economic Co-operation and Development (OECD), European Union-Evaluation, Authorization and Restriction of Chemicals (EU-REACH), that has been listed and characterized as EDCs. The outcome was directed at the public health risk implications, Targeted Hazard Quotient (THQ) and Cancer Risk (CR) for children and adult populations, including endocrine-related disease burden risk (reproductive/metabolic problems, developmental disorders) and all other determinant public health risk factors that constitute risk in Nigeria. There was no limitation on the year of publication, and only studies published in English language were included. Studies that do not fall within these criteria were excluded.

### 2.3. Data synthesis and extraction

For this study, we adopted a quantitative approach for data synthesis. Three (3) independent authors (ORI, PN and DMO) conducted a blind and independent screening of all the literature according to the criteria provided in Section 2.2 above using the EpiData software [v4.6, Odense, Denmark] and/or MS-Excel spreadsheet (see Excel file in Supporting Information: SI-1). The reviewers scanned through all sources identified in the various databases for potentially relevant studies. Secondly, full text of eligible studies was considered for data extraction after duplicate papers have been excluded. After the initial screening of titles and abstracts, we selected 128 studies for full-text review. In case of conflicting decisions during initial screening and discussions, the respective study was included in the full text screening. After the full-text screening, we excluded 25 publications based on the above criteria (see Section 2.2) and categorized the remaining 103 studies into three (3) groups, namely - Surface water, River sediments and aquatic food resources and then used them for the study (Fig. 1). The study characteristics extracted information on the possible human health effects of EDCs in drinking water and aquatic food resources, type of EDC, aquatic food resource, drinking water source, known or potential pollution source, title of study, aim/objective of the study, methods of the study (e.g. data sources, study design, chemical and bio-analytical methods used, type of publication, publication year, study duration, study settings, inclusion and exclusion criteria of the study) (see Excel file in Supporting Information SI-1).

### 2.4. Concentration of EDCs

We extracted the published data on EDCs concentrations in the environmental matrices (water, river sediment and aquatic food resources) by study. To compare EDCs concentrations between studies, we converted all the tissues and sediment concentrations so that they were expressed as  $\mu\text{g/g}$ , while EDC concentrations in drinking water were expressed as  $\mu\text{g/L}$  (SI Tables 1–8). EDCs concentrations were included when the mean  $\pm$  standard deviation (SD) from each study were reported or could be derived. For studies that did not report the mean and SD, but provided the median, maximum and minimum range, and sample size, we used the method of Hozo et al. (2005) to estimate the mean and SD. For the meta-analysis,

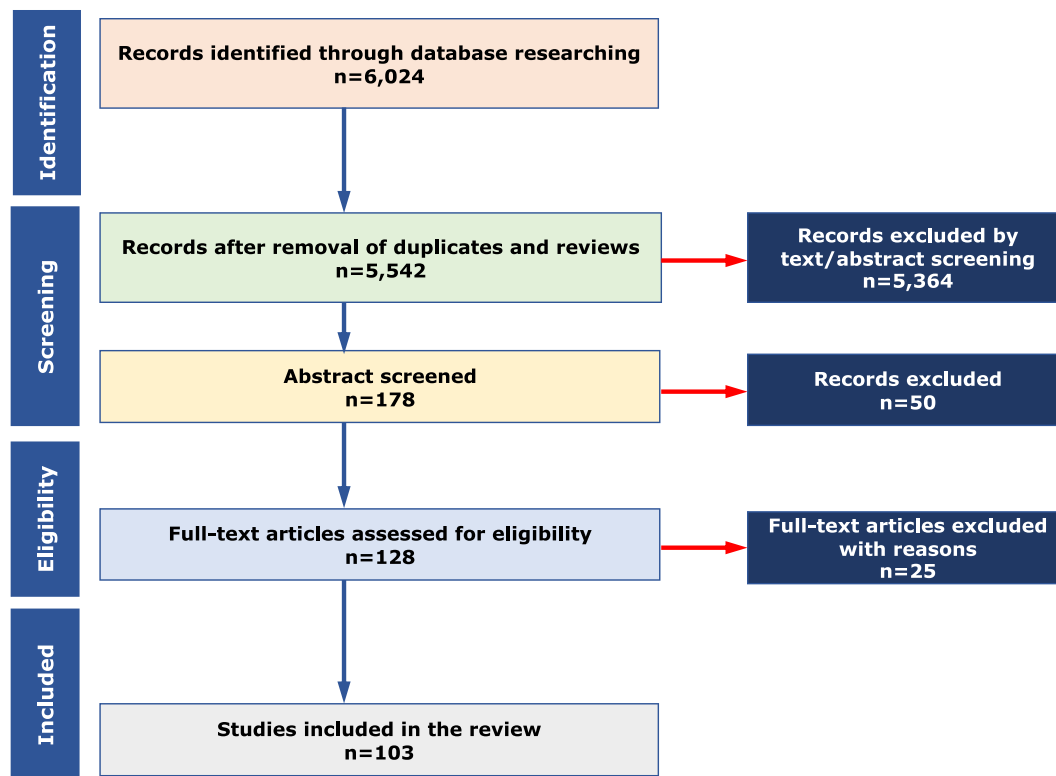


Fig. 1. PRISMA flow diagram of selection and inclusion of articles for the study. Modified from Moher et al. (2009).

we excluded studies that did not report mean, range, SD, SE, and sample size. We compared means and SD for each EDC concentrations in water, river sediments and aquatic food resources and reported the highest level for each. The percentage (%) trends and methods of EDC publications and analysis were also computed and reported, while biological effects identified, implied, or demonstrated were also computed and reported in percentage (%). The Joanna Briggs Institute's critical appraisal tool for cohort research study was used to assess the methodological quality of all publications included in this study, including the extent to which the primary studies have addressed the possibility of bias in its design (Ouzzani et al., 2016).

## 2.5. Data analysis

We performed a descriptive analysis and statistical synthesis of quantitative data that were extracted from eligible literature on EDCs in drinking water and aquatic food resources from Nigerian inland waters showing the trend and concentrations, including their potential public health risk. THQ for humans (adult and child population) drinking hazardous EDCs contaminated water and eating contaminated aquatic food resources from Nigerian inland waters was calculated using the USEPA and WHO statistical models (USEPA, 1989). All data analysis (descriptive charts, percentages, visualized tables, and narrative summaries) was performed using the GraphPad Prism 7.0 (GraphPad Software, San Diego, CA) and OriginPro® 2022 version.

