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The title of the paper:

Association between Exposure to bisphenol A or Phthalates and the Risk of Human Thyroid Cancer

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Association between Exposure to bisphenol A or Phthalates and the Risk of Human Thyroid Cancer

Abstract

Background: Thyroid cancer has become a significant global health concern with a sharp rise in incidence over recent decades. The potential association between endocrine-disrupting chemicals (EDCs) and thyroid cancer development has raised substantial concern, yet the evidence remains inconclusive.

Methods: To comprehensively review the relevant literature, a robust search was conducted in four electronic bibliographic databases: Medline, Scopus, Embase, and Amed. Six studies were included, which investigated the influence of exposure to Endocrine-disrupting chemicals, including phthalates and bisphenol A, on the risk of developing thyroid cancer. The included studies utilized various approaches, outcome measurements, and demographic data.

Results: A total of one thousand and thirteen individuals were analyzed across the six studies, with participants of both sexes, varying ages, and diverse body mass indices. The results showed potential link between Endocrine-disrupting chemicals exposure and thyroid cancer, particularly papillary thyroid carcinoma. Notably, phenols such as bisphenol A, bisphenol F, and bisphenol S were found to be associated with Papillary Thyroid Cancer prevalence. Overall, among the six studies reviewed, one study suggested a protective effect of bisphenol A exposure (OR 0.38; 95% CI 0.19-0.77; p=0.006). While the majority of the studies (four studies) indicated a positive association between BPA exposure and thyroid cancer 83.3%. One study did not find a statistically significant association. Therefore, approximately of the studies found a protective effect, while approximately found a positive association, and One study did

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not find a statistically significant association between bisphenol A exposure and differentiated thyroid cancer (OR 3.71; 95% CI 0.67-20.34; p=0.142).

Conclusion: This systematic review indicates that exposure to Endocrine-disrupting chemicals may increase the chance of developing thyroid cancer, specifically Papillary Thyroid Cancer. The findings underscore the importance of considering Endocrine-disrupting chemicals exposure in public health strategies for thyroid cancer prevention. However, due to the limited number of studies and potential heterogeneity, further extensive prospective research is warranted to validate these relationships and explore underlying biological mechanisms.

Keywords: thyroid cancer, endocrine-disrupting chemicals, EDCs, bisphenol A, phthalates, papillary thyroid carcinoma.

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Introduction:

Thyroid cancer is a significant global public health concern, with a worrisome increase in incidence observed in recent decades (Kim, J., Gosnell, J. E., & Roman, S. A., 2020). As the most common endocrine malignancy, it poses a substantial burden on patients and healthcare systems worldwide (Sawka et al., 2020). For example, in the United States, the American Cancer Society estimated approximately 43,720 new cases of thyroid cancer in 2023, accounting for 2.2% of all new cancer cases, with 2,120 associated deaths [National Cancer Institute, 2023]. While advancements in medical understanding and diagnostics have improved detection, the precise etiology of thyroid cancer remains incompletely understood (Kithara & Sosa, 2020). Emerging research indicates that environmental factors may play a crucial role in this rising trend (Fiore et al., 2019).

Endocrine-disrupting chemicals (EDCs) have garnered attention as potential contributors to thyroid cancer development. Among them, Bisphenol A (BPA) is a well-known EDC that has become ubiquitous in the environment and daily lives For in-text citation in APA style, you would write:

(Vogel, 2009);(Rubin, 2011). BPA is commonly found in plastic bottles, food containers, and can linings, and numerous animal studies have demonstrated its detrimental effects on various systems and organs (Ma et al., 2019). Although the precise impact of BPA on human health remains uncertain, it has been linked to thyroid disorders and several types of cancer (Zhang et al., 2023); (Sonnenschein & Soto, 2010).

