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Research Article

Public Awareness and Knowledge Regarding Toxicovigilance of Xenoestrogens in Iraq: A Cross-sectional Study

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Abstract

Background: Xenoestrogens are synthetic chemicals found in various plastics, sealants, consumer goods, preservatives, and pesticides. They can disrupt the endocrine system and have been linked to numerous health issues, including reproductive problems, hormonal imbalances, developmental abnormalities, and an increased risk of certain cancers. **Objective:** To identify the awareness, knowledge, and usage rate of XEs among individuals in different Iraqi governments and the human risk assessment for potential toxicity. **Methods:** This descriptive cross-sectional study utilized a random convenience sampling method from January to June 2024 throughout various regions of Iraq. Participants aged 18 to 70 years who provided verbal consent were recruited prior to enrollment in this study (n=304). The participants filled out the questionnaires in the presence of researchers, who then collected them for assessment. The questionnaire, partially modified from a prior study, gathered data on educational status, basic knowledge, and awareness of xenoestrogens and their health effects, as well as the safety and frequency of use of containers presumed to harbor xenoestrogens. **Results:** The findings will provide insights into the level of awareness and knowledge among healthcare providers, medical students, and academic professionals in Iraq regarding xenoestrogens and their potential health risks. Detailed results will be analyzed to determine the extent of knowledge and gaps that need to be addressed. **Conclusions:** Most of the Iraqi people did not have enough awareness and knowledge of XE's effects on general health and the environment. This highlights the importance of improving knowledge and awareness about these chemicals.

Keywords: Bisphenol A, Endocrine disruptors, Healthcare awareness, Iraq, Xenoestrogens.

الوعي العام والمعرفة بخصوص اليقظة السمية لشبيهات الاستروجين في العراق: دراسة مقطعية

الخلاصة

الخلفية: Xenoestrogens عبارة عن مواد كيميائية اصطناعية موجودة في العديد من المواد البلاستيكية والمواد المانعة للتسرب والسلع الاستهلاكية والمواد الحافظة والمبيدات الحشرية. يمكن أن تعطل نظام الغدد الصماء وقد تم ربطها بالعديد من المشكلات الصحية، بما في ذلك مشاكل الإنجاب، والاختلالات الهرمونية، وتشوهات النمو، وزيادة خطر الإصابة ببعض أنواع السرطان. **الهدف:** تحديد الوعي والمعرفة ومعدل استخدام XEs بين الأفراد في مناطق مختلفة من العراق وتقييم المخاطر البشرية للسمية المحتملة. **الطرائق:** استخدمت هذه الدراسة الوصفية المقطعية طريقة أخذ العينات العشوائية المريحة من يناير إلى يونيو 2024 في مناطق مختلفة من العراق. تم تجنيد المشاركين الذين تتراوح أعمارهم بين 18 و 70 عاما والذين قدموا موافقة شفوية قبل التسجيل في هذه الدراسة (العدد = 304). قام المشاركون بملاء الاستبيانات بحضور الباحثين، الذين قاموا بعد ذلك بجمعها للتقييم. جمع الاستبيانات، المعدل جزئيا من دراسة سابقة، بيانات عن الحالة التعليمية والمعرفة الأساسية والوعي بـ xenoestrogens وآثارها الصحية، بالإضافة إلى سلامة وتواتر استخدام الحاويات التي يفترض أنها تحتوي على xenoestrogens. **النتائج:** أوضحت النتائج رؤى حول مستوى الوعي والمعرفة بين مقدمي الرعاية الصحية وطلاب الطب والمهنيين الأكاديميين في العراق فيما يتعلق بهرمون الاستروجين ومخاطره الصحية المحتملة. تم تحليل النتائج التفصيلية لتحديد مدى المعرفة والفجوات التي تحتاج إلى معالجة. **الاستنتاجات:** لم يكن لدى معظم الشعب العراقي ما يكفي من الوعي والمعرفة بتأثيرات XE على الصحة العامة والبيئة. هذا يسلط الضوء على أهمية تحسين المعرفة والوعي حول هذه المواد الكيميائية.

