R. M. (Max) Mawhinney
"Kentucky Blue"
677 Topdale Road
Walcha NSW 2354

Reference; Application Number SSD-10471
Location; Approximately 6.5 Km north-east of Walcha NSW.
Applicant; Winterbourne Wind Pty Ltd
Council Areas; Walcha and Uralla Shires.
Consent Authority; Minister for Planning or Independent Planning Commission.

This submission is made in relation to the Environmental Impact Statement Application number SSD-10471 submitted by Winterbourne Wind Pty Ltd, ultimately an associate company of VESTAS AG of Denmark.

Introduction.

Wind Turbine Blades contain significant amounts of Bisphenol A, a highly toxic endocrine disrupting chemical. Wind turbine blades are manufactured using a number of materials however the most significant being epoxy resins (approximately 60% by weight of each wind turbine blade) which contain approximately 35% Bisphenol A. The use of Bisphenol A in wind turbines in the proposed Winterbourne Wind development has been confirmed by Doug Landfear, the project director for and on behalf of Winterbourne Wind. (See Annexure 1)

The toxic nature and health impacts to humans and other organisms of Bisphenol A (commonly referred to as BPA) has been widely studied and acknowledged however recent studies have demonstrated that the "safe" level of BPA exposure is many log multiples lower than currently accepted levels.

Wind turbine blades erode over a period of time releasing large quantities of micro dust particles containing BPA which are spread over extensive areas of the surrounding environment by the very wind that operate the wind turbines.

Dust particles can either contain unadulterated BPA or erode through the process of hydrolysis and/or photolysis (the chemical breakdown of the bound monomers in the epoxy resin) exposing humans to BPA. Claims that BPA is completely chemically bound at time of manufacture is incorrect. Unbound BPA can "bloom" to the surface over a period of time and be blown into the surrounding environment. Claims that Epoxy resins containing BPA do not break down to their individual chemical components is also incorrect. Numerous studies support the fact that BPA is given off materials such as drink bottles over time. See text later in this submission.

BPA as an Endocrine disrupter.

In January 2022, a consortium including the Endocrine Society (global representative body of endocrinologists), Environmental Defense Fund, Breast Cancer Prevention Partners, Clean Water Action Fund, Healthy Babies Bright Future and Dr Linda Birnbaum (former Director National Institute of Environmental Health Sciences and National Toxicology Program), took the extraordinary step of lodging a formal petition to the USA Food and Drug Administration seeking to rescind its approval of Bisphenol A (BPA) in adhesives and coatings and set strict limits on its use in plastics that contact food.

To quote from the attached Endocrine Society January 27th 2022 press release, " New findings from a panel of experts convened by the European Food Safety Authority (EFSA) indicate that harmful

effects from BPA exposure can occur at levels 100,000 times lower than previously thought. This new level is more than 5,000 times below what FDA says most Americans are safely exposed to."

"Without a doubt, these values constitute a high health risk and support the conclusions that uses of BPA are not safe."

Under US law, the FDA are obliged to investigate and respond to a formal petition.

The petition calls for the reduction of levels of BPA to under 1/2 of 1 billionth of BPA/ kilogram of food.

See Annexure 2.

According to Publication PMC 6982222 of the Institute Journal of Environmental Research and Public Health, low concentrations of BPA, exert toxicity with numerous health impacts on humans, particularly in-vitro and newly born babies (due to the immature nature of their hormonal system).

Bisphenols exert toxicity effects due to their potential to induce "oxidative stress, mitochondrial dysfunction, impaired inflammatory function and endocrine disruption activity. The BPA toxicity can manifest as Endocrine disruption including reproductive abnormalities impacting follicle-stimulating hormones resulting in premature puberty, ovarian dysfunction, sex hormone abnormalities, premature birth and reduced birth weights.

BPA has also been associated with obesity and diabetes, cardiovascular toxicity, Hepatotoxicity and Neurotoxicity together with Immunotoxicity.

See Annexure 3

According to research from John Hopkins University, Bloomberg School of Public Health, BPA has been linked with increases in levels of Asthma symptoms in children.

See Annexure 4

It is thought that the "phenol" action of BPA can induce breast cancer along with other cancers.

BPA acts in a similar manner to estrogen confusing the bodies Endocrine system creating unnecessary responsive reactions.

Does BPA leach from plastics and epoxy resins?

A 2009 study by Harvard T.H. Chan School of Public Health provides evidence that BPA leaches from drinking bottles with a two-thirds increase in BPA in urine with people drinking from plastic bottles as opposed to control groups.

A number of countries have banned the use of BPA in baby bottles and sippy cups given the leaching of BPA into the container and subsequent ingestion by the infant.

See Annexure 5

Wind Turbine Blade Erosion

One of the major issues all Wind Turbine Manufacturers have is dealing with "leading edge erosion".

Wind turbine blades are constantly spinning with the leading edge of the blade subjected to severe weather conditions exacerbated by the speed of the blade. The outer tip of an 80 metre blade (the

length of blade proposed at Winterbourne) may be travelling at up to 360 kilometres/hour, greater than a category 5 Cyclone. The impact of wind, particularly when rain/hail/sleet or snow experienced in the Winterbourne area are added, creates a wearing of material which increases with the age of the turbine blades. Once the protective outer coating of the blade is breached, the underlying epoxy resin, containing toxic BPA, is exposed to erosion.

As previously mentioned, this eroded material is then spread through the surrounding environment by the very wind that operates the turbine blades. Given the height above ground level of the turbine blades, the eroded dust would travel uninterrupted over significant distances. Material from dust storms can travel many hundreds of kilometres therefore it is likely that toxic dust from turbine blades could travel many 10's of kilometres landing on roofs that collect drinking water and dust on surfaces used for food preparation along with rivers and streams potentially contaminating water supplies and poisoning the marine ecology.