Phthalates, another group of EDCs, are prevalent in cosmetics, personal care products, and plastic toys. Like BPA, phthalates can also interfere with the endocrine system, disrupting hormonal regulation and potentially leading to adverse health outcomes (Dworakowska & Grossman, 2020);(Mughal, Fini, & Demeneix, 2018). Given the pervasive presence of BPA and phthalates in the environment and their ability to enter the human body through various routes, including ingestion, inhalation, and skin

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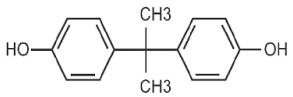
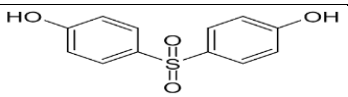
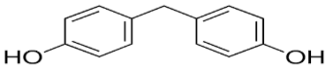
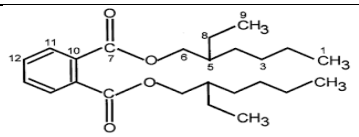
contact, concerns have arisen about their potential impact on human health (Andrianou et al., 2016). The thyroid gland, as a hormone-regulated organ, is particularly vulnerable to disruptions caused by these endocrine-disrupting properties (Zoeller et al., 2012). Thyroid cancer, being highly hormone-dependent, is sensitive to hormonal imbalances, making it essential to understand the potential impact of EDC exposure on thyroid cancer risk.

Despite the growing attention to the potential link between EDCs and thyroid cancer, the evidence remains limited and inconsistent (Schug, Janesick, Blumberg, & Heindel, 2011). Some studies have reported a possible association, while others found no conclusive evidence of such a link. The conflicting findings and limited data call for a comprehensive systematic review to analyze and synthesize the current scientific literature on this topic. By consolidating evidence from multiple studies, a more comprehensive understanding can be obtained of the potential relationship between BPA and phthalate exposure and the risk of developing thyroid cancer.

A table with abbreviations defined and list of bisphenols and phthalates with generic structures.

Abbreviation	Compound Name	Generic Structure
BPA	Bisphenol A	
BPS	Bisphenol S	
BPF	Bisphenol F	
DEHP	Di(2-ethylhexyl) phthalate	

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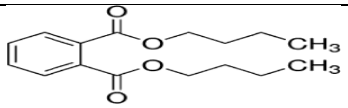
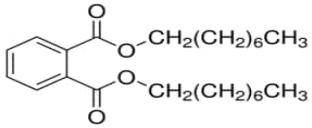
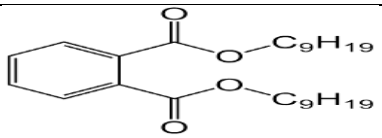
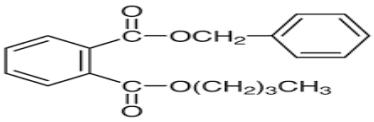
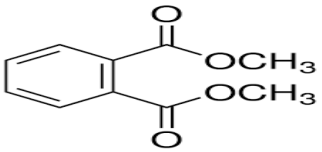
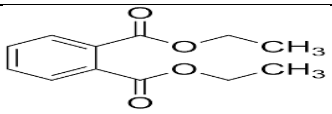
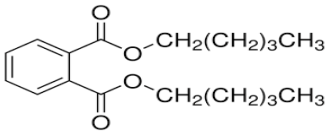
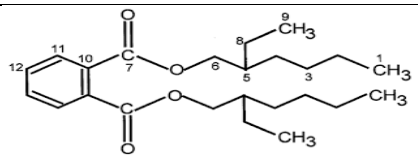
DBP	Dibutyl phthalate	
DNOP	Di-n-octyl phthalate	
DINP	Diisononyl phthalate	
BBP	Benzyl butyl phthalate	
DMP	Dimethyl phthalate	
DEP	Diethyl phthalate	
DCP	Dicyclohexyl phthalate	
DOTP	Di(2-ethylhexyl) terephthalate	

Rationale for the Review:

This systematic review aims to collate the evidence on the association between BPA and phthalates exposure and the likelihood of developing thyroid cancer in humans. Understanding the link between EDC exposure and thyroid cancer will help develop

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prevention strategies and regulations. Additionally, it will identify research gaps, advancing the understanding of the complex relationship between environmental factors and thyroid cancer.

Objectives

The objectives of this review were to assess 1) If there is a causal relationship between BPA exposure and thyroid cancer in humans 2) if phthalates exposure increases thyroid cancer risk, especially in younger adults 3) understand the underlying biological mechanisms linking BPA, phthalates, and thyroid cancer risk.

