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Research Article

Exploring the Crucial Health Impact of Phthalates on Women: A Critical Review

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ABSTRACT

The exposure of women to phthalate esters has emerged as a significant concern, given its potential threat to their health. Exposure to phthalates can be detrimental to health, especially for women who are more susceptible due to spending a significant amount of time indoors. This review aims to address the health risks associated with phthalates in women, encompassing conditions such as breast cancer, endometriosis, obesity, diabetes, respiratory diseases, ovarian dysfunctioning, coronary heart disease, and liver toxicity, among others. It further elucidates the properties and applications of phthalates and routes of exposure. In addition, this review delves into the impact of phthalates in various phases of the steroidogenic process and helps identify the proper mechanisms to regulate phthalate exposure and increase awareness of the health risks associated with phthalic acid esters.

Key words: Breast cancer, Coronary heart disease, Endometriosis, Ovarian dysfunctioning, Phthalates, Women's health.

1. INTRODUCTION

When we discuss phthalate esters, we usually refer to dialkyl esters of phthalic acid. The word "phthalate" comes from "naphthalene," which also relates to phthalic acid. In polymer science, phthalates are particularly valued for their ability to facilitate the sliding of polyvinyl chains, thereby enhancing the flexibility and processability of plastics. Chemically, phthalates are odorless, colorless liquids that less soluble in water but soluble in oil. In industries, phthalates are formed by the reaction between phthalic anhydride and alcohol in the presence of an acid catalyst, as shown:

Due to their chemical and physical properties, phthalates are widely used in various technical applications. They are used as anti-foaming agents in paper production, and also find applications in dielectrics in capacitors, glues, paints, dyes, additives, and coatings [1]. In addition, they play an important role in the production of plasticizers, which enhance the durability of plastics [2]. Plasticizers derived from phthalic acid esters are widely applied in the production of electronics, automotive parts, food packaging, toys, and textile fibers. This widespread use has expanded significantly over recent decades due to the increased demand for flexible and durable plastic materials [3]. Over four hundred seventy million pounds of phthalate are manufactured and imported each year in the United States [4,5]. Due to their weak chemical bond with plastic material such as polyvinyl chloride (PVC), phthalates easily leach out into the atmosphere during production, storage, and disposal stages [6]. Daily use of various products such as cosmetics [7], toys [8], home furnishings [9], cleaning agents [10], cooking oil [11], and even the air we breathe [12], contributes significantly to the phthalate exposure among individuals [13]. The effect of phthalate on human health has increased global public health attention. Di(2-ethylhexyl) phthalate (DEHP), di-n-octyl phthalate (DiNOP), butyl benzyl phthalate (BBP), diisobutyl phthalate (DiBP), diethyl phthalate (DEP), and dimethyl phthalate (DMP) have been registered as environmental contaminants by the U.S. EPSA (2014) [14]. Phthalates have been identified as endocrine-disrupting compounds because they interfere with the hormones present in the human body and affect reproduction system [15], placental development [16], and homeostasis [17]. According to Mariana *et al*. [18], phthalates can disrupt hormones, causing different types of health problems in women, fetuses, and children [19,20]. Phthalate esters (PAEs), even at low concentrations, have the potential to alter human biological processes and increased risks of cancer [1,21], fetal harm [22], and mutations [21,23]. As per Heindel *et al*. and Gray *et al*. [23,24], phthalate analogues with two to eight carbon atoms exhibit developmental toxicity with varying potency. Dibutyl phthalate (DBP) and DEHP have been identified as disruptors of the endocrine system based on experimental evidence. Usually, these chemicals do not bind together the androgen and estrogen receptors due to their intricate mechanisms of action. DEHP reduces ovary estradiol synthesis in mature females by preventing the enzymatic aromatase's transcription and causes ovulation and fertilization [25].

Importantly, women are more vulnerable to phthalates exposure because they spend approximately 70% of their time indoors and typically have higher levels of certain hormones, such as estrogen, compared to men, which may enhance susceptibility to endocrine-disrupting effects [26,27]. Therefore, this review aims to provide a comprehensive overview of exposure to phthalate on women, focusing on their health impacts, mechanisms of action, and associated risk assessments [Figure 1].