Strachclyde University of Glasgow, Scotland calculated a leading edge loss of up to 62 kilos of blade `material per blade per year. The Winterbourne Turbine blades proposed will weigh 28,100 kilos per blade or 84,300 kilos per turbine or 10 million kilos of turbine blades. Over 2 million tonnes of toxic BPA will be imported (from China) into the the Walcha district.

Given the high level of BPA contained in turbine blades, a shedding of 62 kilos per blade by 3 blades per turbine by 119 turbines proposed at Winterbourne will result in potentially 22,000 kilos of material contaminating the surrounding environment.

With epoxy resins making up about 60% by weight of turbine blades and BPA being approximately 35% of the epoxy resin, this represents over 4,600 kilos of BPA per annum being constantly blown into the surrounding environment. Over a 20 year period this equates to 92,000 kilos of BPA.

See Annexure 6 (Paper presented by VESTAS)

Conclusion

With the World Endocrine Society petitioning the USA FDA to reduce to 1/2 billionth of a gram/ kilo of food, the citizens of Walcha will be exposed to potentially thousands of times the recommended maximum exposure level. The exposure will be ongoing day by day, year by year and will increase as turbine blades erode.

Bisphenol A (and other members of the Bisphenol family of toxic chemicals) are rapidly being seen for what they are at the international level. Toxic chemicals that should not be used in association with food or drinking water. BPA will emerge as the new "asbestos" or "cigarette smoke" of this decade.

The construction of wind turbines containing BPA should immediately be banned as the level of BPA that the Winterbourne wind project will expose the Walcha community to is completely unacceptable.

Governments have a responsibility to protect Australian citizens from toxic chemicals, not approve projects that expose them to highly toxic chemicals.

Yours faithfully

R. M. (Max) Mawhinney

Annexure 1

Vestas Confirmation of the use of bisphenol A

From: rgreig71@gmail.com
To: Cameron Greig > Damien Timbs > Michael Luchich > Kate Durack > Jim and Jules Young > Max Mawhinney > banchorynsw@gmail.com > Mark Fogarty >
19 December 2022 at 5:56 pm

Rachel Greig

"Oak Hill"
390 Aberbaldie Rd
Walcha, NSW 2354
0428 776490

From: Doug Landfear <info@winterbournewindfarm.com.au>
Sent: Monday, 19 December 2022 5:42 PM
To: rgreig71@gmail.com
Subject: Re: Contact Us - Winterbourne Wind Farm

Hello Rachel

Bisphenol A is a chemical plasticizer which is combined with a momomeric resin, a hardener, and an accelerator to form epoxy resin. The bisphenol A is consumed in the chemical reaction between these components.

Epoxy resins are used in the manufacture of turbine blades. Epoxy resins are also used to make paints, protective coatings, adhesives, linings on food and beverage containers, and other common household and industrial uses.

Regards

Doug Landfear | **Project Director**
M: +61 436 927 806
E: doug@winterbournewindfarm.com.au
W: winterbournewindfarm.com.au

On Tue, 6 Dec 2022 at 10:25, Rachel Greig <admin@webk.com.au> wrote:

Annexure 2

Groups petition FDA to restrict bisphenol A in food packaging

https://www.endocrine.org/news-and-advocacy/news-room/2022/groups-petition-fda-to-restrict-bisphenol-a-in-food-packaging

PRESS RELEASE

Groups petition FDA to restrict bisphenol A in food packaging

Washington, DC January 27, 2022

New findings show BPA can have harmful effects at levels 100,000 times lower than previously thought

The Endocrine Society joined a coalition of physicians, scientists and public health and environmental organizations to send a formal petition to the Food and Drug Administration (FDA), calling on the agency to rescind its approvals for bisphenol A (BPA) in adhesives and coatings and set strict limits on its use in plastics that contact food.

New findings from a panel of experts convened by the European Food Safety Authority (EFSA) indicate that the harmful effects from BPA exposure can occur at levels 100,000 times lower than previously thought. This new safe level – based on recent scientific evidence – is more than 5,000 times below what FDA says most Americans are safely exposed to.

Without a doubt, these values constitute a high health risk and support the conclusion that uses of BPA are not safe. The petition calls on FDA to limit uses of BPA in food contact articles that may result in migration into food above 0.5 nanograms per kilogram of food.

"The process EFSA used to reassess the safety of bisphenol is a template for how FDA should be doing it for the hundreds of chemicals it approved decades ago. Transparent, thorough, and grounded in the science," said Tom Neltner, EDF's senior director for safer chemicals. "With Americans overexposed to BPA by more than 5,000 times, the agency must make this a top priority and make a final decision by the 180-day statutory

deadline."

The petition was filed by Environmental Defense Fund, the Endocrine Society, Breast Cancer Prevention Partners, Clean Water Action/Clean Water Fund, Consumer Reports, Environmental Working Group, Healthy Babies Bright Futures, Dr. Maricel Maffini, and Dr. Linda Birnbaum, former director of the National Institute of Environmental Health Sciences and National Toxicology Program.

BPA is used to make polycarbonate and other plastics, which are commonly used in hard items such as food containers, pitchers, tableware, storage containers and more. The chemical is also used in epoxy resins that line the inside of metal products and bottle tops. Small amounts of BPA can migrate from containers or equipment into food and beverages.

Industry has taken steps in the past to limit the use of BPA in can linings and plastic baby bottles. These actions followed 2008 findings from the Centers for Disease Control and Prevention indicating the chemical showed up in 92% of US adults and additional studies that showed BPA can act like the female sex hormone, estrogen, in humans and disrupt normal development.

Findings from EFSA's expert panel show that BPA's effects are much worse than previously understood and that people are exposed at levels dramatically above what is safe. Extremely low exposures to BPA can lead to an overactive immune system producing out of control inflammation, as well as changes in the ovaries, endocrine disruption, and reduced learning and memory, according to the EFSA panel.

"FDA has an obligation to protect us from toxic chemicals that can come in contact with our food," said Maricel Maffini, Ph.D., scientist and coauthor of the petition. "These new findings should be a wakeup call to the FDA and all of us that our health is in jeopardy unless we take swift action to limit the amount of BPA that can come into contact with our food."