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INTRODUCTION

Xenoestrogens are synthetic industrial chemicals found in various plastics, sealants, consumer goods, preservatives, and pesticides (Figure 1).

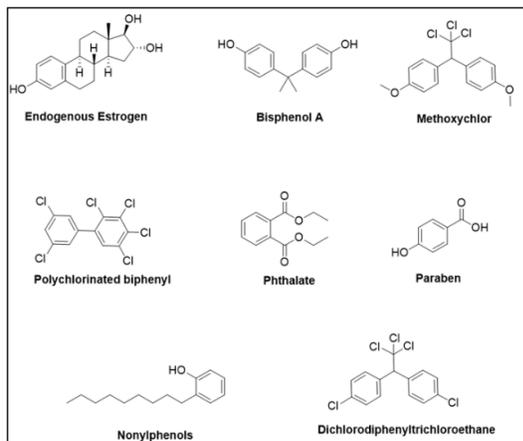


Figure 1: The chemical structures of endogenous estrogen (Estradiol), and xenoestrogens (Bisphenol A, Methoxychlor, DDT, polychlorinated biphenyl, phthalate, paraben, and nonylphenol).

Xenoestrogen activity is when chemicals interact with different kinds of estrogen receptors, mostly estrogen receptor alpha ($ER\alpha$) and estrogen receptor beta ($ER\beta$), acting like natural estrogen and acting either as estrogen or as an anti-estrogen. $ER\alpha$ binding is pro-oncogenic, while $ER\beta$ is a tumor-suppressive estrogen receptor in the body [1,2]. Xenoestrogens can disrupt the normal functioning of the endocrine system, which regulates various bodily processes, including growth, metabolism, and reproduction; hormonal imbalances; reproductive issues; developmental abnormalities; and an increased risk of certain cancers. Exposure to xenoestrogens during critical developmental periods, such as prenatal and early childhood, can have long-lasting health effects and increase susceptibility to certain diseases later in life [3,4]. An extensively studied xenoestrogen is bisphenol A (BPA). BPA was first used as a pharmaceutical estrogen in the 1930s but is now commonly used in the manufacture of polycarbonate plastics and epoxy resins used in food containers, water bottles, and other protective coatings [5]. BPA has a molecular structure that is similar to estrogen. Bisphenol compounds all have two phenol rings connected by a bridging carbon atom, which lets them bind to estrogen receptors and cause estrogen-like effects. BPA has been shown to disrupt ER activity by mimicking, enhancing, or inhibiting endogenous estrogens, causing a direct impact on the intracellular signal transduction pathways [6]. It has a relative binding affinity of 0.01 for both $ER\alpha$ and $ER\beta$ and has been strongly correlated with an increased risk for breast, prostate, and uterine cancer. Because of this, many organizations concerned with the environment have suggested that the public avoid using items made with BPA [7,8]. Modifications in the chemical structure of bisphenol compounds can impact their estrogenic activity. For instance, changing the phenol rings' size,