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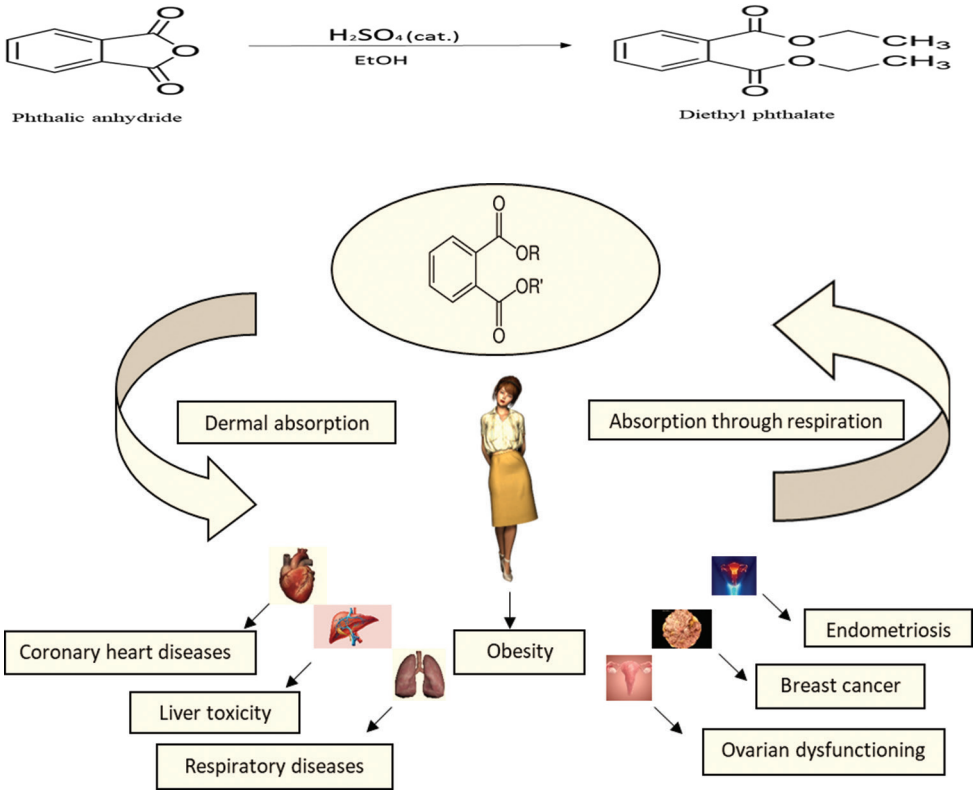

Figure 1: Effect of phthalates on women.

2. ARTICLE SELECTION PROCESS

The PubMed database search engine was utilized to conduct a literature search on the health effects of PAEs. 4,248 selected articles were obtained from the first search; the chosen articles were published between 1990 and 2025. In summary, the overall number of phthalate-related research articles shown in [Figure 2] linked to the following health problems was 1335: respiratory disease (190), obesity (325), liver toxicity (362), coronary heart disease (12), diabetes (256), breast cancer (BC) (129), and endometriosis (61). The initial investigation of abstracts and titles was conducted to reduce the total number of potentially relevant papers to 452 articles. After reviewing and assessing the remaining potentially eligible full papers, 152 articles were ultimately included. The highest percentage of papers involving phthalate exposure published until July 2023 was related to BC and liver toxicity.

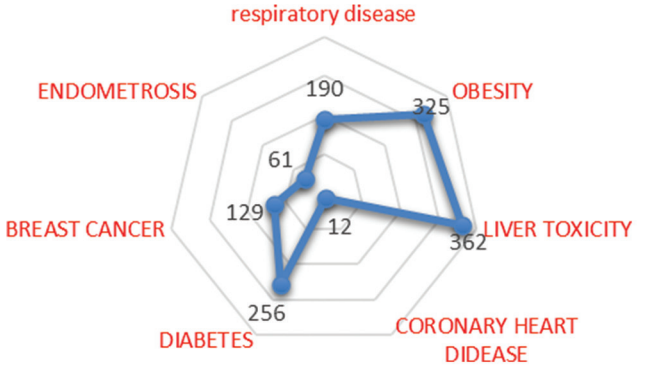

Figure 2: Overall number of phthalate-related research articles.

3. WOMEN'S EXPOSURE

Phthalates are synthetic chemical compounds found in various sources, including food, water, air, soil, dust, and clothing. Women's body can absorb phthalates through various routes, that is, oral ingestion, inhalation, and transdermal absorption. Notably, these chemical compounds are capable of crossing the placental barrier, thereby posing risks to fetal and neonatal development [28].

Women are exposed to phthalates through numerous sources of everyday items, such as food packaging [29], plastic bottles, cooking aids (utensils etc.) [30]. Indoors air, dust, scents products, etc., contribute to inhalation exposure. While dietary supplements, medical tools (bags, tubes, implants, containers, etc.) are additional sources. Beauty products such as fragrances, creams, deodorants, shampoos, nail polish, hair dyes, etc. [7], introduce phthalates directly to dermal absorption. Phthalates are also present in clothing (artificial leather, waterproof clothing, gloves, footwear, ornaments, etc.), playthings (putting in mouth, rubbing, playing), denture prosthesis materials (soft liners, molds, etc.), building supplies, automotive components [8,9,12].

Wang *et al*. [31] discovered that the primary pathway for most PAEs entering the body is oral or dietary exposure through food ingestion [32]. However, besides this, there are two additional ways by which phthalates can enter women's bodies that are inhalation and dermal absorption [33].

The packaging materials used for various foods serve as a major source of phthalate contamination [34]. Cirillo *et al*. [35] observed that cooked foods had increasing amount of di(n-butyl) phthalate (DnBP) and DEHP both before and afterward packaging, with rises 125% and 113%, consecutively. These findings suggest that DEHP and DnBP are the most common plasticizers used in food packaging, and phthalates have the potential to transfer from food containers into food.

In urban environments, phthalates are recognized as predominant semi-volatile organic compounds (SVOCs), as demonstrated in a

Paris-based study measuring 58 SVOCs in both indoor and outdoor air [36]. Studies have shown that in urban areas concentration of phthalates in indoor air is higher than outdoor air, primarily because indoor environments serve as direct sources and phthalates degrade more rapidly outdoors [37,38]. Phthalate concentrations were higher in urban areas than in suburban or forest areas across various locations [38]. Contributing factors include increased plastic production and use, human activities, and environmental conditions that cause phthalates to volatilize, significantly raising their levels in urban atmospheric deposits.

Overall, women can be exposed to phthalates through a combination of personal care items, cosmetics [7], food packaging [29], medical devices [39], cooking oil [12], inhalation, and dermal absorption [11].