FDA has long collaborated with EFSA on risk assessment and risk communication related to food safety, including working together to increase understanding of risks from chemicals used in food packaging, like PFAS. The agency now needs to listen to the warnings on BPA from its expert counterparts at EFSA and take steps to dramatically

reduce our exposures to the chemical.

"These findings are extremely concerning and prove the point that even very low levels of BPA exposure can be harmful and lead to issues with reproductive health, breast cancer risk, behavior and metabolism," said Endocrine Society BPA expert Heather Patisaul, Ph.D., of North Carolina University in Raleigh, N.C. "The FDA needs to acknowledge the science behind endocrine-disrupting chemicals and act accordingly to protect public health."

About Endocrine Society

Endocrinologists are at the core of solving the most pressing health problems of our time, from diabetes and obesity to infertility, bone health, and hormone-related cancers. The Endocrine Society is the world's oldest and largest organization of scientists devoted to hormone research and physicians who care for people with hormone-related conditions.

The Society has more than 18,000 members, including scientists, physicians, educators, nurses, and students in 122 countries. To learn more about the Society and the field of endocrinology, visit our site at **www.endocrine.org**. Follow us on Twitter at **@TheEndoSociety** and **@EndoMedia**.

FILTER BY:

Topics Year

PRESS RELEASE

Experts explain treatment options for a common cancer complication

December 21, 2022

Experts provide the first framework for treating a common and life-threatening metabolic complication of cancer known as hypercalcemia of malignancy in the Endocrine Society's new Clinical Practice Guideline.

PRESS RELEASE

Women who take more steps per day may have a lower risk of diabetes

December 13, 2022

Wearable fitness devices offer new insights into the relationship between physical activity and type 2 diabetes, according to a new analysis of the National Institutes of Health's All of Us Research Program data published in the Endocrine Society's Journal of Clinical Endocrinology & Metabolism.

PRESS RELEASE

New Endocrine Society Clinical Practice Guideline examines better ways to manage hypoglycemia in people with diabetes

December 07, 2022

People with diabetes are benefiting from advances in medications and technologies to lower their risk of hypoglycemia, according to a Clinical Practice Guideline issued today by the Endocrine Society.

PRESS RELEASE

People with diabetes may benefit more from a pancreas transplant than other treatments

November 15, 2022

Results of pancreas transplantation continue to improve and up to 90% of recipients with diabetes enjoy freedom from both insulin therapy and the need for close glucose monitoring following the procedure, according to a new paper published in the Endocrine Society's Journal of Clinical Endocrinology & Metabolism.

PRESS RELEASE

Endocrine Society condemns Florida ban on gender-affirming care

November 04, 2022

The Endocrine Society rebukes the Florida Board of Medicine's decision to ban gender-affirming care for transgender and gender-diverse teenagers.

Annexure 3

Bisphenols as a Legacy Pollutant, and Their Effects on Organ Vulnerability

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6982222/

International Journal of Environmental Research and Public Health

Int J Environ Res Public Health. 2020 Jan; 17(1): 112.
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PMID: 31877889

Bisphenols as a Legacy Pollutant, and Their Effects on Organ Vulnerability

Jong-Joo Kim,[1,†] Surendra Kumar,[2,†] Vinay Kumar,[3] Yun-Mi Lee,[1] You-Sam Kim,[1] and Vijay Kumar[1,*]

Abstract

Bisphenols are widely used in the synthesis of polycarbonate plastics, epoxy resins, and thermal paper, which are used in manufacturing items of daily use. Packaged foods and drinks are the main sources of exposure to bisphenols. These chemicals affect humans and animals by disrupting the estrogen, androgen, progesterone, thyroid, and aryl hydrocarbon receptor functions. Bisphenols exert numerous harmful effects because of their interaction with receptors, reactive oxygen species (ROS) formation, lipid peroxidation, mitochondrial dysfunction, and cell signal alterations. Both cohort and case-control studies have determined an association between bisphenol exposure and increased risk of cardiovascular diseases, neurological disorders, reproductive abnormalities, obesity, and diabetes. Prenatal exposure to bisphenols results in developmental disorders in animals. These chemicals also affect the immune cells and play a significant role in initiating the inflammatory response. Exposure to bisphenols exhibit age, gender, and dose-dependent effects. Even at low concentrations, bisphenols exert toxicity, and hence deserve a critical assessment of their uses. Since bisphenols have a global influence on human health, the need to discover the underlying pathways involved in all disease conditions is essential. Furthermore, it is important to promote the use of alternatives for bisphenols, thereby restricting their uses.

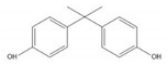
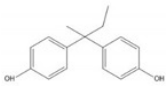
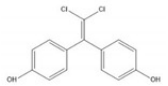
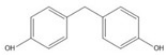
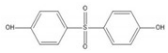
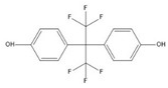
Keywords: bisphenols, endocrine disruptors, obesity and diabetes mellitus, hepatic toxicity, neurotoxicity, immunotoxicity

1. Introduction

Bisphenols (Bisphenol A (BPA), Bisphenol B (BPB), Bisphenol C (BPC), Bisphenol S (BPS), Bisphenol F (BPF) and Bisphenol AF (BPAF)) are phenolic organic compounds (Table 1). These compounds are commonly used in the manufacturing of plastic containers, epoxy resins, food and drink cans, water pipes, electronic equipment, thermal paper, kitchen utensils, toys, and dental sealants [1,2,3,4,5]. Bisphenols are generally used for the hardening of plastic and are easily dissolved in foods and drinks. The general population is therefore exposed to bisphenols, both directly (through oral and/or topical routes) and indirectly (through environmental pollution and/or food chain) [5,6,7,8,9,10]. Due to their extensive uses and long-term discharge from plastic products, humans always have a concentration of bisphenols in their body fluids, even without intentional exposure [11,12].

Table 1

Chemical formula, IUPAC name, and chemical structure of common bisphenols.