or the way they are replaced can change how well they bind to estrogen receptors and how strong the estrogenic response is. Several studies have looked into the SAR of bisphenol compounds by making analogs with different structural changes to see how well they bind to estrogen receptors and how strong their estrogenic effects are [9]. Another xenoestrogen of interest is the estrogenic pesticide dichlorodiphenyltrichloroethane (DDT), which has been banned in the US for almost 50 years. DDT was a commonly used pesticide sprayed across many agricultural fields and homes, acting as an insect neurotoxin to kill mosquitoes and other insect vectors that carry malaria, typhus, and other insect-borne diseases. It is still widely used in India and southern Africa, and its metabolites may have an endocrine-disrupting potential, potentially affecting the reproductive system through estrogenic or androgenic activity [10,11]. DDT and its metabolites are endocrine-disrupting chemicals (EDCs) that mimic the action of estrogen, disrupting the estrogen receptor (ER) pathways. DDT and its metabolites exhibit a relative binding affinity of 0–0.01 and 0–0.02, respectively, to the estrogen receptor (ER). Receptor-binding assays show that *o,p'*-DDT has weak estrogenic activity, while *p,p'*-DDE is an androgen receptor antagonist. DDT was previously not associated with increased cancer risk, but it has been linked to increased breast cancer, especially during certain WOS exposures [12]. Despite an abundance of research showing the harmful effects of both BPA and DDT, these two xenoestrogens continue to be used today. Even though epidemiological studies have linked BPA exposure to lower-quality sperm in males, the material is still utilized in plastics [13]. However, it is alarming that, despite being outlawed in the US for fifty years, DDT is still used in areas where malaria is endemic. This is because clinical and epidemiological data have linked DDT exposure to reduced semen volume, concentration, motility, and normal morphology [14]. Methoxychlor (DMDT) was created as a replacement for DDT for vector control when it was outlawed. It was employed to keep pests like cockroaches, mosquitoes, and other insects away from cattle, crops, and pets. Even though there is mounting proof that DMDT is an $ER\alpha$ agonist and an $ER\beta$ antagonist, with relative binding affinities of less than 0.01% for both, leading to a greater suppression of estrogen binding, the drug is still in use today. The risk of ovarian cancer has been linked to DMDT, but not to other malignancies in humans [15]. Polychlorinated biphenyls (PCBs) are a group of synthetic halogenated organic compounds used in electrical equipment, hydraulic fluids, and plasticizers. They can eventually end up in landfills, where they can re-enter the environment via soil and air release [16]. PCBs have relative binding affinities for estrogen receptors ($ER\alpha$ and $ER\beta$) between 0.01 and 3.4 and <0.01 and 7.2, respectively. Despite a two-fold difference in $ER\beta$ binding affinity compared to $ER\alpha$,

PCBs are associated with increased breast cancer risk. On the other hand, PBDEs are used in flame retardants, electrical equipment coatings, construction materials, textiles, and furniture padding. Despite the fact that PBDEs have a higher binding affinity to estrogen receptors than PCBs, there is no clear relationship between PBDE exposure and breast cancer risk. Recent studies have shown that PBDEs induce the expression of estrogen-responsive genes, particularly those related to cell proliferation in cancer cells [17,18]. In addition, phthalates, parabens, and nonylphenols (NP) are notable examples of xenoestrogens. In soft packaging plastics, phthalates are present and have the ability to competitively block E2 binding to ER [19]. In the meantime, NP is a component of consumer goods including laundry detergents, personal hygiene, automobile care, and grass care items, as well as being utilized in a number of industrial operations. In comparison to other xenoestrogens, NP has a modest relative binding affinity (0.0032–0.037) to the ER. On ER+ breast cancer cells, they can nevertheless show estrogen-like action [20]. The present study aims to estimate the knowledge and awareness about the xenoestrogens as endocrine disruptors and their risks of cumulative toxicity of these synthetic chemicals among a sample of Iraqi people.

METHODS

Study design and setting

This descriptive cross-sectional study utilized a random convenience sampling method from January to June 2024 throughout various regions of Iraq. Participants aged 18 to 70 years who provided verbal consent were recruited prior to enrollment in this study (n= 304). The participants filled out the questionnaires in the presence of researchers, who then collected them for assessment.

Data collection

The research instrument was created following an assessment of numerous published sources; it aimed to gather data regarding educational status, fundamental knowledge and awareness of xenoestrogens and their health effects, the safety of containers and tools presumed to harbor xenoestrogens utilized in daily activities, and the frequency of daily usage of these containers and tools. The questionnaire has been partially modified from a prior study concerning knowledge and attitudes of xenoestrogens [21], with additional questions incorporated. The questionnaire underwent validation via a pilot study.