### 2.5.1. Public health risk assessment

**2.5.1.1. Estimated average daily intake (EADI).** The EADI (Eq. (1)) was computed by multiplying the mean residual EDC concentration by the estimated water or fish consumption rate (L/day).

$$\text{EADI (mg/kg/day)} = \text{Residual concentration} \times \text{water consumption/body weight (bw)} \quad (1)$$

where: Residual concentration is the concentration of specific EDC type in water or fish sample ( $\mu\text{g/L}$  or  $\mu\text{g/g}$ ), a conservative ingestion rate of water

per day was estimated to be 1 L for a 10 kg child and 2 L for adult (Calabrese, 1992), with body weight set at 70 kg for adult population (Fianko et al., 2011). The EADI was compared to the reference dose (RfD) which represents the threshold exposure below which it may be unlikely for sensitive populations to experience adverse health effects (USEPA, 1989). RfD is a term used in evaluation of risk of toxic effects for various 145 chemicals on humans and RfD is defined by USEPA as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

### 2.5.2. Target hazard quotient (THQ)

THQ represent the ratio of the EADI (mg/kg/bw/day) of a chemical (e.g. EDC) to a reference dose (RfD, mg/kg/day) and defined as the maximum tolerable daily intake (MTDI) of a specific EDC that does not result to deleterious health effects (Eq. (2)) (USEPA, 1989):

$$\text{THQ} = \text{EADI}/\text{RfD} \quad (2)$$

THQ value equal or above 1 (i.e.  $\text{THQ} \geq 1$ ) indicates that in the exposed population, the consumption of contaminated water or fish is likely to produce obvious deleterious effects. An increase in THQ value, parallels the increase in the probability of hazard risk on human health.

### 2.5.3. Cancer risk assessment model

The carcinogenic risk for children and adult population drinking EDCs contaminated water and consuming aquatic food fish species was determined using deterministic and probabilistic methods (Nwaneshiudu et al., 2007; Singh and Agarwal, 2018a). The highest concentration of each contaminant was used to estimate the exposure dose/chronic daily intake rates for the Nigeria population using Eq. (2):

$$\text{Chronic daily intake (CDI, in mg/kg-day)} = \frac{\text{CF} \times \text{IR} \times \text{FI} \times \text{EF} \times \text{ED}}{\text{BW} \times \text{AT}} \quad (3)$$

where CF = concentration of contaminant in water or food (mg/L; mg/kg), IR = ingestion rate of water or fish for children (100 g/day) and adult (200 g/day), FI = fraction of ingested food assumed to be 0.4 (Nwaneshiudu et al., 2007), EF = exposure frequency (365 meals/year), as stipulated by the EPA, ED = exposure duration (6 years for children and 30 years for adults), BW = body weight (10 kg for children and 70 kg for adult) and AT = average time (25,550 days or 70 years). The generated data of the CDI from the deterministic and probabilistic risk analysis approaches were then used to calculate cancer risk (CR) using Eq. (4):

$$CR = CDI \times SF \quad (4)$$

where, CR = calculated cancer risk for water and fish. CDI = chronic intake (mg/kg/day and mg/L/day) and SF = slope factor 7.3 (mg/kg/day and mg/L/day) as provided by the USEPA Integrated Risk Information System.

### 3. Results

#### 3.1. Overview, trends, and methods of EDC publications and analysis

The percentage number of EDC studies per year in Nigeria is shown in Fig. 2A. Out of the 103 publications describing EDC contamination in drinking water sources and aquatic food fish species from Nigeria, majority (70.8 % or  $n = 73$ ) were published between 2015 and 2020 (Fig. 2A). OCPs concentration from Warri River was the first reported EDC publication in Nigerian aquatic environment (Fig. 2A). A total of 11 EDCs were identified from Nigerian inland rivers and aquatic food resources ranging from OCPs,

PCBs, PAHs, PEs, BPA, PCs, OTs, PPCPs, PBDEs, sterols and n-alkanes. Similarly, OCPs were the most analyzed, studied and reported EDCs from Nigeria aquatic and food fish species constituting 25 % ( $n = 26$ ), followed by PCBs (24.1 %;  $n = 25$ ) and PAHs (21.3 %;  $n = 22$ ), while sterols, n-alkanes and PBDEs were the least studied EDCs constituting only 1 % each (Fig. 2B). Studies analyzing EDC concentrations in Nigeria used different analytical methods ranging from LC-MS/MS, HPLC, GC-FID, GC-ECD and GC-MS. Overall, GC-MS (42.7 %) was the most used analytical method for EDC analysis in Nigeria, followed by GC-ECD (27.1 %), while LC-MS/MS (1.9 %) was the least applied method (Fig. 2C). A total of about 54 different aquatic food resources consisting of fish, prawns, crabs, molluscs and benthos have been used to evaluate EDC concentrations in Nigeria with *Chrysichthys nigrodigitatus*, *Clarias gariepinus* and *Tilapia* species as the most frequently used fish for EDC studies in Nigeria (SI Table 9). No studies are available on the concentrations of PBDEs, OTs, PPCPs, sterols and n-alkanes in aquatic food resources from Nigeria.

#### 3.2. Concentration of EDCs in drinking water, river sediments and aquatic food resources

All data on EDC concentrations in different environmental matrices (water, sediments, and aquatic food resources) is presented in SI Table 1–8 and were mostly from wildlife. The highest BPA concentration in Nigeria was recorded in sediment ( $66.6 \pm 1.6 \mu\text{g/g}$ ) and water ( $63.6 \pm 6.7 \mu\text{g/L}$ ) samples from the Calabar River, while *C. gariepinus* from rivers and lagoons in Southwest Nigeria had the highest BPA concentrations  $2.7 \pm 0.9 \mu\text{g/g}$  (Fig. 3A). Ori stream in Iwo and Ogun River had the highest