Sl. No.	Bisphenol	Chemical Formula	IUPAC Name	Chemical Structure *
1.	Bisphenol A (BPA)	$C_{15}H_{16}O_2$	4-[2-(4-hydroxyphenyl)propan-2-yl]phenol	
2.	Bisphenol B (BPB)	$C_{16}H_{18}O_2$	4-[2-(4-hydroxyphenyl)butan-2-yl]phenol	
3.	Bisphenol C (BPC)	$C_{14}H_{10}Cl_2O_2$	4-[2,2-dichloro-1-(4-hydroxyphenyl)ethenyl]phenol	
4.	Bisphenol F (BPF)	$C_{13}H_{12}O_2$	4-[(4-hydroxyphenyl)methyl]phenol	
5.	Bisphenol S (BPS)	$C_{12}H_{10}O_4S$	4-(4-hydroxyphenyl)sulfonylphenol	
6.	Bisphenol AF (BPAF)	$C_{15}H_{10}F_6O_2$	4-[1,1,1,3,3,3-hexafluoro-2-(4-hydroxyphenyl)propan-2-yl]phenol	

* Chemical structures were drawn using ChemDraw version 18 (PerkinElmer, MA, USA).

Bisphenols exert toxic effects due to their potential to induce oxidative stress, mitochondrial dysfunction, impaired inflammatory function, and endocrine disruption activity. Bisphenol exposure leads to mitochondrial dysfunction, deregulation of cellular signaling pathways, and generation of reactive oxygen species (ROS) subsequent to decreased antioxidant enzymes [5,13,14,15,16,17,18,19,20]. Elevated ROS levels result in oxidative stress, DNA damage and cell death, by activating the caspase cascade as well as mitogen-activated kinases (MAPK) signaling pathways [16,19,20,21,22,23,24,25]. Bisphenols induce inflammatory responses via various signaling pathways and alteration of various immune cells. Bisphenol exposure stimulates the production of pro-inflammatory cytokines and inhibits the production of anti-inflammatory cytokines [20,23,26]. Human studies also have determined that bisphenol toxicities are associated with oxidative stress and inflammatory responses [27,28,29,30].

Bisphenols bind to androgen, estrogen, progesterone, thyroid, and aryl hydrocarbon receptors, which are, in turn, associated with endocrine and other systems of the body, especially the reproductive, respiratory, and nervous systems [31,32,33,34,35]. Exposure to bisphenols disrupts the activity of several hormones, including sex hormones, insulin, and thyroxin, causing different organ toxicities [15,36,37]. Hence human exposure to bisphenols has increased the risk of obesity, diabetes mellitus, liver dysfunction, cardiovascular diseases, reproductive, and developmental abnormalities [38,39,40,41]. Bisphenols are metabolic disruptors, and even early-life exposure at low concentrations can result in impaired metabolic functions and toxicity to several organs or systems. These complications are further reviewed in the following subsection. Moreover, BPA is known to interact with therapeutic drugs and may affect the outcomes of chemotherapy [42].

2. Endocrine Disruption and Reproductive Abnormalities

Bisphenol toxicity studies have revealed that these chemicals disrupt the endocrine functions and cause reproductive toxicity [43,44,45,46]. Even a low dose of chronic exposure to bisphenols suppresses the luteinizing hormone, follicle-stimulating hormones, and prolactin, exhibiting estrogenic and antiandrogenic effects and affecting spermatogenesis [12,47,48]. Common reproductive abnormalities include premature puberty, ovarian dysfunction, implantation failure, abnormal sperm function, fertilization failure, sex hormone abnormality, premature birth, and lower birth weight [48,49,50,51,52]. Bisphenols interact with both membrane-bound and nuclear estrogen receptors. BPA mimics the action of the natural estrogen 17-β estradiol, and their metabolites have greater estrogenic activities [53,54,55].

In a prospective study of 1841 pregnant women, Zhang et al. found that BPAF and BPS are potential risk factors for gestational diabetes mellitus (GDM). The authors observed the endocrine-disrupting effects of BPAF and BPS on blood glucose metabolism among Chinese pregnant women. Moreover, multivariable logistic regression analysis revealed an association of urinary BPAF with the risk of GDM [56]. In a cross-sectional study on 167 men, Meeker et al. found that urinary BPA level is inversely related to the estradiol:testosterone ratio, indicating that BPA probably modulates the estrogen and androgen synthesis gene expression [37]. A positive correlation between urinary BPA level and higher expression of two estrogen-responsive genes (encoding ERβ and ERRα) were found in the European population [57]. Increased urinary BPA level has also been associated with decreased thyroid-stimulating hormone and increased levels of free triiodothyronine hormone in a Chinese population aged 40 years or older [58]. BPA, BPF, and BPS have also been detected in human breast milk samples from Spanish mothers [59,60] (Table 2).

Table 2

Effect of bisphenol exposure in the human population.

Sl No.	Human Population Study	Bisphenols Studied	Finding	Reference
1	A case-controlled study (251 each)	BPAF, BPA, BPS	Urinary BPAF and BPS concentrations are positively associated with DM2	[78]
2	NHANES-2003-08	BPA	Urinary BPA levels are associated with diabetes mellitus and Peripheral Arterial Disease	[38,79]
3	485 adults (259 men, 92 premenopausal women, and 134 postmenopausal women)	BPA	Urinary BPA levels are associated with oxidative stress and inflammation in postmenopausal women	[27]
4	Case-control study	BPA, BPAF, BPS	Urinary concentrations of bisphenols are positively associated with DM2 risk	[78]
5	Meta-analysis; human population	BPA	BPA exposure is positively associated with DM2 risk	[80]
6	A cross-sectional study in Chinese school children	BPA	BPA exposure increases the BMI in school children	[81]
7	Cross-sectional study (n = 3390; age ≥ 40 years)	BPA	BPA is positively associated with generalized obesity, abdominal obesity, and insulin resistance	[82]
8	Cross-sectional study (n = 3394; age ≥ 40 years)	BPA	Urinary BPA levels are associated with increased thyroid function	[58]
9	Cross-sectional study (n = 2838; age 6–19 years); NHANES-2003-08	BPA	Urinary BPA levels are associated with obesity	[83]
10	Cross-sectional study (n = 1455 (2003–2004) and n = 1493 (2005–2006); age 18–74 years); NHANES-2003-06	BPA	Urinary BPA levels are associated heart disease	[84]
11	Cross-sectional study (n = 167 Men; age 8–55 years);	BPA	Urinary BPA levels are associated with altered serum thyroid and reproductive hormone levels in men	[37]
12	A prospective study (n = 1841; pregnant women)	BPA, BPS, BPF, BPAF	BPAF and BPS might be potential risk factors of gestational diabetes mellitus	[56]
13	A repeated-measures, longitudinal study (n = 2336, age ≥ 40); non-diabetic adults; Chinese population	BPA	BPA is independently associated with dyshomeostasis of glucose before the development of diabetes in women (age ≥ 40)	[85]