Inclusion and exclusion criteria

The inclusion criteria consisted of individuals of both genders aged 18 to 70 years, with diverse educational backgrounds, and dwelling in various districts of Iraq. The exclusion criteria encompassed incomplete forms and individuals who do not speak English.

Ethical consideration

The study was conducted after obtaining the approval of the Ethics Review Committee (ERC) of the College of Medicine, University of Sulaimani (No: 15:4 on Feb 28, 2024). No identifying data were included in the questionnaire.

Statistical analysis

The data were analyzed by using GraphPad Prism version 8.4.3 (GraphPad Software, Boston, MA 02110, USA). Descriptive statistics and a comparison of the variables were carried out, and statistical differences were analyzed using Chi-square and Fisher's exact tests. Values are considered significantly different at $p < 0.05$.

RESULTS

Table 1 shows the survey findings for xenoestrogens, which emphasize major demographic characteristics of the participants. The respondents' average age was 31.6 years, with a standard deviation of 13.5 years. The 18-24 age group accounted for 158 (51.9%) of the participants, which was statistically significant with a p-value of < 0.0001 . Participants were divided into four age groups: 25-35 years (46, 15.1%), 36-45 years (52, 17.2%), 46-55 years (32, 10.5%), and 56-65 years (16, 5.3%). In terms of gender distribution, males represented 166 participants (54.6%), while females made up 138 (45.4%). The difference in gender distribution was statistically significant with a p-value of 0.028. In terms of educational status, most respondents (139 in total) were medical students (45.7%). Other educational backgrounds included non-medical graduates (50, 16.4%), MSc holders (48, 15.8%), BSc holders (29, 9.5%), Ph.D. candidates (21, 6.9%), teachers (8, 2.6%), and others (9, 3.0%). The educational status also demonstrated a significant difference, with a p-value of less than 0.0001.

Table 1: Demographic characteristics of participants (n=304).

Characteristics	Value	p-value
<i>Age (year)</i>		
Mean±SD	31.6 ± 13.5	----
18-24	158(51.9)	
25-35	46(15.1)	
36-45	52(17.2)	<0.0001†
46-55	32(10.5)	
56-65	16(5.3)	
<i>Gender</i>		
Male	166(54.6)	
Female	138(45.4)	0.028*
<i>Educational status</i>		
Medical student	139(45.7)	
Ph.D.	21(6.9)	
MSc	48(15.8)	
BSc	29(9.5)	<0.0001†
Non-medical	50(16.4)	
Teacher	8(2.6)	
Other	9(3.0)	

The values were expressed as mean ± SD for numerical variable and n (%) for categorical variables; SD: Standard deviation; n: Number; *Fishers, exact test; † Chi square test.

These findings highlight the significance of demographic characteristics in comprehending the survey results for xenoestrogens, suggesting that age, gender, and educational background may impact perceptions and knowledge of these substances. The results in Table 2 provide an insight into participants' awareness of xenoestrogens and their perceived impact on personal health and the environment. The majority of respondents,

173 (56.9%), expressed no awareness of xenoestrogens, with a statistically significant p -value of 0.002. In comparison, only 131 individuals (43.1%) reported knowing nothing about these substances. When questioned about their awareness of estrogens in general, 196 participants (64.5%) stated they were informed, whereas 108 participants (35.5%) understood a lack of knowledge, with a highly significant p -value of <0.0001 .

Table 2: Knowledge of participants about xenoestrogens and their impact on the personal health and environment.

Knowledge type	n (%)	p-value*
Having knowledge about xenoestrogen		
No	173(56.9)	0.002
Yes	131(43.1)	
Have knowledge about estrogen		
No	108(35.5)	<0.0001
Yes	196(64.5)	
Xenoestrogens negatively impact the environment		
No	161(53)	0.168
Yes	143(47)	
Plastic bottles are environmentally friendly		
No	217(71.3)	<0.0001
Yes	87(28.7)	
Chemical pesticides are environmentally harmful		
No	270(88.8)	<0.0001
Yes	34(11.2)	
The environment affects personal health		
No	270(85.5)	<0.0001
Yes	44(14.5)	
Have a knowledge about BPA-free products		
No	226(74.3)	<0.0001
Yes	78(25.7)	

The values were expressed as n (%); n: Number. * Fishers, exact test.