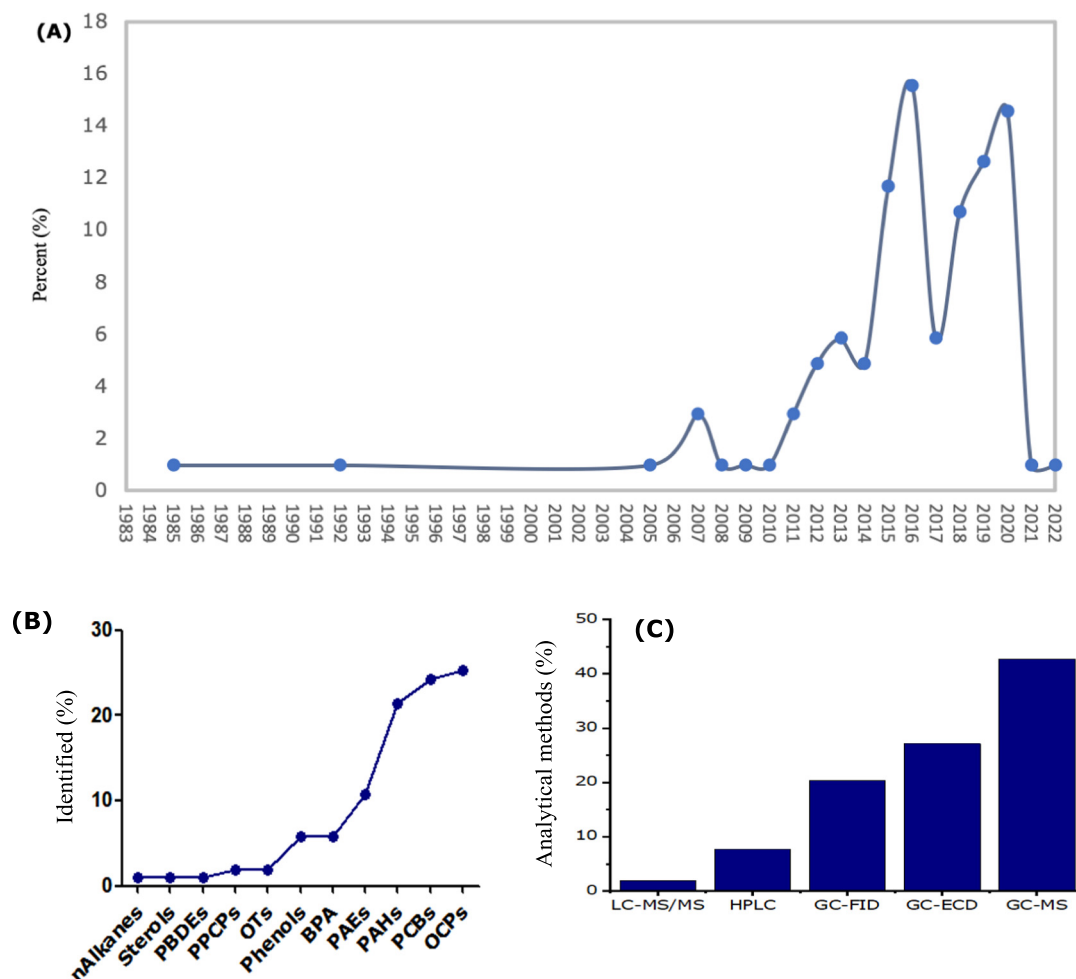
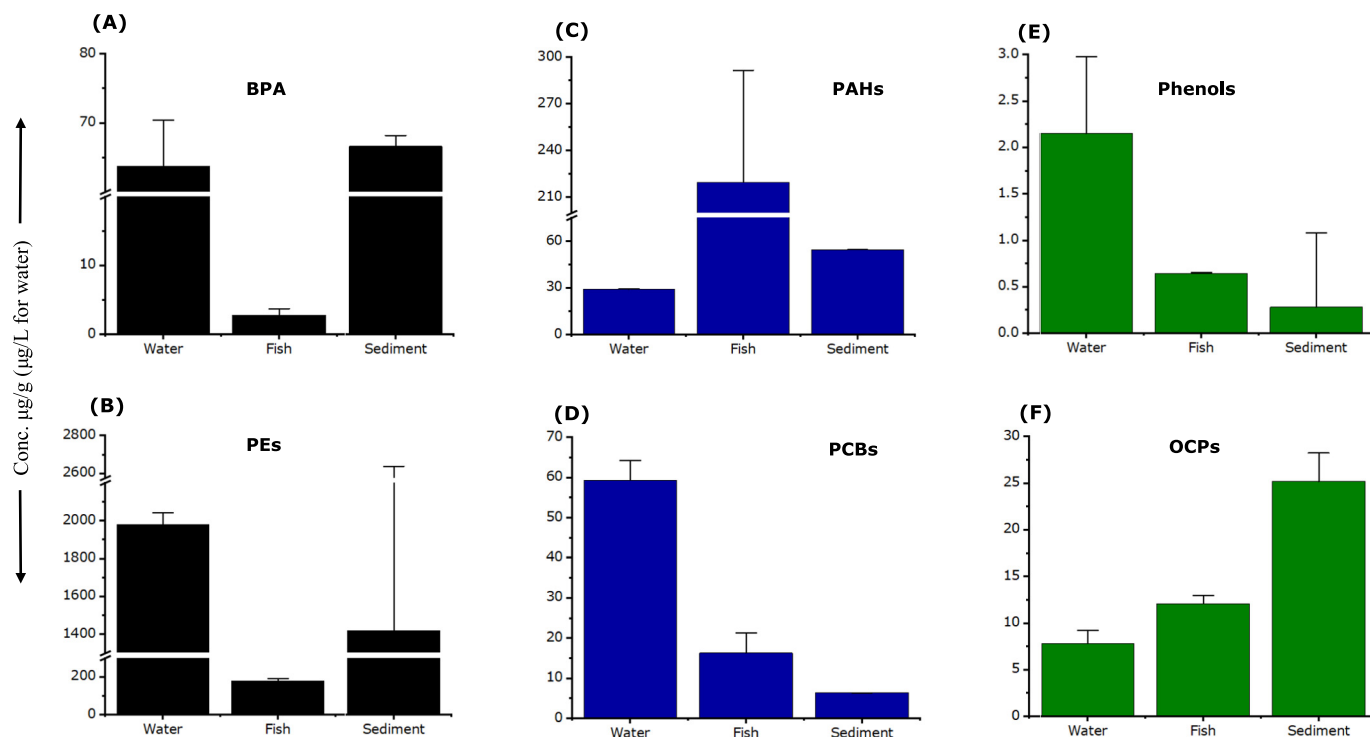


Fig. 2. Trend (A) identified (B) and analytical methods (C) used for evaluating endocrine disrupting chemicals (EDCs) in water, river sediments and aquatic food resources from Nigerian inland waters. Data are given as percentage (%) in all variables.