Bisphenol A (BPA); Bisphenol S (BPS); Bisphenol F (BPF); Bisphenol AF (BPAF); Bisphenol B (BPB); reactive oxygen species (ROS); mitogen-activated kinases (MAPK); diabetes mellitus type 1 (DM1); diabetes mellitus type 2 (DM2); National Health and Nutritional Examination Survey (NHANES); body mass index (BMI).

Numerous studies in animal models have reported the deleterious effects of exposure to bisphenols. Tian et al. found that male CD-1 mice exposed to BPA had decreased testis weight, damage to basal lamina of seminiferous tubules and tight junctions between Sertoli cells, and decreased levels of the androgen-binding protein [61]. BPA exposure of pregnant CD-1 mice results in altering the tissue organization of ovaries and mammary glands, and alters the estrous cycle in adulthood via modulation of their morphogenesis specific genes' expression [62]. Intraperitoneal administration of BPA (25 mg/kg BW /day; 9 days) to 8-week-old female Wistar rat decreased catalase expression, and increased lipid peroxidation and nitric acid levels in granulosa cells of the ovary. BPA exposure also decreases the estrogen and progesterone levels, and increases pro-inflammatory cytokine levels [63]. Sub-acute oral administration of BPA (10 mg/kg BW/day) in adult Wistar rats increases the serum estrogen level and prostate-specific antigen, causing vascular congestion and hyperplasia of the prostatic epithelium [64]. BPA at low doses decreases the synthesis of estradiol and inhibits the growth of antral follicles isolated from wild-type and Ahr knock-out mice, through partial involvement of the aryl hydrocarbon receptor pathway [32]. BPA exposure results in decreased sperm counts and motility, and increased ROS and lipid peroxidation in mice testes [25] (Table 3).

Table 3

Effect of Bisphenol exposure in different experimental models.

Sl No.	Study	Bisphenols	Dosing	Finding	Reference
			In-Vivo Studies		
1	Streptozotocin-induced type 1 diabetes mellitus male mice model	BPA	5 mg/kg BW for 5 days, gavage	Disruption of calcium homeostasis; insulin resistance	[86]
2	Eight-week-old female Wistar rats	BPA	25 mg/kg BW/day for 9 days, intraperitoneal	Catalase plays a role in mediating reproductive damage in granulosa cells exposed to BPA	[63]
3	Non-obese diabetic mice	BPA	0, 1, and 100 mg/L BPA in drinking water	Long-term BPA exposure at a dose three times higher than the tolerable daily intake of 50 µg/kg, appears to accelerate spontaneous insulitis and diabetes development in non-obese diabetic mice	[87]
4	Male and female Sprague-Dawley rats	BPA	0.04, 0.4, and 4 mg/kg/day	Juvenile BPA exposure disturbs the spatial memory in male rats, but not in female rats, in a dose-dependent manner; alteration of the excitatory plasticity; downregulates the spine density and glutamate receptor expression levels in the hippocampus	[88]
5	Male Sprague-Dawley adult rats	BPA	40 µg/kg; subcutaneous injection	Acute BPA exposure impaired memory and block synaptic plasticity processes	[89]
6	Zebrafish (*Danio rerio*)	BPA	10^{-9} M	Alters the expressions of genes involved in thyroid hormone synthesis and of thyroid-specific transcriptional factors, in a dose- and time-dependent manner	[75]
7	T-cell receptor transgenic mice	BPA	10 mg/L, for 2 weeks; drinking water	Reduces interleukin-2, 4, and interferon γ secretions, and increases the productions of IgA and IgG2a	[90]

Bisphenol A (BPA); Bisphenol S (BPS); Bisphenol F (BPF); Bisphenol AF (BPAF); Bisphenol B (BPB); reactive oxygen species (ROS); mitogen-activated kinases (MAPK); diabetes mellitus type 1 (DM1); diabetes mellitus type 2 (DM2); National Health and Nutritional Examination Survey (NHANES); body mass index (BMI).