Methods:

A systematic search was conducted in four electronic bibliographic databases, namely Medline, Scopus, Embase, and Amed. The search strategy incorporated MeSH terms and keywords related to bisphenol and its synonyms, as well as phthalates, combined with terms associated with thyroid cancer using Boolean Operators. The search covered the period from 1946 to May 2023. The detailed search strategy employed in Medline is outlined in Appendix 1.

Study Strategy

The citations identified were imported into RefWorks, a reference management software, to eliminate duplicate entries. A screening process was then conducted to evaluate the titles and abstracts of the identified studies for their relevance to the research questions. Full texts of the studies meeting the inclusion criteria were critically appraised.

Inclusion and Exclusion Criteria

All peer-reviewed original research articles published in English-language. Only studies with human subjects were included regardless of age, gender, or race. Included studies were required to report outcomes directly related to thyroid cancer, such as

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disease incidence, prevalence, or biomarkers associated with thyroid cancer using quantitative measures, such as odds ratios or relative risks.

Non-original research articles, including reviews, editorials, and letters were excluded. Animal studies and studies conducted at a cellular or model level, as well as those focusing on in vitro were excluded. Studies with a small sample size of fewer than 10 people were excluded to ensure statistical robustness. Finally, studies exclusively focusing on children and adolescents were not included in the review due to the possibility of them being exposed to endocrine-disrupting chemicals (EDCs) indirectly through their mothers rather than through direct exposure (Mughal, Fini, & Demeneix, 2018).

Data Quality and Assessment

The Joanna Briggs Institute (JBI) Critical Appraisal Tools for case-control studies were utilized to examine the quality of the included studies and assess how they addressed potential biases in their design, conduct, and analysis.

Data Analysis

Due to the variability among the included studies, conducting a meta-analysis was deemed unsuitable. The heterogeneity were identified in study designs, variations in measurements, and differences in population characteristics. Additionally, the lack of longitudinal data in all the included studies limited the ability to establish causality. Instead, a comprehensive analysis of the results was conducted using a narrative synthesis approach.

Results:

Literature search and selection

A comprehensive search conducted in four databases result in a total of 186 potentially relevant studies (Medline: N=48, Scopus: N=73, Embase: N=64, and