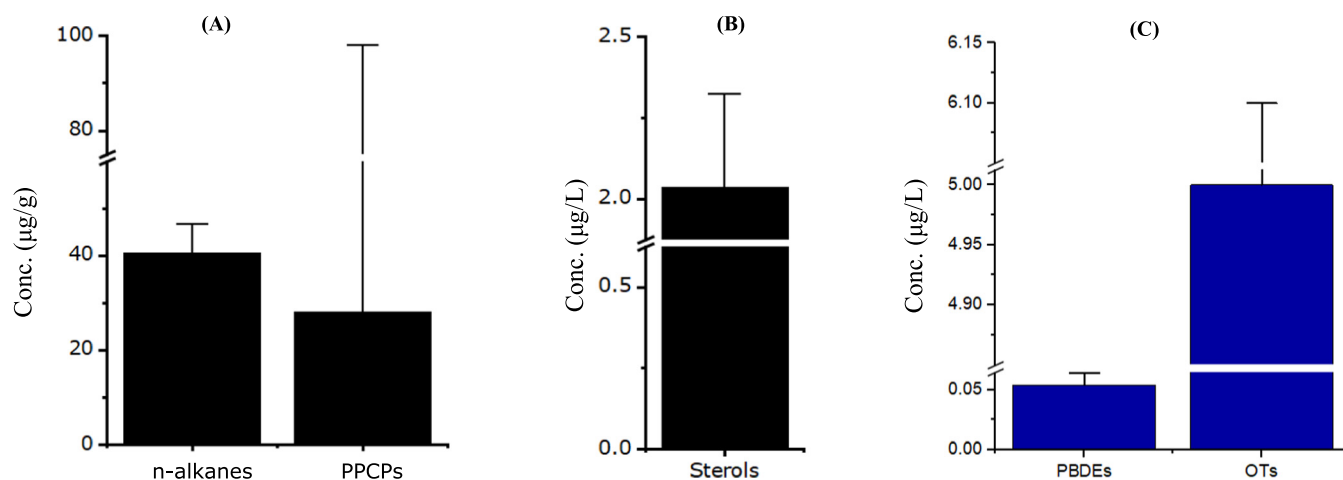
**Fig. 3.** Highest concentration of endocrine disrupting chemicals reported in water ( $\mu\text{g/L}$ ), River sediments and aquatic food resources ( $\mu\text{g/g}$ ) from Nigerian inland waters. (A) bisphenol-A (BPA), (B) phthalate esters (PEs), (C) polyaromatic hydrocarbons (PAHs), (D) polychlorinated biphenyls (PCBs), (E) Phenolic compounds, and (F) organochlorine pesticides (OCPs).

PEs concentrations in water and sediments ( $1980.0 \pm 62.0 \mu\text{g/L}$  and  $1420.0 \pm 1216.2 \mu\text{g/g}$ , respectively), while *Cyprinus carpio* from Ona River had the highest PEs ( $178.1 \pm 12.2 \mu\text{g/g}$ ) concentration in fish (Fig. 3B). For PAHs, Qua Iboe River ( $29.1 \pm 0.3 \mu\text{g/L}$ ) and Lagos lagoon ( $54.6 \pm 71.9 \mu\text{g/g}$ ) had the highest concentrations in water and sediments, respectively, while the brackish water prawn (*Macrobrachium macrobrachium*) from the Badagry Creek had the highest PAHs concentration for aquatic food resources (Fig. 3C). PCBs concentrations were highest in Eleyele Lake ( $59.3 \pm 4.9 \mu\text{g/L}$ ) water and Lagos lagoon sediments ( $6.41 \pm 0.0 \mu\text{g/L}$ ), while *C. nigrodigitatus* from the Lagos lagoon ( $16.3 \pm 5.0 \mu\text{g/g}$ ) had the highest PCBs concentrations (Fig. 3D). Phenolic compounds were highest in Calabar River ( $2.2 \pm 0.8 \mu\text{g/L}$ ) and Lagos lagoon sediments ( $0.3 \pm 0.8 \mu\text{g/g}$ ), while *C. nigrodigitatus* from Lagos lagoon showed the highest concentrations of phenolic compounds in food fish species from Nigeria

(Fig. 3E). For OCPs, Owena River ( $7.8 \pm 1.4 \mu\text{g/L}$ ) and Ondo River ( $25.2 \pm 3.1 \mu\text{g/g}$ ) had the highest concentrations in water and sediment, respectively. While *C. nigrodigitatus* from Warri River ( $12.1 \pm 0.9 \mu\text{g/g}$ ) had the highest OCPs concentration in Nigeria (Fig. 3F). The levels of n-alkanes, PPCPs and sterols were only reported in sediment samples showing the highest concentrations of  $40.7 \pm 6.0$ ,  $2.0 \pm 0.3$ , and  $28.2 \pm 69.9 \mu\text{g/g}$  from Great Kwa River, Calabar river and Ikpa river basin, respectively (Fig. 4A and B). The Lagos lagoon sediments had the highest concentrations of PBDEs and OTs at  $0.05 \pm 0.0$  and  $5.0 \pm 1.1 \mu\text{g/g}$ , respectively (Fig. 4C).

### 3.3. Sources, biological and public health risk

Industrial, agricultural, and domestic activities were the three (3) sources of EDCs into drinking water and aquatic food resources



**Fig. 4.** Highest concentration of (A): n-alkanes and pharmaceuticals and personal care products (PPCPs), (B): sterols, and (C): polybrominated diphenyl ethers (PBDEs) and organotin (OTs).