4. PHTHALATES METABOLISM IN THE WOMEN

As phthalate enter the body, they undergo hydrolysis and conjugation reactions before being excreted through feces, perspiration, and urine [40]. Initially, phthalates are indeed hydrolyzed into their primary metabolite monoester phthalates by esterases and lipases present in the parenchyma and intestines. This process is important for the metabolism of phthalates [41,42]. The hydrolytic monoester can undergo subsequent oxidation reactions that may alter its carbon chain. Another interesting point is that glucuronic acid can be employed to conjugate the hydrolytic monoester and oxidized secondary metabolites, which will eventually be excreted from the body through urine. Mono-methyl phthalates and mono-ethyl phthalate, respectively, are hydrolyzed metabolites of DEP and DMP, which are hydrophilic and are emitted without undergoing oxidation. DiBP and DnBP are primarily released with hydrolyzed monoesters (around eighty-four percent and seventy percent, respectively, of the given dosage), and their overall fraction in the urine of humans is around ninety percent within 24 h of oral administration [43,44].

The metabolic pathway of high molecular weight phthalates, like DEHP, is complex due to its branched chain. In the first step of metabolism, DEHP is hydrolyzed to mono (2-ethylhexyl) phthalate (MEHP) catalyzed by unspecific lipase [45]. Then, MEHP is further oxidized to 5oxo MEHP or 5ox MEPP. Excretions only contain a small percentage of their metabolites, while the 24 h excretion rate decreases with an increase in molecular mass [46]. Phthalates and their biochemical routes are shown in Figures 3 and 4, while several studies have found PAEs in saliva, breast milk, amniotic fluid, and the circulatory system [47,48]. Furthermore, PAEs have been discovered in fetal meconium [49] and adipose tissue of adults connected to human hair at less concentration [50].

5. EFFECT OF PHTHALATES ON THE WOMEN BODY

Phthalates are chemicals that do not bond to polymer molecules covalently. These chemicals can easily be leached into the atmosphere and pose threaten human health due to environmental pollution. According to Golestanzadeh *et al*. [51], phthalates can cause several diseases in women. Phthalates have both genomic and non-genomic effects [44]. The genomic effect causes hypermethylation, hypomethylation, and aromatase [52].

5.1. Endometriosis

Endometriosis is a disorder marked by the presence of endometrial-like tissue on the uterine surface or frequently found within the peritoneal cavity, affecting 6–10% of women of motherhood age. An increasing amount of evidence has shown that phthalates may have had a role in the etiology of endometriosis over the past decade [53]. Endometriosis affects approximately 15% women of reproductive age, rendering it one of the most prevalent illness [54,55]. Dyspareunia, persistent pelvic discomfort, dysmenorrhea, and menorrhagia – all of which can result in infertility addressed [56]. Numerous researches have suggested associations between PAEs exposure and endometriosis. This condition, arising from the aberrant development of tissue outside the uterus, can result in infertility, ovarian cancer, ovarian cysts, pelvic discomfort, and hormonal issues within the peritoneal cavity and endometrium [57]. Exposure of phthalates may contribute to the onset of endometriosis by increasing proliferative and invasive activities of endometrial cells [47]. According to several studies, women with endometriosis were exposed to endocrine-disrupting chemicals (EDCs), such as DEHP and DiBP metabolites. Although some researchers hypothesised that DEHP boosts the viability of endometrial cells, oxidative stress, and invasive potentially leading to the development of endometriosis [58]. Phthalates may be linked to the development of endometriosis given the increased levels of these compounds in the plasma of endometriosis patients compared to fertile controls [59].

However, additional investigation is necessary to recognize the exposure of DEHP and MEHP, which raise the rate of excretion of prostaglandin F2-α and reduce the excretion of prostaglandin E2 [60]. Oxidative stress is also linked to the endometriosis. Cho *et al*. investigated that endometrial stromal cells exposed to DEHP showed raised levels of a peroxide-sensitive fluorescent marker, indicating increased generation of reactive oxygen species (ROS). This exposure also resulted in decreased expression of key antioxidant enzymes – superoxide dismutase, glutathione peroxidase, heme oxygenase, and catalase – which normally protect cells from ROS-induced damage [61].

Matrix metalloproteinases (MMPs) enzymes are play a key role in the early endometriosis development**.** MMPs are crucial for variable changes in the endometrial cycle, particularly through vascular formation and tissue remodeling [62]. Kim *et al*. found that DEHP treatment significantly enhanced MMP-2 and MMP-9 activity in cultured endometrial cells [63]. Moreover, DEHP exposure was shown to raise the phosphorylation levels of extracellular-signal-regulated kinase (Erk) and boost the expression of p21-activated kinase-4. These molecular changes are allied with increased cellular proliferation and a heightened resistance to apoptosis – both key features in the pathophysiology of endometriosis [63,64].

DEHP interacts with peroxisome proliferator-activated receptors, forming a complex with retinoid X receptors within the cytoplasm [Figure 5]. This complex then moves into the nucleus, where it effects the transcription of specific genes [65]. Huang *et al*. found that DEHP vulnerability was linked to increased levels of several inflammation-related markers, including interleukin-1β, interleukin-8, MMP2, intercellular adhesion molecule-1, cyclooxygenase-2, and peroxisome proliferator-activated receptor gamma (PPARγ). Their findings suggest that DEHP may trigger an inflammatory cascade through pathways mediated by PPARγ [66,67]. Human endometrial cells from the eutopic endometrium of patients with endometriosis showed increased expressions of aldo-keto reductase (AKR) 1C1, AKR1C2, AKR1C3, and AKR1B10 after exposure to DEHP, so they may play a role in the development of endometriosis through the resistance to progesterone and prostaglandin synthesis [68].