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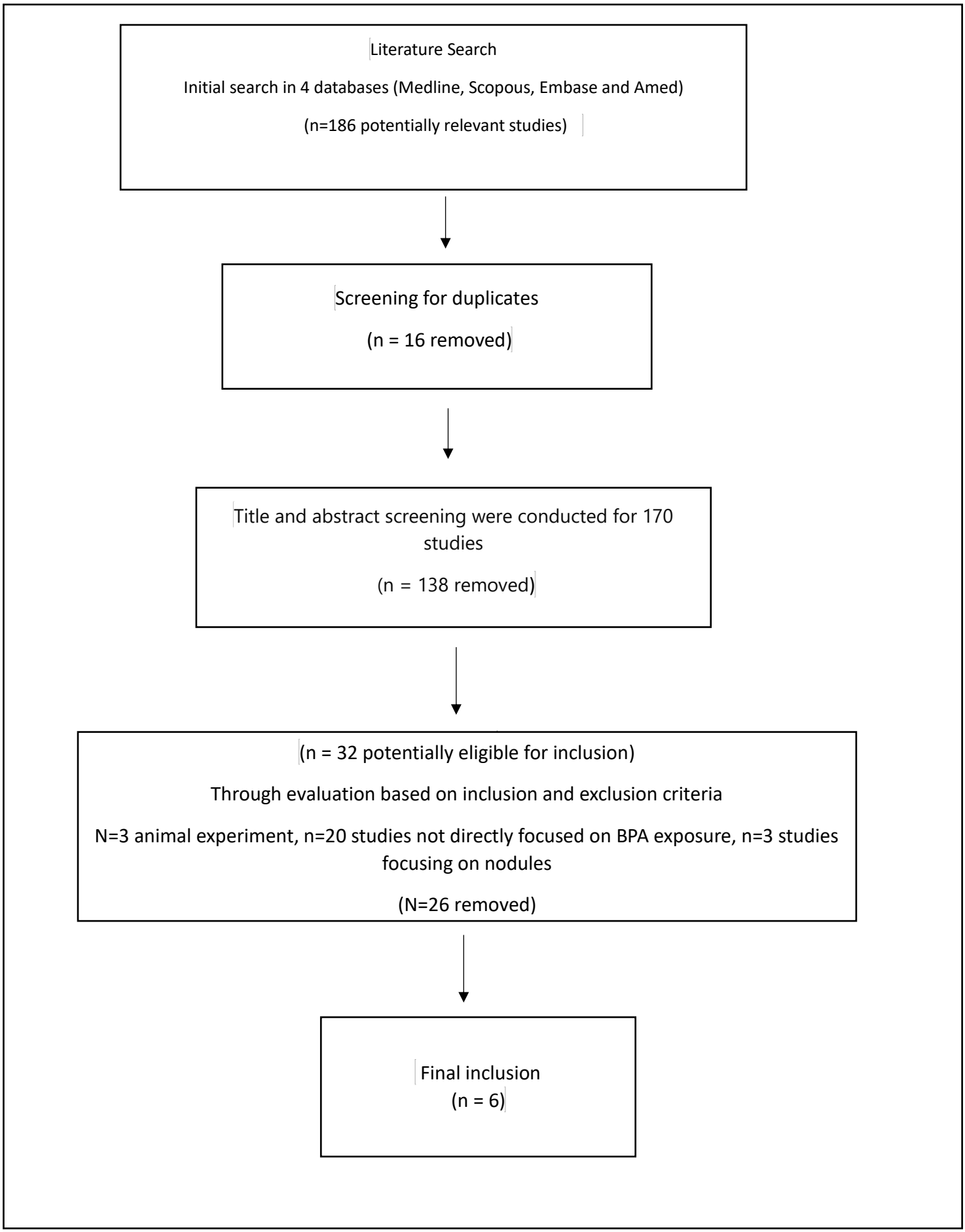
Amed: N=1). After removing duplicates (N=16), 170 research studies were scanned. Following the initial title/abstract screening, 32 literature studies were identified as potentially eligible. Subsequently, a thorough evaluation based on the inclusion and exclusion criteria was performed, leading to the exclusion of 3 animal experiments, 20 studies not directly focused on BPA exposure, and 3 studies that specifically focused on nodules, which are rare and not directly related to cancer. Finally, 6 original studies met the criteria for inclusion in this systematic review. PRISMA flow chart detailing the literature screening process is represented below in Figure I.

Figure I. PRISMA Flow Chart



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Characteristics of Included studies.

The included studies demonstrated variations in sample sizes, ranging from 95 to 367 participants. Out of the 6 studies, 3 were cross-sectional studies (Zhou et al., 2017), (Marotta et al., 2019), (Marotta et al., 2023). Two studies were case-control studies (Li et al., 2021) and (Chen et al., 2022). Additionally, one study adopted a cross-sectional case-control design: (Zhang et al., 2023). The type of (EDCs) Investigated in these studies included BPA, BPS, BPF, DEHP, MEHP, BPAF, BPE, TCS and TCB. Regarding the assessment of (EDCs) exposure, three studies utilized blood samples (Li et al., 2021), (Marotta et al., 2019), and (Marotta et al., 2023). Two studies relied on urine samples (Zhang et al., 2023) and (Chen et al., 2022), while one study employed both urine and blood samples (Zhou et al., 2017). Geographically, four studies were conducted in China (Zhang et al., 2023), (Zhou et al., 2017), (Li et al., 2021) and (Chen et al., 2022), whereas two studies were carried out in Italy: (Marotta et al., 2019) and (Marotta et al., 2023). Comprehensive overview of the characteristics of the included studies is presented in Table II.

Table II. Basic characteristics of the included studies.