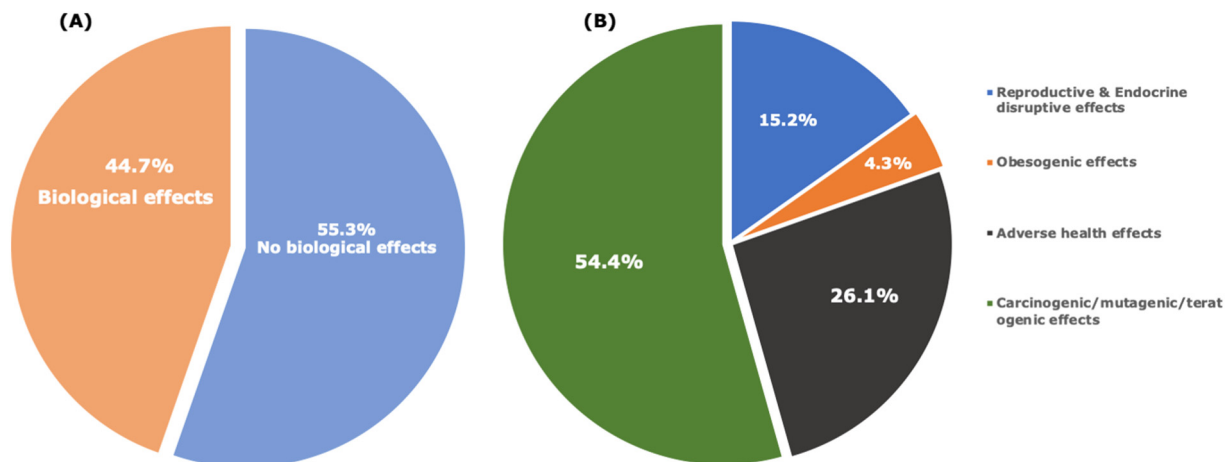


Fig. 5. Percentage (%) biological effects related to endocrine disrupting chemicals (EDCs) in Nigeria (A and B).

from inland rivers. Out of the 103 publications reviewed in this study, only 44.7 % indicated biological effects in humans and wildlife (Fig. 5A). Recorded biological effects included - reproductive and endocrine disruptive effects, such as modulations in vitellogenin expression, hormonal alterations, intersex (ovo-testis) and other hepato-, gonadohistopathological changes, obesogenic effects, such as activation of lipids and glucose metabolism signaling pathways, adverse health effects and carcinogenic, mutagenic, and teratogenic effects (Fig. 5B). Carcinogenic, mutagenic, and teratogenic effects were the highest toxicological effects identified, constituting 54.4 %, followed by adverse health effects (26.1 %), while reproductive/endocrine disruptive effects and obesogenic effects were the least identified biological effects - constituting 15.2 and 4.3 %, respectively, (Fig. 5B).

### 3.4. Public health risk exposure assessment

The public health exposure risk resulting from EDCs consumption in drinking water and contaminated food fish species for the different categories (children and adults) of Nigerian populations was modeled using the deterministic and probabilistic methods, showing higher THQ and cancer risk in children, compared to the adult population (Fig. 6). OCPs (2.2), PAHs (8.1), PCBs (16.5) and PEs (330.3) produced the highest THQ values in children population, while only PAHs (2.3), PCBs (4.7) and PEs (95.6) showed THQ for the adult population drinking EDC contaminated waters (Fig. 6A and B). PEs produced the highest THQ for all EDCs in drinking water, evaluated for both children and adult population in Nigeria (Fig. 6B). No THQ was recorded in both children and adult populations

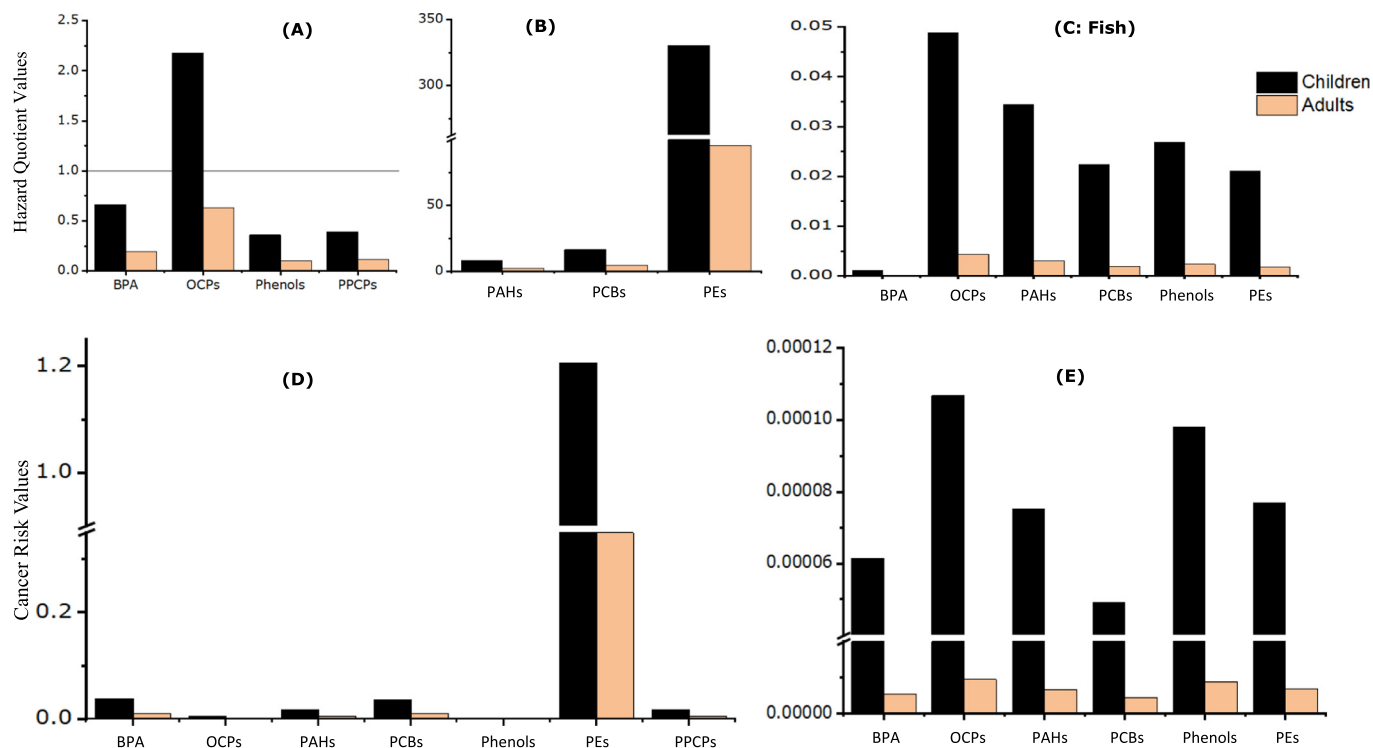


Fig. 6. Targeted hazard quotient (THQ: A-C) and cancer risk (CR: E-F) in children and adults population consuming endocrine disrupting chemicals (EDCs) contaminated drinking water and aquatic food resources in Nigeria.

eating EDCs contaminated aquatic food resources in Nigerian (Fig. 6C). Generally, children population showed significantly higher cancer risk, compared to the adult population, with PEs (1.2) in water and OCPs (0.00011) in food fish, constituting the highest cancer risk in the children population (Fig. 6D and E).