Antiandrogenic and estrogenic activities of BPF and BPAF are similar to BPA [65,66,67,68,69]. BPF exposure decreases the basal testosterone secretion by human fetal testes, and induces the production of 17β-estradiol [70,71]. Zebrafish larva exposed to BPF promotes the production of estrogen, which causes phenotypic feminization and alters sexual differentiation [72]. BPA, BPF, and BPS exposure to mouse embryonic stem cells (mESCs) disrupt numerous processes during mESC global and neural differentiation, thereby triggering the onset of cardiovascular/neural diseases and cancer [73]. BPA exposure also exerts differential effects on the mouse GC-1 spermatogonial cell line by altering the cell growth, global DNA methylation, histone level, and MAPK signaling pathways [20]. In a similar study, exposure of the mouse spermatocyte GC-2 cell line to BPA, BPF, and BPS altered the DNA methylation and steroidogenesis-related gene expressions [46]. Both BPA and BPS exposure results in modified activities of the ABCB1 promoter in human placental 3A cells, which affect the placental P-glycoprotein efflux transporter levels. Such changes in the levels of placental P-glycoprotein significantly affects fetal exposure to xenobiotics [74]. Gentilcore et al. reported that exposure of thyroid immortalized cell line (FRTL-5) and zebrafish embryos to BPA (10^{-9} M) affects the thyroid follicular cells through an altered expression of the thyroid-specific gene and transcriptional factors [75]. Sheng et al. found that low dose BPA (10^{-9} M) treatment of CV-1 cells derived from *Cercopithecus aethiopis* monkey kidney suppresses the thyroid hormone receptor transcription [76]. Neuregulins are a member of the epidermal growth factor family proteins involved in embryogenesis and the development of many internal organs. A study in a pig model reveals that low and high dose exposures of BPA (0.05 and 0.5 mg/kg BW/day) alters the number of neuregulin-1-positive fibers and their neurochemical properties, in both uterine muscular and mucosal layers [52]. BPA (2000 and 4000 µg/L) exposure to zebrafish embryo during the first 24 h of development has been shown to impair the migration of primordial germ cells [77].

3. Obesity and Diabetes

Studies on humans and animals have revealed that bisphenol toxicity is associated with obesity and impaired glucose homeostasis [5,82,83,96,97,98,99]. BPA exposure alters the glucose-stimulated insulin/C-peptide response in humans [100]. In a repeated-measures, longitudinal study from China, Wang et al. found that BPA exposure is associated with impaired glucose homeostasis in women (aged ≥ 40 years), and has a high urinary BPA level. However, no significant associations were found between glucose metabolic markers and urinary BPA in men [85]. By disrupting the endocrine activity, bisphenol exposure resulted in increased body weight. Bisphenols are also reported to bind to the α and β receptors of fatty tissues and modulate their functions. BPA exposure also disrupts thyroid signaling by affecting the metabolism of the thyroid hormone [101].

A prospective study from a Swedish population (n = 1016, mean age = 70 years) reported that serum BPA levels are positively associated with adiponectin and leptin, and inversely associated with the gut-hormone ghrelin. BPA is also shown to interfere with the hormonal control of hunger and satiety [102]. A cross-sectional study of 2838 participants in the USA reported that urinary BPA levels correlated with increased body weight in children and adolescents [83]. An epidemiological study conducted in a Chinese population found a dose-related association between high urinary BPA concentration and increased body weight in 9–12 year old girls [97]. Another study from China reported that increased urinary BPA levels of both girls and boys (aged 8–15 years) are related to increased body mass index [81]. In a Chinese population case-control study of 251 cases of diabetes mellitus type 2 (DM2) and 251 controls, urinary concentrations of bisphenols (BPAF and BPS) were found to be positively correlated with DM2 [78]. A meta-analysis study determined that BPA toxicity is related to an increased risk of DM2; they reported that both urine and serum BPA levels are positively associated with the risk of DM2 [80]. In a cross-sectional study on the middle-aged and elderly Chinese population, a positive association was found between generalized obesity, abdominal obesity, and insulin resistance [82]. In an epidemiological study in the USA, Shankar et al. found a positive association between increased urinary BPA concentration and diabetes mellites, which was independent of confounding diabetes risk factors [79] (Table 2). In a meta-analysis study, Kim et al. reported that BPA exposure in children is associated with the risk of obesity [103].

Bodin et al. found that long-term BPA toxicity accelerates spontaneous insulitis and diabetes mellitus type 1 (DM1) development in non-obese diabetic mice [87]. Zhao et al. showed that 1 and 10 µg/L BPS exposure to male zebrafish significantly increases the fasting blood glucose levels, decreases insulin levels, and impairs glucose homeostasis [96]. Liu et al. showed time and gender-dependent effects of maternal BPA (100 µg/kg/day) exposure on the body weight and glucose homeostasis disorder in C57BL6 mice offspring. These offspring have glucose intolerance and decreased insulin secretion [104] (Table 3).

4. Cardiovascular Toxicity

Several studies have established the role of bisphenol in cardiovascular diseases, including myocardial infarction, cardiomyopathy, and hypertensive heart disease [105,106,107,108,109]. A survey conducted in the United States shows the correlation between urinary BPA levels and increased prevalence of heart disease [84]. Shankar et al. found that increased serum BPA concentration is associated with the development of peripheral arterial disease in United States adults. The observed association was independent of their lifestyle (smoking and alcohol), body mass index, hypertension, cholesterol level, and diabetic status [106]. Another study confirmed that BPA exposure is associated with decreased heart rate variability and increased blood pressure in elderly subjects (≥60 years old). The risk of hypertension was also increased with increasing urinary BPA concentration in participants [110]. In a cross-sectional study (n = 1016 subjects; age = 70 years), Olsen et al. found positive associations between the serum concentration of BPA and LDL cholesterol levels [111] (Table 2).

Feiteiro et al. observed that BPA inhibits the L-type calcium channels in rat aorta smooth muscles, leading to the relaxation of vascular smooth muscles, which was found to be dependent on the concentration of BPA [94]. BPA escalates the worsening of DM1 by disrupting calcium homeostasis in the mouse pancreas, resulting in endoplasmic reticulum stress in pancreatic cells and promoting insulin resistance [86]. Perinatal exposure of bisphenols (BPAF, BPA, and BPF) regulate the expressions of hepatic glucose and lipid metabolism specific genes, and hence inhibit their homeostasis in adolescent female mice offspring [112]. Furthermore, they differentially influence oxidative damage and metabolic disorders in the livers of male mice offspring [113] (Table 3).

5. Hepatotoxicity

BPA exposure leads to hepatotoxicity by oxidative stress, mitochondrial impairment, and inflammatory pathways [15,114,115,116,117]. Nicolucci et al. found BPA in human plasma samples and observed an association between BPA exposure and liver health status [118].