5.2. Ovarian Dysfunction

Research has revealed that women in their reproductive stage have higher levels of mono-ethyl phthalate (MEP), mono-n-butyl phthalate (MBP), MEHP, and mono-benzyl phthalate (MBzP) in their bodies compared to men [69,70]. This is likely because men use less cosmetic and personal care items, such as lotion, nail polish, hairspray, and

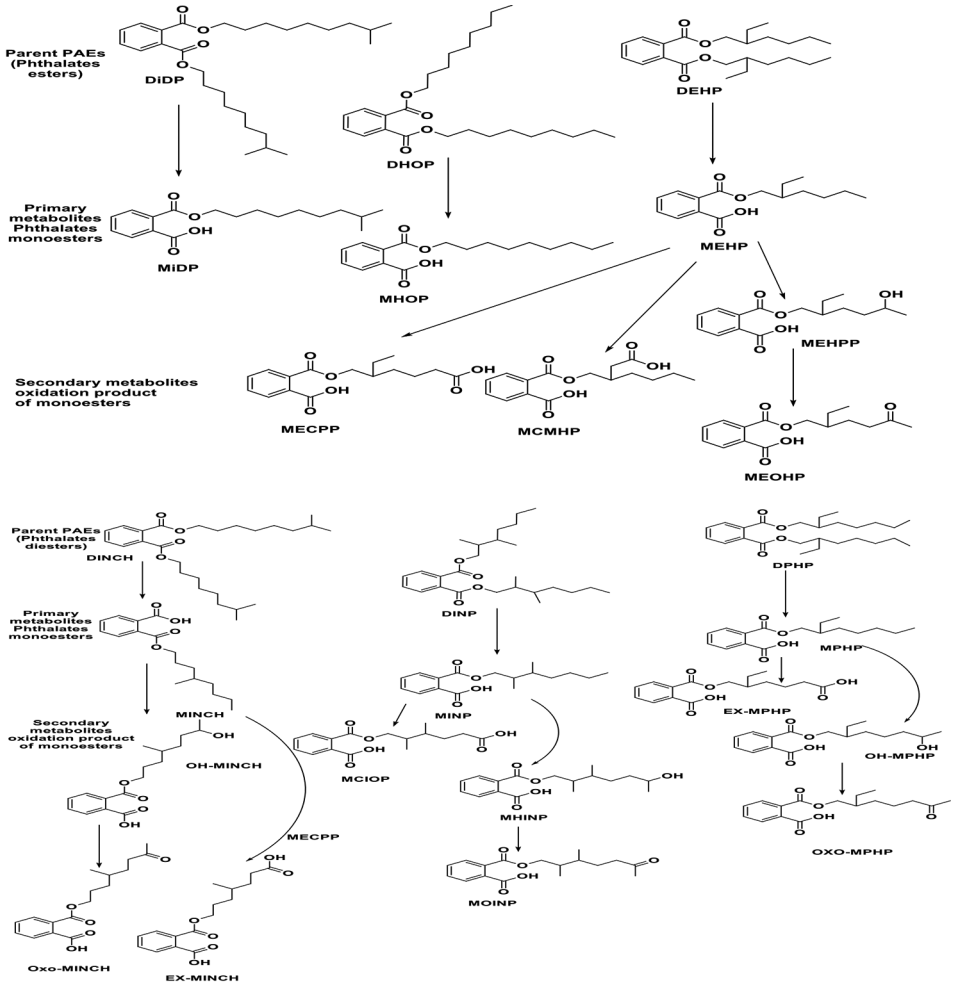

Figure 3: Metabolism of high molecular weight phthalate.

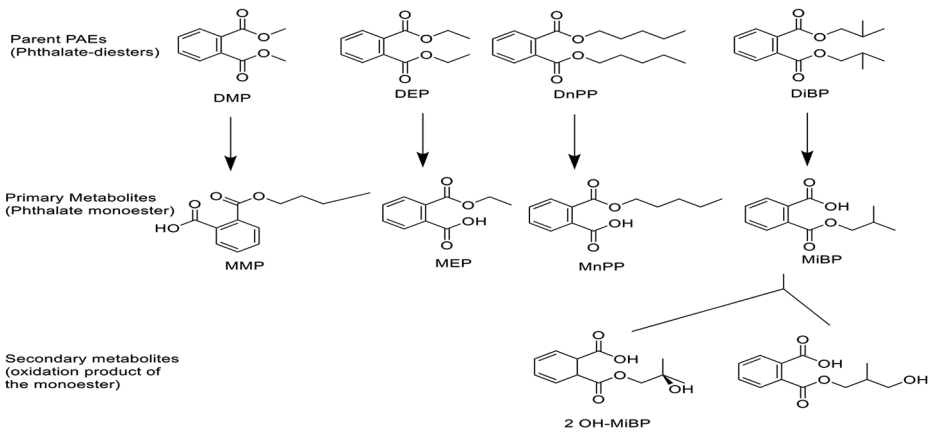

Figure 4: Metabolism of Low molecular weight phthalate.