Author/Year and Country	Study Design and Duration	Sample Size / Age / Gender	Case/Control	Type of Endocrine-disruptor Chemicals (EDCs) Investigated	Methods Used to Assess EDCs Exposure
Marotta, V. et al. (2019)/Italy	Multicenter, cross-sectional study 4 months	n=55 patients (≥18, Range 19-77 yrs), 18 males and 37 females	27 with benign nodules (control), 28 with Differentiated Thyroid Cancer	Bisphenol AF and Diethylhexylphthalate (DEHP) , BPA, BPS, BPF, BPE, BPB, BPAF, BPDGE	Blood samples from the antecubital vein (5 mL)

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Marotta, V. et al. (2023)/Italy	Multicenter, cross-sectional 24 months	n=96 patients (≥18 years, Range 19–77 yrs), 30 males and 66 females	55 benign nodules, 41 thyroid cancers, 28 normal weight, and 68 overweight/obese	Bisphenol A, phthalates (PHTs) diethylhexyl phthalate (DEHP), and its monoester metabolite mono (2-ethylhexyl) phthalate (MEHP)	Blood samples from the antecubital vein (5 mL)
Zhang, L. et al. (2023)/China	Cross-sectional case-control study 4 months	n= 222 participants, mean age 42.5 yrs, 50 males and 172 females	Non-Papillary Thyroid Cancer = 111, Papillary Thyroid Cancer = 111	Bisphenol A, bisphenol F, and bisphenol S	Urine samples (5 mL)
Chen, P.-P. et al. (2022)/China	Case-control study 9 months	N=367 cases, (264 females, 103 males)	<30 = 40, 30-50 = 161, ≥50 = 166	Triclosan (TCS), bisphenol A, bisphenol AF, bisphenol F, bisphenol S	Urine samples (0.5 mL
Li, L. et al. (2021)/China	Case-control study 17 months	N=95 participants, <50 yrs = n= 48, ≥50 yrs = n= 47	45 Papillary Thyroid Cancer patients (9 males, 36 females), Control 50 (11 males, 39 females)	Bisphenol A (BPA)	Venous blood (5 mL)
Zhou, Z. et al. (2017)/China	Cross-sectional study 7 months	N=178 participants male = n= 50, female = n= 128	53 Papillary Thyroid Cancer group, 60 Nodule Goiter group, and 65 healthy control group	Bisphenol A (BPA)	Blood and spot urine samples were collected

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BPA exposure and thyroid cancer

Six studies, encompassing a total sample size of n= 1013, were conducted in two countries (China and Italy) as presented in Table 1. All of these studies investigated the association between BPA exposure and thyroid cancer. Among them, three studies focused on a specific type of cancer, PTC: (Zhang et al., 2023), (Zhou et al., 2017), and (Li et al., 2021). One study examined differentiated thyroid cancer (DTC): (Marotta et al., 2019), one studied thyroid nodules: (Marotta et al., 2023), and one looked into thyroid cancer in general: (Chen et al., 2022).

The study conducted by (Zhang et al., 2023) observed that individuals with higher BPA exposure had a lower risk of developing PTC, suggesting that BPA exposure might have a protective effect against the development of PTC (OR 0.38; 95% CI 0.19-0.77; p=0.006). However, the study by (Marotta et al., 2019) did not find a statistically significant association between BPA exposure and DTC (OR 3.71; 95% CI 0.67-20.34, p=0.142).

The other 3 studies by (Marotta et al., 2023), (Chen et al., 2022), (Li et al., 2021), and (Zhou et al., 2017) showed significant increase in Odds Ratio (Table 2) suggesting that BPA exposure may act as a risk factor for the development of thyroid nodules, papillary thyroid cancer (PTC), or thyroid cancer. Additionally, (Chen et al. 2022) revealed that oxidative stress is a significant contributing factor to the formation and progression of cancer, wherein the urinary 8-isoPGTF2 plays a mediating role in this association. The details of the association between BPA and thyroid cancer are presented in Table III.

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Table III**: Association between BPA exposure and thyroid cancer**.