Regarding the environmental effect of xenoestrogens, 143 participants (47%) agreed that these compounds had a detrimental influence on the environment, though this finding failed to reach statistical significance ($p=0.168$). The results showed that 217 (71.3%) participants mistakenly regarded plastic bottles as environmentally friendly ($p<0.0001$). A vast majority of 270 participants (88.8%) believed that chemical pesticides are damaging to the environment ($p<0.0001$). Furthermore, 270 individuals (85.5%) thought that the environment influences personal health, indicating a significant p -

value of <0.0001 . Lastly, awareness of BPA-free items was particularly low, with 226 individuals (74.3%) ignorant of such products, while only 78 participants (25.7%) reported being educated, reaching statistical significance ($p<0.0001$). These findings indicate a widespread absence of understanding about xenoestrogens and their effects, emphasizing the need for more education and outreach on this critical public health problem. The results in Table 3 revealed the participants' understanding of the effects of xenoestrogens on human health.

Table 3: The knowledge about the impacts of xenoestrogens on human health

Knowledge about health impacts of xenoestrogens	n(%)	p-value
Do you have a knowledge about endocrine disrupting xenoestrogens		
No	163(53.6)	0.088*
Yes	141(46.4)	
How do you feel when you know the risks of endocrine disrupting xenoestrogens?		
Bad	217(71.4)	<0.0001 #
Good	76(25)	
Excellent	11(3.6)	
Can you name any specific endocrine-disrupting xenoestrogen?		
No	185(60.8)	<0.0001 *
Yea	119(39.2)	
Can you score (ascending 1-5 scale) their harmful effects?		
1	9(2.9)	<0.0001 #
2	22(7.2)	
3	74(24.3)	
4	130(42.8)	
5	69(22.8)	
Do you know their association with a specific health disorder?		
No	90(29.6)	0.0001*
Yes	214(70.4)	

Values were expressed as frequency and percentage. * Fishers, exact test. # Chi square test.

The majority of respondents, 163 (53.6%), reported having no awareness of endocrine-disrupting xenoestrogens, while 141 (46.4%) claimed to be aware of them. A *p*-value of 0.088 demonstrated that this difference was not statistically significant. When asked about their feelings following learning about the hazards connected with endocrine-disrupting xenoestrogens, most participants exhibited negative emotions: 217 individuals (71.4%) felt "bad," 76 (25%) felt "good," and just 11 (3.6%) felt "excellent." This conclusion was statistically significant ($p < 0.0001$), showing a strong emotional response to being informed about the hazards. In terms of having the ability to identify specific endocrine-disrupting xenoestrogens, 185 people (60.8%) were unable to do so, whereas 119 (39.2%) were able to. This finding was statistically significant ($p < 0.0001$), indicating a widespread lack of particular knowledge of these chemicals among the participants. Participants were also asked to rate the detrimental effects of xenoestrogens on a scale of one to five. The score

distribution indicated that 9 individuals (2.9%) evaluated the effects as "1," whereas 22 (7.2%) ranked them as "2." A greater group, 74 individuals (24.3%), rated the effects "3," whereas 130 participants (42.8%) ranked them "4." Finally, 69 individuals (22.8%) evaluated the harmful effects as "5," suggesting significant worry about the potential impacts of xenoestrogens ($p < 0.0001$). Furthermore, when asked about the link between xenoestrogens and certain health issues, 90 people (29.6%) said they didn't know, whereas 214 participants (70.4%) agreed. This finding was statistically significant ($p = 0.0001$). Overall, these findings reveal a serious information gap about xenoestrogens and their health consequences, despite a strong emotional reaction to the dangers they bring. The results in Table 4 provided useful insights into participants' awareness of the safety of infant care and skincare products with respect to xenoestrogens. When asked if infant toys had xenoestrogen effects, 204 respondents (67.1%) agreed, while just 100 (32.9%) disagreed.