perfume, as compare to the women, which contain phthalates, particularly MBP [71]. Studies have shown that phthalates can affect female reproductive health, causing defects in folliculogenesis and steroidogenesis, leading to non-reproductive disorders, increased pregnancy complications, miscarriages, infertility, and a diminished ovarian reserve [72,73]. While the impacts of phthalates on follicle development are still being studied, it has been suggested that they can disrupt the initial phases of folliculogenesis and influence ovarian and oocyte development [74,75]. There is evidence to suggest that DEHP exposure during sexual development can inhibit oocyte formation [76]. Proper guideline of ovarian steroidogenesis is essential for reproductive as well as non-reproductive health. However, various studies have shown that phthalates can dysregulate steroidogenesis in multiple ways. Specifically, phthalates have been found to interfere with the synthesis and release of several sex steroid hormones in both *in vitro* and *in vivo* systems, leading to a reduction in estradiol levels [33,34]. Moreover, phthalates have a direct negative impact on the generation of steroid hormones by targeting several steroidogenic

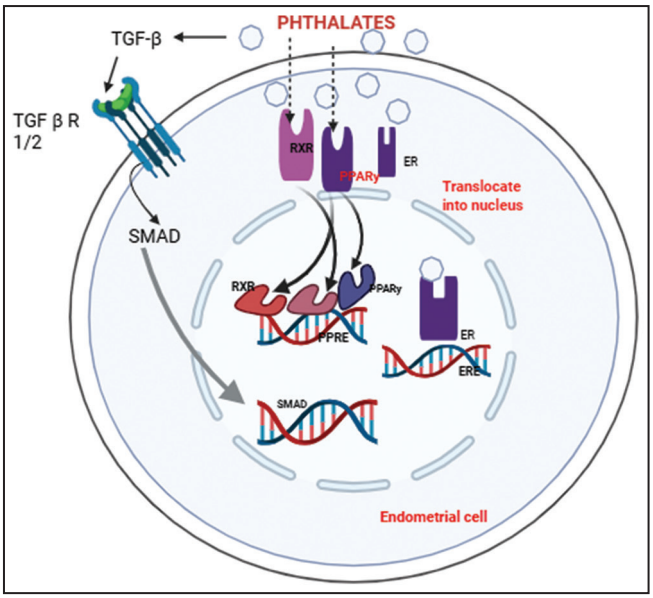

Figure 5: The action of phthalate on endometrial cell.

cell types in the ovary [77]. Figure 6 shown how these phthalates (DEHP, MEHP, DBP, BBP) affect ovary. When DEHP comes in contact with the ovary, it increases the levels of cholesterol hormones produced by the ovary [78]. Progesterone, a sex hormone crucial for pregnancy, is affected by DEHP, MEHP, DBP, and BBP, which decrease its levels in the ovary and can lead to difficulties in pregnancy [79]. Testosterone, converted into estradiol, plays a role in the development and rebuilding of reproductive tissues in women. However, DEHP and its metabolites (MEHP) decrease its levels [80], as shown in Figure 6.

Primary ovarian insufficiency is the decline in ovarian function in women under the age of 40. Detection of primary ovarian insufficiency is made with the presence of menstrual irregularity for at least 4 months and the indication of low concentration of estrogen and high concentration of follicle-stimulating hormone [81]. The POI is primarily caused by a lack of information about potential underlying causes. In this regard, the probable impact of the environmental aspects, such as exposure to endocrine-disrupting compounds is emphasized. A recent retrospective study by Du *et al*. [82], suggests that phthalate exposure may impair granulosa cell development and, as a result, reduce ovarian reserve, as indicated by an observed inverse association between urinary phthalate levels and inhibin B. Research has shown that phthalates can exert antioestrogenic, antiandrogenic, anti-progestogenic, and antithyroid effects. Modern lifestyles contribute to continual exposure to complex mixtures of harmful environmental agents and EDCs, which can accumulate in bodily tissues and fluids. This persistent exposure, especially during sensitive developmental windows, poses significant threats to reproductive health [83]. Özel *et al*. [84] conducted Prevalence as well as case-control studies involving 30 women diagnosed with Primary ovarian insufficiency and 30 healthy, fertile controls. Their analysis of serum phthalate diesters showed high concentration of certain phthalate metabolites – particularly mono-n-butyl phthalate (MnBP) – in women with Primary ovarian insufficiency. Based on these findings, the researchers observed that MnBP could indicated a notably risk factor in the development of primary ovarian insufficiency. Furthermore, high urinary levels of MiBP were linked to reduced estrogen levels and increased follicle-stimulating hormone levels, recommended a disruption in endocrine feedback mechanisms. In conclusion, phthalates appear to promote the development of Primary ovarian insufficiency, potentially through disruptions in the hypothalamic–pituitary–ovarian axis or by directly affecting ovarian cells. Further, research has shown that higher levels of urinary phthalate metabolites are linked with an earlier starts of menopause [85]. These conclusions emphasized the threat posed by environmental contaminants to human reproductive health, as they adversely impact hormonal and reproductive systems. Addressing this issue requires equipping healthcare professionals to identify individuals at risk for primary ovarian insufficiency, support their reproductive planning, and minimize exposure to harmful factors [86].