#### 4. Discussion, conclusions, and recommendations

As a developing country, Nigeria lacks national or regional guidelines or regulations on EDCs. Overall, the present review targeted to provide evidenced-based data that will help inform environmental regulations and policies on EDCs in Nigeria. A recent call for action on EDCs in Africa was made during the first endocrine society meeting in South Africa 2017. Thus, our review represents a rapid response arising from the South African meeting. The National Environmental Standards and Regulatory Enforcements Agency (NESREA) is the Nigerian agency responsible for regulating national environmental problems and the body currently lacks research capacity, infrastructures, funding, and support necessary to perform comprehensive EDCs studies that could provide the scientific basis to inform environmental policies. The inability of developing countries such as Nigeria to enforce environmental policies, regulations and laws, including lack of drinking water quality framework has resulted to an increasing release of contaminants into the environment with corresponding adverse effects on public health and wildlife (Adeogun et al., 2016a). Environmental contaminant projections have indicated a paradigm shift in global chemical production and consumption by 2020 to respective 31 and 33 %, in developing countries (Gore et al., 2015), with increased likelihood for humans and wildlife exposures (Bergman et al., 2013). While 28 % of disease burden in Africa has been linked to environmental pollution, poverty, poor sanitation and hygiene (WHO, 2015). Pollutants monitoring programs has indicated that exposure to some chemical contaminants with endocrine disrupting effects maybe higher in African and Asia, compared with other parts of the world, suggesting significant higher risks in these populations (Fång et al., 2015; Stuetz, 2006). For example, the number of obese and overweight children (metabolic effects) in Africa has increased from 5.4 to 10.3 million over the past 24 years (Group, 2017), and about 100,000 annual new cancer cases are diagnosed in Nigeria (Ekanem and Parkin, 2016; Jedy-Agba et al., 2012; Morounke et al., 2017). Environmental pollution and climate change, lifestyle, feeding habit and genetic history has been identified as major contributing factors to these illnesses (Morounke et al., 2017). Other epidemiological reports have suggested that the presence of elevated levels of these groups of environmental contaminants have paralleled the growing rate of several non-communicable diseases, reproductive, endocrine and metabolic problems (obesity and diabetes), hormonal imbalance, including cancer burden in Nigeria (Ekanem and Parkin, 2016; Jedy-Agba et al., 2012; Morounke et al., 2017; Orisakwe, 2021).

Reports on the occurrence, distribution, and concentrations of EDCs in drinking water sources and aquatic food fish species from Nigeria are eminent. There is no systematic plan, actions, or policy towards effective control, prevention, mitigation, and management in Nigeria. Given the potential adverse public health, wildlife, biodiversity, and ecosystem effects of these group of contaminants, we have presented a holistic, coordinated comprehensive meta-analytical approach on the state of the science on EDCs in Nigeria. This is targeted at developing a scientific and technical basis for sustainable environmental policy formulations and enforcements towards public health intervention, wildlife safety and environmental management. We have identified the occurrence of significantly high concentrations of legacy and emerging environmental contaminants with endocrine disrupting effects in drinking water and aquatic food resources from Nigerian inland rivers. These concentrations highlight significant public health concern mostly for humans who depends on these water sources for drinking, domestic use, and aquatic resources for food and sustainable livelihood. Interestingly, our data indicate a higher THQ and cancer risk in children compared with adult population in Nigeria.

Our review shows that out of 54 species reported so far, only 3 dominant ecological and economically important food fish species (*C. nigrodigitatus*, *C.*

*garipepinus* and *Tilapia* species) were the most frequently used species for EDCs monitoring studies in Nigeria. This may perhaps reflect the fact that these species are the most commercially important, dominant, and highly valued food fish species occurring in several Nigerian inland ecosystems (Olaifa et al., 2004; Holzloehner et al., 2007; Ama-Abasi et al., 2019; Ama-Abasi and Uyoh, 2020). Further, their ability to adapt to a wide range of ecological zones (occurring in polluted and non-polluted ecosystems), trophic and feeding characteristics including all year-round availability (Skelton et al., 1994; Mdegela et al., 2010), may explain their frequent use or dominance as indicator species for aquatic pollution monitoring in Nigeria. Given the geographically widespread and importance of these 3 species across the country, it could be suggested that these species be adopted for harmonization of aquatic food fish species for EDCs monitoring in Nigeria.

An evaluation of the common chemical analytical methods used for EDCs monitoring in Nigeria indicates that GC-MS was the most frequently used method. However, we believe that this may be related to the availability, wide and competent technical/analytical handling, robustness, specificity, simplicity and sensitivity of GC-MS in Nigeria, compared with other methods (Chew et al., 2021). OCPs concentration in Warri River was the first EDC report in Nigeria (Atuma and Eigbe, 1985), and still remains the most EDC value constituting 25.2 % of total EDCs reported from Nigeria. This is not surprising, considering the fact that Nigeria is an agricultural country with significant application and use of pesticides for pest and vector control (Ezemoye et al., 2015; Ogbeye et al., 2018; Chukwuka et al., 2019) with no regulations or action for controlled chemical usage. Current information indicates that agriculture contributed 21.1 % to the nominal GDP in the first quarter of 2022 and this is associated with significant pesticides usage and may explain the elevated OCP levels, compared to other EDCs in Nigeria (Akinagbe and Akinbobola, 2022).