Stud(year) and /country	Type of Cancer	Methods Used to Assess EDCs Exposure	Sample size	Odd ratio (OR)	95% Confidence interval (CI)	P- value
Marotta et al. (2019), Italy	differentiated thyroid cancer (DTC)	Blood samples from the antecubital vein (5 mL)	Total 55, 18 males, 37 females	3.71	0.67-20.34	0.142
Marotta, V. et al. (2023)/Italy	thyroid nodules	Blood samples from the antecubital vein (5 mL)	Total 96, 30 males, 66 females	5.3	1.07–26.18	0.028
Zhang et al. (2023), China	Papillary Thyroid Cancer (PTC)	Urine samples (5 mL)	Total 222, 50 males, 172 females	0.38	0.19-0.77	0.006
Chen et al. (2022), China	Thyroid Cancer	Urine samples (0.5 mL	Total 367 male103, female 264	1.78	1.12-2.84	0.015
Li, L. et al. (2021)/China	Papillary Thyroid Cancer (PTC)	Venous blood (5 mL)	Total 95, 20 males, 75 females.	57.8% of the patients (26/45) were concluded to harbour the BRAFV600E.		
Zhou, Z. et al. (2017)/China	nodular goiter (NG) and papillary thyroid carcinoma (PTC	Blood and spot urine samples were collected	Total 178, male 50, female 128	- Bisphenol A(BPA) concentrations (UBC) were significantly higher in both the non-goiter (NG) and papillary thyroid carcinoma (PTC) groups compared to the healthy control group. - Serum BPA concentrations did not show any significant differences between the groups.		

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BPS exposure and thyroid cancer

The association between BPS and Thyroid cancer was investigated in three studies: (Zhang et al., 2023), (Marotta et al., 2019), and (Chen et al., 2022). Among these studies, (Zhang et al., 2023) and (Chen et al., 2022) reported a significant potential protective effect of BPS exposure against the development of PTC and TC. However, (Marotta et al., 2019) found no statistically significant relationship between BPS exposure and DTC (OR 10.1; 95% CI 0.51 -197.32); p=0.111) [18]. Table IV below shows the Association between BPS and Thyroid cancer.

Table IV: The association between BPS and Thyroid can**cer**

Stud(year) and /country	Type of Cancer	Methods Used to Assess EDCs Exposure	Sample size	Odd ratio (OR)	95% Confidence interval (CI)	P- value
Marotta et al. (2019), Italy	differentiated thyroid cancer (DTC)	Blood samples from the antecubital vein (5 mL)	Total 55 18 males, 37 females	10.1	0.51-197.32	0.111
Zhang et al. (2023), China	Papillary Thyroid Cancer (PTC)	Urine samples (5 mL)	Total 222, 50 males, 172 females	0.63	0.43-0.93	0.02
Chen et al. (2022), China	Thyroid Cancer	Urine samples (0.5 mL	Total 367 female 264, male103	0.55	(0.34-0.88)	0.012

BPF exposure and thyroid cancer

The association between BPF and Thyroid cancer among the same studies is mixed. (Zhang et al., 2023) observed a statistically significant positive association between BPF exposure and PTC, indicating an increased risk (OR 1.80; 95% CI 1.27-2.54;

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p=0.001). However, (Marotta et al., 2019) and (Chen et al., 2022) did not find statistically significant associations with DTC and overall thyroid cancer, respectively (Table V).

Table V: the association between BPF and Thyroid cancer

Stud(year) and /country	Type of Cancer	Methods Used to Assess EDCs Exposure	Sample size	Odd ratio (OR)	95% Confidence interval (CI)	P- value
Marotta et al. (2019), Italy	differentiated thyroid cancer (DTC)	Blood samples from the antecubital vein (5 mL)	Total 55, 18 males, 37 females	5.18	0.23-111.22	0.490
Zhang et al. (2023), China	Papillary Thyroid Cancer (PTC)	Urine samples (5 mL)	Total 222, 50 males, 172 females	1.80	(1.27–2.54)	0.001
Chen et al. (2022), China	Thyroid Cancer	Urine samples (0.5 mL	Total 367, male103, female 264	0.73	(0.47-1.14)	0.169

DEHP exposure and thyroid cancer

The association between DEHP and thyroid cancer was explored in two studies: (Marotta et al., 2019) and (Marotta et al., 2023). Both studies reported statistically significant positive associations between DEHP exposure and thyroid conditions albeit with wide confidence intervals, specifically DTC and thyroid nodules, respectively. The results suggest that higher DEHP exposure may be linked to an increased risk of developing these thyroid conditions (Table VI).