5.3. BC

According to the World Health Organization (WHO) in 2020, BC emerged as the leading health condition among women and approximately 15% of all female deaths occurs due to BC [87]. This complex disease is influenced by various factors, such as PAEs, pesticides, C_6H_5OH, and Hg, etc. [88]. PAEs are a type of endocrine disruptor that can potentially affect the production, transport, emission, and binding of hormones in the women's body. Endocrine disruptors can also make cancer cells resistant to chemotherapy. For instance, exposure to PAEs or 4,4'-(propane-2,2-dial)diphenol can trigger the release of proinflammatory factors that lead to doxorubicin-induced cardiotoxicity and chemoresistance. When women exposed to phthalates, BC cells undergo changes in genes that regulate cell cycle and promote cell growth become more active. These changes in gene expression support the growth and survival of cancer cells [25]. Phthalates can also interfere the microenvironment of tumor cells, which is essential for the development of any malignancy. Studies have found a link between phthalates and BC, specifically explaining how MEP and DEP can cause cancer in pre-menopausal women [89,90]. Exposure to DEHP has also been shown to upsurge the invasiveness of MDA-MB-231 BC cells [91], and PAEs such as DEHP, BBP, and DBP have been found to promote cell growth in estrogen-positive BC cell lines [92]. Interestingly, treating cells with phthalates before administering tamoxifen and other BC treatments can lower the mortality of the cell line [25]. Future research can focus on using advanced genomics and *in silico* methods to identify other potential cellular prey and ways to reveal the full structure of the disease progression caused by PAEs in humans. Despite being a significant research problem, this aspect has not been adequately addressed.

5.3.1. MECHANISM OF BC CAUSED BY PHTHALATE

Pathogenesis of BC is a very knotty process. The epigenetic, genes, cellular functional, and microenvironmental changes are responsible for cancerous cell. In BC, activation of proto-oncogenes, deoxyribonucleic acid (DNA) re-arrangement, amplification or loss of functions is responsible for mutation in women body. In BC, inactivation of TP53 and P21 (tumor suppressor gene) is prevalent condition [93]. From of an epigenetic perspective, methyl group are added to DNA, chemical alteration occurs in histone protein, and RNA interference regulates gene expression [94]. Notably, hypermethylation of the BRCA1 tumor suppressor gene is frequently detected in BC, while mutations in BRCA1 and BRCA2 genes are recognized as contributors to BC development in women [95].

Like other carcinogens, phthalate can promote the growth of hormone-dependent cancers, such as BC, by affecting cell proliferation, angiogenesis, and programmed cell death. Phthalate exert their effects through the aryl hydrocarbon receptor (AhR)-cyclic adenosine monophosphate(cAMP)-protein kinase A (PKA)-cAMP-responsive element-binding protein (CREB1) signaling pathway. The AhRa ligand-activated transcription factor, stabilized by heat shock protein 90, becomes activated on exposure to halogenated aromatics, polycyclic aromatic hydrocarbons, and endogenous ligands in a dose-dependent manner. In research, it was found that treatment with benzyl butyl phthalate led to enhanced localization of AhR at the plasma

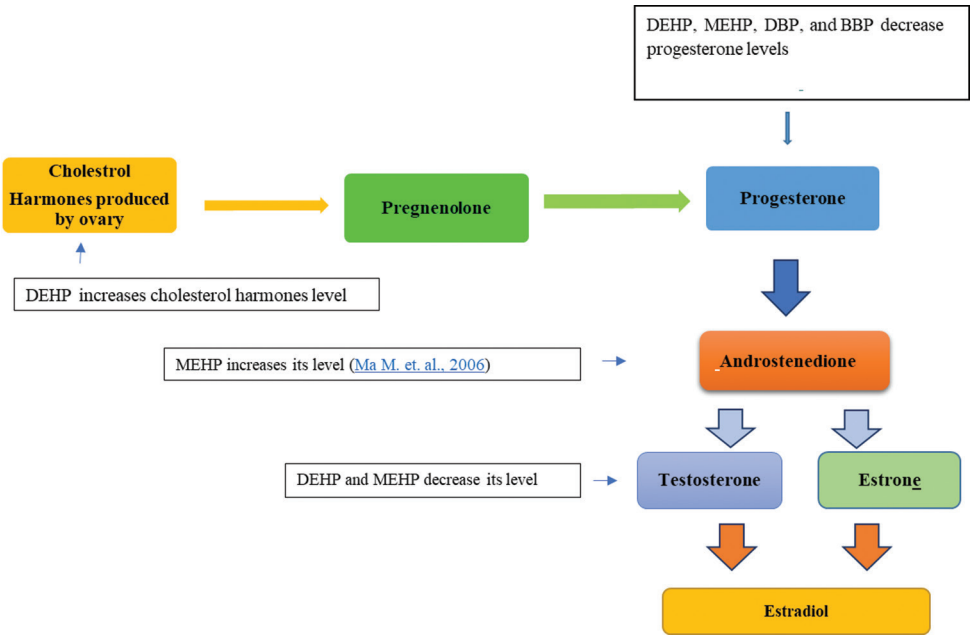

Figure 6: Phthalates influencing the steroidogenic process.

membrane, accompanied by increased cAMP levels and elevated CREB1 phosphorylation, implicating activation of this signaling cascade [96,97].