The trends for EDCs monitoring in Nigeria indicates that, while the occurrence and concentration of OCPs have been reported as early as 1985, relatively very few publications are available with majority of EDCs studies available between 2015 and now. This may be related to the fact that Nigeria and indeed many developing countries in African lack research capacity development, state of the art analytical tools, infrastructure and funding needed to perform comprehensive environmental and human health monitoring studies (Bornman et al., 2017). This is of serious concern and calls for immediate action from government, legislature, ministries, environmental monitoring agencies and non-governmental organizations, in view of the current environmental and public health risk associated with the occurrence and concentration of these contaminants in the Nigerian aquatic food fish species and environmental matrices.

Given the high concentrations of EDCs reported in the reviewed publications, we examined if biological effects have been related or implicated in wildlife and public health risk outcomes. We found that 44.7 % of the entire studies have either indicated, implicated, or demonstrated these associations. The order of biological effects was - carcinogenic/mutagenic/teratogenic (54.4 %), followed by adverse health effects (26.1 %), while reproductive/endocrine disruptive effects and obesogenic effects were the least biological effects reported and constituting 15.2 and 4.3 %, respectively and other effects (Fig. 7). It is important to highlight that these contaminants may be directly considered as procarcinogens, because their metabolism results in the formation of more toxic complexes (metabolites) that may lead to DNA adduct formation (Meehan et al., 1977; Meehan and Straub, 1979; Stading et al., 2021). DNA adducts represent critical events in the initiation of carcinogenesis and subsequent promotion and progression to cancer formation (Stading et al., 2021; Guengerich, 1988; Hemminki, 1993). DNA adduct formation has been associated with alterations in genes implicated in human and wildlife cancers (Stading et al., 2021; Chaturvedi and Lakshman, 1996; Wei et al., 1996). Other possible mechanisms of carcinogenesis by these contaminants may be related to epigenetic modulations with resulting DNA methylation, histone modification via acetylation and deacetylation (Stading et al., 2021).

In this study, the THQ and CR model showed that EDCs in drinking water and food fish species in Nigeria produced higher public health risk



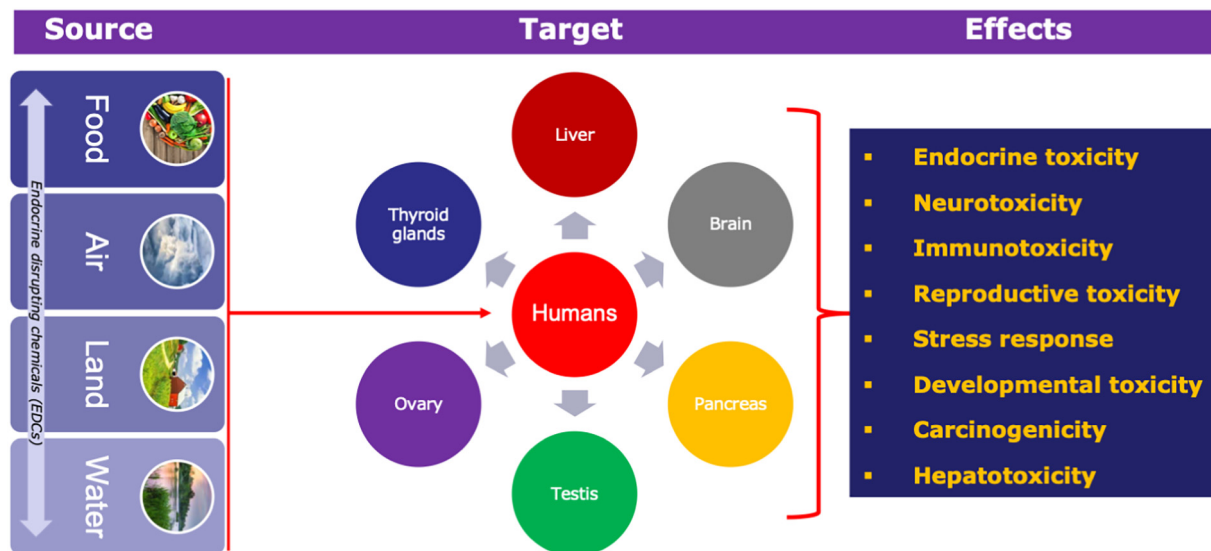


Fig. 7. Schematic representation of endocrine disrupting chemical (EDC) sources, organ targets and corresponding effects in humans.

in children, compared to the adult population, suggesting that exposure toxicity may be age dependent. This observation may be related to the fact that children are the most vulnerable population group due to their active developmental events for neuro-behavioral, immune, endocrine and metabolic physiology with potential reduced capacity to metabolize xenobiotics, compared with the adults (Chance, 2001). Consistent with our findings, higher cancer risk in children exposed to PAHs through diet, compared with adults in Indian population has been reported (Singh and Agarwal, 2018a). Further, contaminant levels in diet and potential cancer risk in exposed organisms have been reported (Singh and Agarwal, 2018a; Singh and Agarwal, 2018b; Yu et al., 2019; Taghizadeh et al., 2021; Chen et al., 2022). Herein, we showed that PEs produced the highest THQ and cancer risk for both children and adult population, compared with other EDCs. This is not surprising, considering the ubiquitous application of PEs as plasticizer, constituting the bulk of plastic pollution in Nigeria. Moreso, PEs have been listed as possible human tumor promoting agent and carcinogen that act via the aryl hydrocarbon receptor (AhR) regulating downstream signaling cascade events that induce or promote tumorigenesis and carcinogenesis (Wang et al., 2012).