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Table VI: The association between DEHP and Thyroid cancer						
Stud(year) and /country	Type of Cancer	Methods Used to Assess EDCs Exposure	Sample size	Odd ratio (OR)	95% Confidence interval (CI)	P- value
Marotta et al. (2019), Italy	differentiated thyroid cancer (DTC)	Blood samples from the antecubital vein (5 mL)	Total 55 18 males, 37 females	14.44	1.69-122.98	0.005
Marotta, V. et al. (2023)/Italy	thyroid nodules	Blood samples from the antecubital vein (5 mL)	Total 96 30 males, 66 females	13.74	2.91–64.89	<0.001

MEHP exposure and thyroid cancer

The same two studies also investigated the association between MEHP and Thyroid cancer, but reported different results. While (Marotta et al., 2019) did not find a statistically significant association with DTC (OR 3.19; 95% CI 0.85-11.87; p=0.121), (Marotta, V. et al., 2023) found a borderline statistically significant positive association with thyroid nodules (OR 2.65; 95% CI 1.01-6.94; p=0.043) [19]. Table VII shows the association between MEHP and Thyroid cancer.

Table VII: The association between MEHP and Thyroid cancer						
Stud(year) and /country	Type of Cancer	Methods Used to Assess EDCs Exposure	Sample size	Odd ratio (OR)	95% Confidence interval (CI)	P- value
Marotta et al. (2019), Italy	differentiated thyroid cancer (DTC)	Blood samples from the antecubital vein (5 mL)	Total 55 18 males, 37 females	3.19	0.85-11.87	0.121
Marotta, V. et al. (2023)/Italy	thyroid nodules	Blood samples from the antecubital vein (5 mL)	Total 96 30 males, 66 females	2.65	1.01–6.94	0.043

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Exposure of remaining EDCs

The remaining EDCs, including BPAF (Bisphenol AF), BPE (Bisphenol E), TCS (Triclosan), and TCB (Tetrachlorobiphenyl), were individually investigated by single studies. (Marotta et al., 2019) conducted a study on the association between BPAF exposure and Differentiated Thyroid Cancer (DTC), revealing a statistically significant positive association with an odds ratio (OR) of 14.44, 95% confidence interval (CI) of 1.69 to 122.98, and a p-value of 0.005. Additionally, (Marotta et al., 2019) also investigated the link between BPE exposure and Differentiated Thyroid Cancer (DTC), and reported a statistically significant positive association with an OR of 4.9, 95% CI of 1.17 to 20.47, and a p-value of 0.028. Furthermore, (Chen et al., 2022) explored the association between TCS exposure and Thyroid Cancer, reporting a statistically significant positive association with an OR of 1.92, 95% CI of 1.21 to 3.06, and a p-value of 0.006. These findings collectively suggest that BPAF, BPE, and TCS exposures may be linked to an increased risk of DTC or Thyroid Cancer.

Quality assessment

Using the JBI assessment tool for assessing the quality of the included studies, all six studies compared well in terms of the groups in terms of age and gender. However, in terms of specific matching criteria, the use of consistent identification criteria for cases and controls were not mentioned, resulting in ‘unclear’ category. Nevertheless, all included studies made efforts to address potential confounding factors by excluding individuals with specific medical conditions and assessing modifications in variables affecting EDCs. All studies also employed strategies like self-reporting questionnaires to deal with confounding factors. All studies, except for (Li et al., 2021) and (Zhou et al., 2017), appropriately applied statistical analysis, with the exception that these two studies lacked impact measurements (such as odds ratios or relative risks) for the relevant association.

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DISCUSSION

The findings from the six included studies offer insightful information on the potential contribution of EDCs to the emergence of thyroid cancer and emphasized the need for additional research in this area. This systematic review found that several EDCs, including phenols, BPA, BPF, and BPS, were linked to a higher risk of PTC as substantiated by other literature review (Kruger et al., 2022). The findings that are held across numerous research add weight to the argument that thyroid cancer risk and EDC exposure may be related. These findings are significant given the prevalence of these chemicals in everyday products and their potential to interfere with the body's hormonal systems (Diamanti-Kandarakis et al., 2009). In spite of the recognition, it is worth noting the paucity of studies in this area and explored only in a few countries.