Meng et al. found that perinatal exposure to bisphenols (BPA, BPF, and BPAF) differentially influences metabolic disorders and oxidative stress in the liver of male mouse offspring. BPF exposure affected the liver antioxidant defense system, whereas BPAF altered the level of β-glucose and glycogen [113]. Oral dosing of BPA to male Wistar rats decreases the antioxidant enzymes and their gene expressions, and increases the liver enzyme activity [15]. Similarly, Moon et al. found that mice exposed to a low dose of BPA might cause structural changes in the liver and mitochondrial dysfunction. Moon et al. confirmed that BPA induces lipid peroxidation, and decreases glutathione peroxidase activity and expression of pro-inflammatory cytokines such as tumor necrosis factor-α and interleukin-6 [13]. BPA exposure in mice also induces lipid accumulation in the hepatic cells by affecting fatty acid synthesis and their transport genes. BPA exposure leads to excessive lipid accumulation in the liver, decreases the levels of autophagy, and induces nonalcoholic fatty liver disease and their associated complications [114,115,116,117]. Long-term BPA exposure (0.5 µg BPA/kg/day, 10 months) on male mice induces hepatic lipid accumulation, which may be due to the epigenetic reprogramming of genes involved in lipid metabolism, such as alterations of DNA methylation patterns [119]. BPA (15 µg/L for 3 and 6 weeks) exposure to *Gobiocypris rarus* fish disturbed the expressions of acetyl-CoA carboxylase, fatty acid synthase, and carnitine palmitoyltransferase 1α, by

altering the sterol regulatory element-binding protein 1 binding to their sterol regulatory elements, subsequently affecting triglyceride synthesis. BPA exposure led to a gender-specific effect on fatty acid β-oxidation in *G. rarus* fish [120].

Human HepG2 hepatoma cells exposed to low concentrations (10^{-4}–10^{-12} M) of BPA showed mitochondrial dysfunction by inducing ROS generation, lipid peroxidation, mitochondrial transmembrane hyperpolarization, and release of interleukin-8 and tumor necrosis factor-α secretion [95] (Table 3).

6. Neurotoxicity

Exposure to bisphenols is associated with several neurological dysfunctions comprising memory and cognitive impairments, including aggression, hyperactivity, anxiety, depression, autism, and neuroinflammation. Children are more prone to bisphenol exposure, and even low concentrations (≤100 μM) are toxic to brain development in both prenatal and childhood stage [89,121,122,123,124,125]. Exposure to BPA in the first trimester of pregnancy is associated with sleep-related problems in preschool children [80]. In a longitudinal birth cohort study in California, Harley et al. observed that prenatal and early childhood BPA exposure of children results in behavioral problems, including anxiety, depression, and hyperactivity [123]. Evans et al. found that prenatal exposure to BPA may be related to increased behavioral problems in school-age boys, but not in girls [126]. Increased serum and urine BPA levels were detected in children with autism spectrum disorder (ASD) [124,127]. Metwally et al. observed that BPA exposure induces oxidative stress in ASD children, which results in mitochondrial dysfunction and behavior impairment [128]. In a similar study, the authors found that serum levels of follicle-stimulating hormone, inhibin B, and estradiol hormones were lower in the ASD group than the control group [129]. (Table 2).

Prenatal BPA exposure of Wistar rats causes changes in the hippocampal expressions of genes associated with ASD in a sex-specific manner. BPA disrupts the expression of ASD candidate genes (*Auts2*, *Foxp2*, and *Smarcc2*) more significantly in the male hippocampus than in females [130]. Subcutaneous injection of 20 μg BPA/kg BW/day in pregnant mice resulted in impaired neurotransmission. BPA increases the levels of dopamine as well as their metabolites, and decreases the levels of serotonin and their derivatives in the brain [131]. In a similar study on pregnant mice, prenatal and lactational BPA exposure (20 μg/kg BW/day), from embryonic day to 21st postnatal day, resulted in impaired murine behavior [132]. Chen et al. found that juvenile BPA exposure impairs the spatial memory only in male rats, in a dose and gender-dependent manner. Such cognitive impairment was due to changes of the excitatory plasticity, such as the downregulated spine density and glutamate receptor expression levels in the hippocampus [88]. High concentrations of BPA (>100 μM) exposure in mice hippocampal HT-22 cells induces apoptosis by increasing the calcium influx and ROS levels, followed by activating the phosphorylation of extracellular signal-regulated kinase, c-Jun N-terminal kinase, and caspase 3 [133]. BPA causes developmental toxicity through antiproliferation and pro-apoptosis in rat embryonic midbrain (MB) cells. Khadrawy et al. found the neurochemical impact of BPA in the cortex and hippocampus region of adult male albino rat brain. The authors found that BPA induces a state of oxidative stress and excitotoxicity-cum-acetylcholinesterase activity in these regions [92]. Long-term, low-level BPA exposure causes impaired learning and memory ability, increases the DNA damage in brain cells, and decreases the cell density in the hippocampus of adolescent mice. [134]. Low concentrations of BPA exposure block the cell cycle progression and increase the induced apoptosis. BPA exposure decreases the phosphorylation of c-Jun N-terminal kinase and cyclic-AMP response binding protein in MB cells, and increases the mRNA expressions of proapoptotic proteins (Bax and p53) [21]. Poimenova et al. conducted a study on 6-weeks old Wistar rat offsprings treated with BPA (orally; 40 μg/kg/day) during pregnancy and lactation. Results showed increased anxiety-like behavior and reduced exploratory behavior in a corticosterone-regulated manner [135].

BPS exposure at concentrations of 0.3 and 3.0 mg/L on zebrafish embryos showed decreased locomotor activity, increased oxidative stress, apoptosis, and altered retinal structure. Moreover, the researchers also found that 3.0 mg/L BPS exposure suppresses the expression of six neuro development-specific genes

(*mbp*, *syn2a*, *α1-tubulin*, *elavl3*, *gap43*, and *gfap*) [91]. Kinch et al. showed that an acute low dose of BPS or BPA (0.0068 mM) exposure on zebrafish modified the growth of hypothalamus and caused hyperactive behavior [93]. A similar study showed that chronic BPS exposure on male zebrafish results in structural impairment of the retina and reduction of their tracking capability [136] (Table 3).