Regulatory test guidelines for monitoring EDCs have adopted the measurement of biological variables such as vitellogenin, zona radiata, oestrogen receptors and intersex inductions in organisms as core biomarkers for assessing endocrine-active compounds (Ibor et al., 2016; Adeogun et al., 2016a; Hyllner et al., 1991; Oppen-Berntsen et al., 2002; Mittwoch et al., 1993; Sumpter, 1993; Arukwe et al., 1997; Tyler et al., 1998; Ibor et al., 2020). For example, a vast number of EDCs have been associated with metabolic problems such as obesity and type II diabetes (Desvergne et al., 2009; Grün and Blumberg, 2009; Hines et al., 2009; Dirinck et al., 2011; Shapiro et al., 2016; Salihovic et al., 2016). Obesogens are natural or synthetic environmental chemicals, that can interfere with the nuclear hormone receptors (peroxisome proliferator-activated receptors - PPARs) promoting obesity by increasing the number and size of adipocytes, changing the amount of calories burned at rest, shifting energy balance to favor storage of calories or altering the mechanisms through which the body regulates appetite and satiety (Janesick and Blumberg, 2011). Furthermore, PPCPs represent a unique group of emerging synthetic environmental contaminants with potential health effects in humans and other non-target species. At low environmental concentration, PPCPs have been shown to produce adverse effects on several species (Liu and Wong, 2013). Unfortunately, this group of contaminants has only received limited attention in Nigeria, with almost non-existent data. The ubiquitous environmental presence of various PPCPs has been confirmed in increasing number of studies and in different environmental compartments, raising concerns on their

health impacts (Ebele et al., 2017). The Organization for Economic Co-operation and Development (OECD) defined EDC as exogenous substances that cause adverse health effects in an intact organism, or its progeny, consequent to changes in endocrine function (OECD, 1996), and PPCPs has been shown as potential EDCs based on this definition due to their alteration of hormonal homeostasis by interfering with synthesis, secretion, transport, binding and/or metabolism (Arukwe and Goksøyr, 2003; Carballa et al., 2004; Lishman et al., 2006; Chang et al., 2009). Therefore, the occurrence and potential health risks associated with the presence of PPCPs should be given priority in Nigeria. Nevertheless, the data presented in this study shows that, reproductive, endocrine, and obesogenic effects represent the least considered biological effects for chemical pollution monitoring in Nigeria. Thus, there is urgent need for actions, development of research capacity and infrastructures necessary to perform molecular and cellular endpoints analysis that will serve as early warning signals towards providing empirical basis to inform public health, wildlife, and environmental safety decisions and policies.

On a global-, overt health and endocrine risks perspective, the non-existent of toxicological data and national regulation and guideline on EDCs in Nigeria, hampers complete exposure and health risks assessment. Previous studies have demonstrated verified adverse reproductive and developmental effects in humans and animals after exposure to EDCs either through intentional or accidental exposure, occurrences of adverse reproductive and developmental effects in several animal species that cannot be attributed to chemical use or industrial activities and of historical profile of reduced sperm quality and elevated incidence of congenital defects, testicular and breast cancer cases (Toppari et al., 1996; Daston et al., 1997; Skakkebaek et al., 2016). According to Toppari and coworker (Toppari et al., 1996), the reproductive health of the male population has decline in a significant number of countries during the 1980s and 1990s. A decline in sperm quality was reported in developed countries such as Belgium, Denmark, France, and Great Britain in the 1990s, with associated increases in the incidence of testicular cancer, hypospadias, and cryptorchidism during the same period (ibid). These human health effects showed direct relationship with comparable reproductive problems that were observed in many wildlife species (Arukwe et al., 1997; Toppari et al., 1996; Wainstock et al., 2019; Sumpter and Jobling, 1995; Jobling et al., 1998; Purdom et al., 1994), showing clear geographic differences in the prevalence of male reproductive disorders. Although several of these human studies were epidemiological in nature, the cause-and-effect relationship for the differences in these effects is still subject to ongoing debate. However, clinical, and empirical studies have over the years, demonstrated that these adverse effects may be inter-related to exposure to common

environmental contaminants with endocrine-disruptive potentials during the organizational-, fetal or childhood life stages.

When the data presented in this study are viewed holistically, it is glaring that the concentration of EDCs in drinking water and aquatic food fish resources from Nigeria are significantly alarming and potentially threatens public health, wildlife, biota, and environmental health. Interestingly, this surge maybe directly or indirectly relate to the growing public health crisis such as increased cancer cases, reproductive, endocrine, hormonal imbalance, and metabolic problems (Fig. 7). Fish and other aquatic food resources represent a significant portion and important source of protein for Nigerians and other developing countries. Previous reports have demonstrated that exposure of feral fish to EDCs produced developmental disorders (Gimeno et al., 1998; Quinn et al., 2004; Stentiford and Feist, 2005; Gimeno et al., 1997). Particularly, the masculinization of fish after exposure to tributyltin (TBT), nonylphenol and octylphenol (and other alkylphenol polyethoxylates), PCBs, and zinc (Ju et al., 2009; Lee et al., 2009) have been reported. Phenols were shown as classical inducers of feminization in male individuals (Gray and Metcalfe, 1997; Gray et al., 1999). These laboratory studies have corroborated field investigations showing altered physiology, gonadal development, and reduced reproductive capacity of fish after exposure to EDC (Bateman et al., 2004; Antuofermo et al., 2017). Thus, the increases in the incidence of reproductive anomalies observed in wild species and the parallel reduction in coastal fisheries yield have raised concerns on the role of endocrine toxicity in the low catch per unit effort of landed fisheries (Food and Agricultural Organization (FAO), 2016) with subsequent direct and indirect health consequences to humans.

Based on the weight of scientific evidence presented herein, we suggest that government agencies and other non-governmental organizations (NGOs) should scale-up advocacy environmental programs and enforcement actions towards reducing EDCs exposures. Public sensitization and training programs for local populations will help educate, provide precautionary measures that may reduce EDC exposures. It is important that government and other NGOs prioritize funding research on EDCs that is directed at establishing a comprehensive biomonitoring database towards providing epidemiological and cohort data on the extend and severity of EDCs on public health and wildlife. This is necessary to benchmark important scientific outcomes that will form an empirical basis for effective drinking water interventions and policy formulation/implementation towards public health and wildlife safety in Nigeria based on the United Nations Sustainable Development Goals 14 (Life below water).

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#### CRediT authorship contribution statement

ORI: Conceptualization; Data curation; Investigation, Formal analysis; Funding acquisition; Visualization; drafted the original draft; PN: Data curation; Writing - review & editing; DMO: Data curation; Writing - review & editing; OI: Data curation; Writing - review & editing; JA: Data curation; Writing - review & editing; DA: Data curation; Writing - review & editing; CO: Data curation; Writing - review & editing; AVC: Data curation; Writing - review & editing; AOA: Data curation; Writing - review & editing; AA: Conceptualization; Formal analysis; Funding acquisition; Project administration; Resources; Supervision; Roles/Writing - original draft; Writing - review & editing.

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#### Data availability

No data was used for the research described in the article.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationship that could have appeared to influence the work reported in this manuscript.

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