This cascade promotes the expression of Histone Deacetylase 6, a gene that activates c-Myc through the β-catenin/lymphoid enhancer-binding factor/T-cell factor 4 complex in estrogen receptor-negative BC cells [97]. The activation of c-Myc increases cell growth, proliferation, and tumor growth. Furthermore, AhR activation increases the transcription of CYP1B1, a monooxygenase enzyme involved in xenobiotic metabolism. CYP1B1 convert s estradiol to 4-hydroxyestradiol by the process of hydroxylates, which can be further oxidized to estrogen-3,4-semiquinone – a potent carcinogenic metabolite. The accumulation of these metabolites, along with ROS and subsequent DNA adduct formation, promotes cancer and tumor growth [98,99]. Mechanisms adopted by phthalates to affect the cancer cells are depicted in Figure 7.

5.4. CORONARY HEART DISEASE

Heart problems are currently the foremost cause of mortality worldwide. Researches have shown that phthalates exposure early in life can disrupt metabolic pathways and developmental endocrine processes, leading to adverse cardiovascular profiles. There have been observed correlations between phthalate exposure and circulatory heart diseases, as well as coronary heart diseases [100]. In fact, in the report of WHO, coronary heart disease is the main cause of death worldwide. Other types of pollutants have also been linked to cardiovascular diseases in women, with studies signifying a link between phthalates and these conditions [101]. DEHP, a type of phthalate, can attach to airborne dust particles and be ingested, inhaled or absorbed through the skin from contaminated items [102]. Some researchers believe there may be a connection between the amount of phthalates in our environment [103]. One particular type of phthalate, DEHP, has been related to elevated blood pressure and is considered a risk factor for cardiovascular disease [18]. MEHP is a chemically active metabolite that has been shown to contribute to the pathogenesis of heart disease [26]. When di-(2-ethylhexyl) phthalate (DEHP) enters the body via inhalation or dermal absorption, it undergoes hydrolysis to form metabolites such as MEHP (mono-(2-ethyl-5-hydroxyhexyl) phthalate) and MEOHP (mono-(2-ethyl-5-oxohexyl) phthalate), as shown in Figure 8. The second step is hepatic glucuronic conjugation, which reduces the compounds' potential biological activity and increases their water solubility for excretion from the human body [104]. The majority of DEHP metabolites in urine are in the glucuronidated form. Studies have found that MEHP cusses to the echogenicity of plaques, echogenicity of the intima-media complex, intima-media thickness of the typical carotid artery, and overt atherosclerotic plaques [105].

Furthermore, exposure to phthalates could potentially contribute to higher levels of plaque echogenicity, intima-media thickness, and echogenicity, which may increase the likelihood of developing hypertension [26]. Research has shown that high levels of MMP may increase the risk of hypertension-related pregnancy complications [106].

Phthalates are known to be related to cardiovascular risk factors, but the evidence supporting this connection is of low-high quality. One reason for this is the short physiologic half-lives of phthalates, which makes it difficult to obtain information on long-term exposure from a single measurement. Another challenge is that different studies have used different metabolites to detect phthalates, making it difficult to compare results. Finally, many of the studies that have been conducted on phthalates and cardiovascular risk factors were not originally intended for this purpose, such as pharmacovigilance studies or population-based surveys [Table 1].

6. RESTRICTIONS ON PHTHALATES

The scientific research and data available today suggest that we need more guidelines to decrease phthalates exposure. Fortunately, a lot of nations have been taken steps to restrict the consumption of phthalates in various goods [Table 2], such as toys, items of child-care, food packaging, and utensils. For instance, Japan prohibited the use of DEHP in food-handling gloves and DiNP and DEHP in toys back in 2001 [107]. In 2007, Europe banned the use of DEHP, DBP, and BBP in toys and childcare products made of PVC and other plasticized materials. DiNP, DiDP, and DnOP were also banned in products intended for children to put in their mouths. Recently, DiBP was included to the list of restricted substances in 28 EU nations in

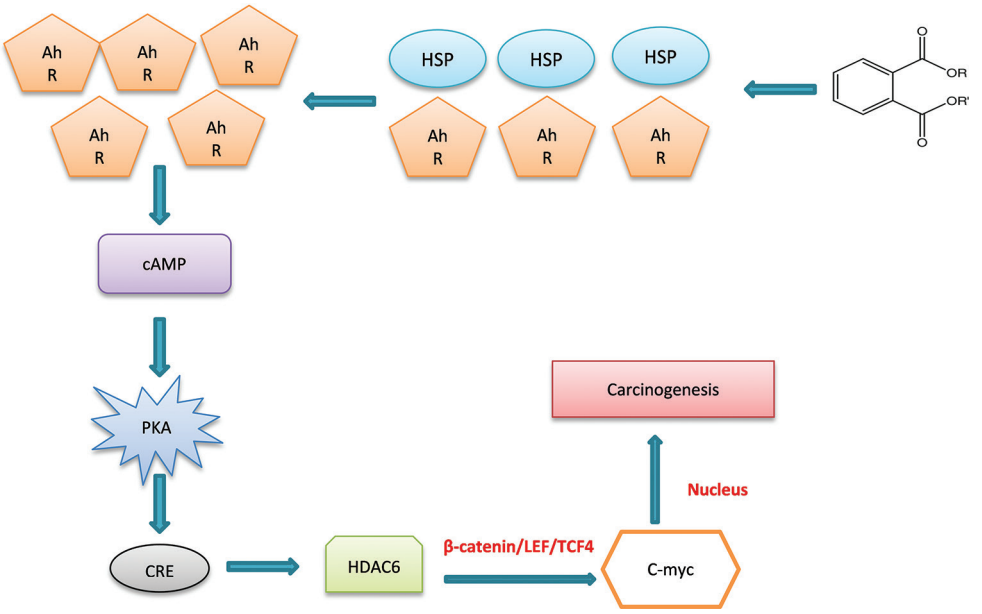

Figure 7: Mechanisms adopted by phthalate esters to affect the cancer cells.