The analyzed studies used various techniques, including determining the EDC concentrations in blood and urine samples. The reliable and validated EDC assessment techniques that confirmed the link between thyroid cancer risk and EDC exposure strengthen the research findings. Other research also examined how exposure to EDC and genetic variables, such as the BRAFV600E mutation interacted (Woodruff, 2011) and they reported that the interaction between genetic mutations and EDC exposure may raise the risk of thyroid cancer and PTC in particular. Understanding these connections is essential for locating high-risk groups and creating individualized preventative plans (Gore et al., 2015). This review also emphasized the importance of oxidative stress biomarkers as potential mediators of the effects of EDCs on thyroid cancer development, including 8-hydroxy-2-deoxyguanosine (8-OHdG) and 8-iso-prostaglandin F2 (8-isoPGF2). These findings offer insights into the biological mechanisms by which EDCs may cause cancer, which may help develop focused therapies to lessen their negative effects (Fiore et al., 2019).

Nevertheless, despite the evidence reported from the studies, there are some limitations that need to be acknowledged. Variations in study designs, sample sizes,

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and participant characteristics could explain variations across different studies (Modica, Benevento, & Colao, 2023) and these differences may introduce some level of inconsistency in the findings and make it challenging to draw definitive conclusions from the collated data. In addition, the cross-sectional design hinders their ability to establish a causal relationship between EDC exposure and thyroid cancer risk. Absence of a standardized method to evaluate EDC exposure, may add bias and make results difficult to compare (Wang & Qian, 2021). Furthermore, it is crucial to acknowledge that both the screening and data extraction were conducted by a single individual (only double checked by the other author), which could potentially introduce bias and limitations in the study's methodology. Additionally, the fact the data are sourced from only two countries and a limited number of studies, raises concerns about the generalizability of these findings. However, it highlights the need for future research. To address these limitations and provide more conclusive evidence of the link between EDC exposure and thyroid cancer risk, it is advisable to conduct case-control studies using larger datasets, implement long-term follow-ups, and extend research to other countries. (Vagi et al., 2017).

This review suggests that exposure to specific EDCs may be linked to a higher risk of PTC. Convincing evidence for the need to address EDC exposure in the context of thyroid cancer prevention and public health measures is provided by the consistent findings. Nevertheless, more investigation is required to pinpoint a link and comprehend the intricate interplay between EDCs, hereditary variables, and the chance of developing thyroid cancer. Expanding the knowledge in this field will contribute to the development of efficient preventative measures and regulations to protect the health of the community which is exposed to various toxins in everyday life (Kiess, Häussler, & Vogel, 2021). It is critical to implement regulatory measures aimed at reducing EDC exposure to safeguard populations at risk for thyroid cancer. The implications of these findings have significant relevance for shaping public health policies and initiatives.

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Conclusion

There is a possible connection between thyroid cancer risk and EDC exposure including phenols, BPA, BPF, BPS, and others with potential function of biomarkers for oxidative stress in modulating the effects of EDCs on thyroid cancer development. It is crucial to remember that the study involved both male and female participants and individuals from various age groups and body mass index (BMI) classifications.

Future research should explore this association in larger datasets in other contexts and geographical regions exposed to higher levels of EDCs. It is imperative to comprehend the involvement of EDCs in the emergence of thyroid cancer in order to focus on preventative strategies and promote public health initiatives to reduce exposure to hazardous chemicals.

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Appendix 1

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions <1946 to June 09, 2023>

Search Strategy:

1 bisphenol.tw. (13414)

2 (bisphenol adj1 A).tw. (12687)

3 (bisphenol adj1 F).tw. (671)

4 (bisphenol adj1 S).tw. (901)

5 (dibutyl adj1 phthalate$).tw. (1551)

6 Dibutyl Phthalate/ (1599)

7 Triclosan$.tw. (4195)

8 Phenol$.tw. (122897)

9 (bisphenol adj1 AF).tw. (317)

10 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 (140903)

11 Thyroid Neoplasms/ (57101)

12 Thyroid Nodule/ (7692)

13 Thyroid Cancer, Papillary/ (6619)

14 (thyroid adj3 (cancer$ or carcinoma$)).tw. (53978)

15 (Thyroid adj3 (tumor$ or tumour$)).tw. (8651)

16 (Thyroid adj3 neoplasm$).tw. (2526)

17 (Thyroid adj3 malignan$).tw. (6534)

18 11 or 12 or 13 or 14 or 15 or 16 or 17 (78121)

19 10 and 18 (48)