Table 4: The knowledge about the safety of baby care and skincare products

Knowledge about safety of baby products and cosmetics	n(%)	<i>p</i> -value
Do these products have xenoestrogen effects?		
<i>Baby's Toys</i>		
No	100(32.9)	0.0001*
Yes	204(67.1)	
<i>Plastic feeding bottles</i>		
No	54(17.8)	<0.0001*
Yes	250(82.2)	
<i>Cosmetics and skincare products</i>		
No	75(24.7)	<0.0001*
Yes	229(75.3)	

The result was statistically significant ($p = 0.0001$), demonstrating a high level of knowledge about the possible dangers connected with infant toys. Concerns about plastic feeding bottles were particularly strong. A significant number of 250 people (82.2%) acknowledged that these bottles may have xenoestrogen effects, while only 54 people (17.8%) disagreed. This finding was statistically significant ($p < 0.0001$), indicating strong worry regarding the safety of plastic feeding bottles in connection with xenoestrogens. Similarly, 229 people (75.3%) agreed that xenoestrogens had an impact on cosmetics and skincare products, while 75 people (24.7%) disagreed. This finding was statistically significant ($p < 0.0001$). Overall, our findings show a significant amount of knowledge among participants about the possible xenoestrogen effects of baby care and skincare products, emphasizing the significance of educating consumers about their safety. Figure 2 demonstrates the number of plastic bottles consumed daily by the participants. Those used for mineral water represent the highest level (3 units/day), and the value was significantly higher than those used for other purposes and the use of non-plastic containers. In Figure 3, the daily use of plastic containers for freezing and keeping food represents the highest level (1.5 units/day) and is significantly higher than those used for food delivery ($p < 0.0001$).

DISCUSSION

This study analyzed the unexplored area of public knowledge and awareness regarding the health impacts and hazards of xenoestrogens in war-torn countries such as Iraq using a quantitative analysis design. Prior research [22,23] has demonstrated that most participants possess inadequate awareness and deficient knowledge regarding endocrine-disrupting chemicals, such as xenoestrogens. Consequently, it has been acknowledged that individuals who possess a sufficient level of understanding regarding xenoestrogens either acquired this knowledge during their academic pursuits or acquired it from media articles. In this study, the participants showed good knowledge about the health impacts and hazards of environmental pollution; however, their knowledge about xenoestrogens as endocrine disruptors is low. This result is compatible with previously published reports [24;25]. The results of the present study showed a relatively high consumption of plastic containers. Many of these products include bisphenol-A, which can be easily leached during heating, cooling, or preserving certain liquids and foods. Even in low quantities, bisphenol A can produce estrogen-like activity that may disturb the normal hormonal integrity [26]. In this regard, it is important to recognize that human exposure to the effects of xenoestrogens like bisphenol A or phthalates is very common through diet or

food containers [27]. In the current study, although the participants have good knowledge and awareness about the safety of cosmetics and the possibility of including xenoestrogens, consumption of these products is relatively high.

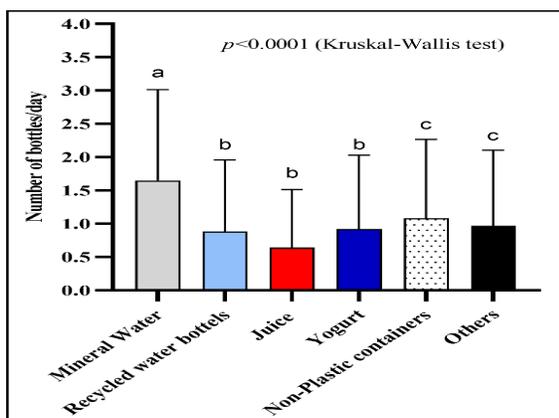


Figure 2: Number of plastic bottles used daily. Values are presented as mean±SD. Values with different letters (a,b,c) are significantly different (Duns, post hoc test, $p < 0.05$).