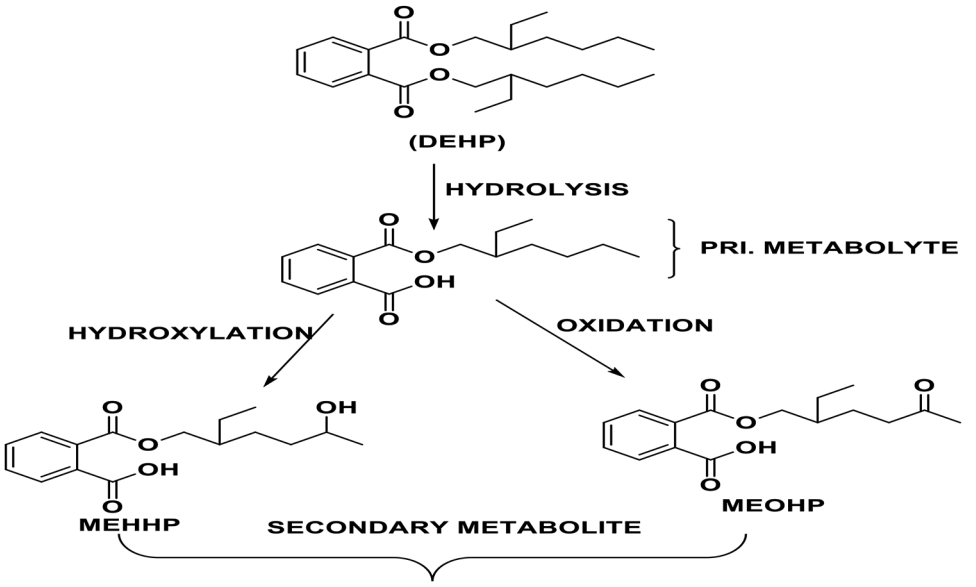

Figure 8: Pathway of diethyl hexyl phthalate in the cardiovascular system.

2018 [108]. The US Congress introduced the Consumer Protection Safety Act (CPSA) in 2008, which prohibited goods containing DEHP, DBP, or BBP at weights >0.1%, including toys and childcare items. Australia also banned the use of products that contain more than 1% DEHP. This includes toys and childcare items, as well as food containers and utensils. Similar bans have been announced for goods exported from Canada and China, the two countries that use and produce the most phthalates. In 2017, China implemented the most recent phthalates regulations (GB 5009.271-2016, GB/T 21928-2008, GB 9685-2016, GB 15593-1995), which restrict the number of phthalates that can be detected in food, food containers, and packaging materials. The maximum amount of dissolved DEHP that should be found in infusion equipment is less than 10 mg/mL (GB 14232.1-2004/ISO 3826-1, GB 24613-2009). Furthermore, a number of healthcare institutions have already taken preventive measures to reduce the usage of PAEs. It is obvious that more regulations are necessary to protect consumers, by limiting the use of PAEs in various products, we can restricting minimalize exposure to these hazardous chemicals and safeguard the health of individuals, mainly women [109].

Table 1: Effect of Phthalates on female's cardiovascular system

S. No.	Phthalates	Effects	References
1.	MMP	Coronary heart disease	[103]
2.	MEHP	The echogenicity of vascular plaques	[105]
3.	DiNP and DiBP	High blood pressure	[18]
4.	MBzP	Pregnancy-induced hypertensive diseases, increased diastolic blood pressure	[106]

MEHP: Mono (2-ethylhexyl) phthalate, MEHHP: Mono (2-ethyl-5-hydroxy hexyl) phthalate, MEOHP: Mono (2-ethyl-5-oxohexyl) phthalate, MMP: Mono benzyl phthalate

Table 2: Restriction in different countries

Country	Constraint	References
Australia	Products containing more than 1% by weight are restricted	[110]
Japan	DEHP is restricted in food handling gloves	[107]
United States	Products containing BBP, DBP, and DEHP, are restricted at more than 0.1% by weight, shall be restricted	[110]

7. CONCLUSION

The health of women is in jeopardy due to the damaging effects of airborne phthalates and their derivatives. Even though the evidence linking phthalate exposure with health problems like cardiovascular disease, respiratory problems, BC, endometriosis, and ovarian dysfunction is limited and inconsistent, it is clear that women are more vulnerable to the toxicity of phthalates because phthalates are endocrine-disrupting chemicals that can harm women's health in various ways, including their reproductive system. Thus, it is crucial to conduct more research with larger sample sizes to achieve more accurate results and a better understanding of the overall impact of phthalates on women's health. Furthermore, future studies should aim to determine the effects of phthalates on female respiratory and reproductive function, such as menstrual cycle, measures of fecundity, fertility, and asthma. Therefore, the present review suggests awareness regarding indoor air phthalates, which have been reported to cause serious health outcomes in women. Also, the study describes the in-depth mechanism involved in the physiology of various health outcomes such as cardiovascular diseases and endometriosis, which will help the future environmentalist and medical practitioner to successfully mitigate and prevent hazardous responses in women, respectively.

8. ACKNOWLEDGMENT

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9. ETHICAL CONSIDERATIONS

Ethical issues (Including plagiarism, informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

10. COMPETING INTERESTS

The authors have no conflict of interest.

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