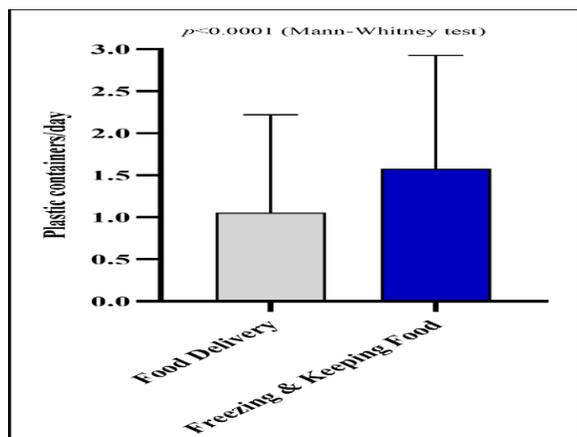


Figure 3: Daily use of plastic food containers. Mann-Whitney test.

Previous studies showed that the use of these products has been linked with many pathological conditions, mostly attributed to endocrine disruption [28,29]. Moreover, skin absorption of xenoestrogens is found to be relatively higher than oral exposure, which may lead to significant endocrine impact [30]. Accordingly, it is also very important to be cautious and careful in using personal care products and checking their labels to lessen exposure to endocrine disruptors [31]. In Malaysia, a study conducted on 15 university students concerning the use of plastic-type food contact materials found that 84% of them had a low level of knowledge regarding endocrine disruptors. It should be noted that the study focused on the use of canned food and bottled mineral water [32]. However, it can still be concluded that the knowledge regarding xenoestrogens as endocrine disruptors is inadequate among participants regardless of the nature of the study sample, the country where the study was conducted, and the products investigated. Additionally, excessive consumption of products

containing endocrine disruptors, like plastic water bottles, cosmetics, and food preservatives, may be associated with impaired normal pubertal development. Therefore, long-term exposure to these products may increase the incidence of breast cancer [33]. The results showed that the study participants ostensibly were aware of the health risks of xenoestrogens, and the majority of them provided a high estimate of the risk factors of these compounds. However, the majority were unaware that some of the daily-used supplies contained these compounds, as demonstrated in this study. This can be attributed to the fact that the targeted sample possesses a solid theoretical understanding of these compounds and their effects on the biological system. However, there is a lack of understanding regarding which daily-use supplies contain these compounds on a practical level. Their response reflects this lack of understanding about the risk factor associated with their daily use. It is strongly advised that additional research be conducted to determine the public's perceptions of xenoestrogens as endocrine disruptors in order to develop effective risk communication strategies. It is challenging for individuals who are involved in health risk prevention campaigns to effectively communicate their message due to the prevalence of xenoestrogens. It is imperative that the information regarding these chemicals be conveyed with precision to prevent individuals from becoming less inclined to take necessary precautions. Xenoestrogen risk communicators in a war-torn country such as Iraq may benefit from the findings of this study to adopt effective strategies to mitigate exposure. This study provides initial insights into healthcare providers' views on xenoestrogens, their sources, and their health effects, but it cannot be generalized to the broader population. Consequently, additional quantitative research is required to determine the factors that influence public risk perceptions regarding exposure to xenoestrogens.

Study limitations

The study's limitations were its relatively small sample size, its small geographic scope, and the fact that it primarily involved academic and healthcare professionals. These were the most significant limitations. Therefore, it is challenging to extrapolate the results of the study to other regions or populations.

Conclusion

There is a lack of knowledge and awareness of xenoestrogens and their negative effects on the health of exposed populations among the surveyed participants with a high educational level. This highlights the importance of improving knowledge about these chemicals in this population. To raise awareness, programs and activities using social media, as well as educational campaigns, must be established.

Conflict of interests

The authors declared no conflict of interest.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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