7. Immunotoxicity

Bisphenols affect inflammation and immune responses through several signaling pathways, and are capable of both initiating as well as inhibiting the activities of immune cells. Bisphenols modulate the immune response by affecting estrogenic receptors, aryl hydrocarbon receptors, and peroxisome proliferator-activated receptors. Exposure to bisphenols can alter the function of cytokines and chemokines, which exacerbates or results in immune-related diseases (e.g., allergy, asthma, multiple sclerosis) [137,138,139]. An epidemiological study conducted in the USA reports the association between higher urinary BPA levels with higher cytomegalo virus antibody titers in the <18-years age group, indicative of the negative impacts of BPA on immunity [36].

BPA exposure decreases neutrophilic activity and inhibits interleukin-6 formation in mice infected with non-pathogenic *Escherichia coli* [140]. Roy et al. showed that the offspring of female mice exposed to BPA were more susceptible to infection by the influenza A virus, which is associated with the modulation of their innate immunity [141]. T-lymphocytes of mice treated with BPA have increased secretion of interferon-γ and decreased secretion of interleukin-4 [142], whereas Lee et al. observed that BPA increases the levels of both interleukins 4 and 8 in mouse T-lymphocytes [143]. BPA (1 μM) exposure to mouse splenic lymphocytes inhibits the mitogenesis of these cells, particularly B lymphocytes [144]. Mice treated with BPA produce lymphocytes with higher amounts of immunoglobulin A and IgG2a. BPA exposure affects the nonspecific immune defenses [90] and modulates proliferation of B cells as well as the production of some cytokines and antibodies [145]. BPF and BPS exposure is reported to increase oxidative stress and the expressions of immunity-related genes in a concentration-dependent manner during the early developmental stages in zebrafish [146]. *Carussius auratus* exposed to BPA results in immunotoxicity, and such fish are prone to infectious diseases [147] (Table 3).

8. Discussion

Bisphenols are widely used as a raw material in the synthesis of polycarbonates, epoxy resins, and thermal paper. These chemicals are used in the manufacturing of numerous products including plastics, water pipes, toys, medical equipment, electronics, food cans, and numerous household applications. These chemicals are leached from the products and are ubiquitous in the environment. Foods and drinks are the most important sources of exposure. Results of both animal and human studies have revealed the toxic effects of bisphenols. Increased levels of bisphenols are found in human body fluids including in urine, serum, placental tissue, umbilical cord blood, and breast milk [60,78,84,97,124]. These chemicals affect animal and human organisms by interactions with estrogen, androgen, and aryl hydrocarbon receptors, and disrupt the function of the endocrine system, including altering the functions of sex hormones, insulin, leptin, adiponectin, or thyroxin. These chemicals exert various effects in living organisms as they are able to interact with receptors, generate ROS, lipid peroxidation, and alter cell signaling. Epidemiological studies have shown that exposure of the general population to bisphenol increases the risk of coronary heart diseases, neurological disorders, and metabolic disorders, including obesity and diabetes. Continuous exposure to bisphenols has shown detrimental effects on reproduction, development, and neural networks. These chemicals also affect the biology of immune cells, and play a significant role in the initiation or exacerbation of inflammatory conditions. Moreover, bisphenols show an age, gender, and dose-dependent effect. Even a low concentration of bisphenol is known to be detrimental; hence, critical assessment of their uses and the global influence on human health is necessary.

Humans and animals are exposed to bisphenols from the prenatal stage to the last day of survival. Bisphenols are present in products used daily, and we are always in contact with these chemicals, either indirectly or directly. Prenatal and childhood bisphenol exposure affects the developmental process and leads to neurological, reproductive, immunological, and endocrine disruption. Even low doses of bisphenols are toxic, and chronic exposure affects almost every body part. Bisphenols induce oxidative stress, inflammation, apoptosis, and impairs the metabolic process. Nowadays, almost every product contains bisphenol and we are unwillingly exposed to it. Foods and drinks stored in plastic containers get easily contaminated with bisphenols, and consumption of such foods results in gradual accumulation of bisphenols in our body. This accumulation eventually leads to toxicity of major body organs including the liver, brain, and kidney, ultimately disrupting the neurological, immunological, reproductive, and endocrine functions.

9. Conclusions

We need to have alternatives of bisphenols and try to minimize their uses because of their continuous exposure and impending toxicity. We have to work on processes/methods which can remove/filter out bisphenols from our body. Furthermore, a shift in focus towards natural plant products for packaging, storing, and other day-to-day activities is required. Soil made products can be promoted for storage of foods and drinks. The use of plastic bags needs to be restricted for shopping and extra packaging, and we need to promote the use of eco-friendly bags made of natural plant products.

Bisphenols have a wide range of toxicity profiles. However, we limited our discussion to the major organ systems. We did not discuss their role in cancer, respiratory system, renal, and developmental toxicity.

Abbreviations

BPA	Bisphenol A
BPB	Bisphenol B
BPC	Bisphenol C
BPS	Bisphenol S
BPF	Bisphenol F
BPAF	Bisphenol AF
ROS	Reactive Oxygen Species
MAPK	Mitogen-Activated Kinases
DM1	Diabetes Mellitus Type 1
DM2	Diabetes Mellitus Type 2

Author Contributions

Conceptualization, J.-J.K., S.K., V.K. (Vijay Kumar); methodology, J.-J.K., S.K., V.K. (Vijay Kumar).; writing—original draft preparation, J.-J.K., S.K., V.K. (Vijay Kumar); writing—review and editing J.-J.K., S.K., V.K. (Vinay Kumar), Y.-M.L., Y.-S.K., V.K. (Vijay Kumar). All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

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Annexure 4

Higher BPA levels linked to more asthma symptoms in children
No link found for closely related chemicals BPS and BPF

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Higher BPA levels linked to more asthma symptoms in children

No link found for closely related chemicals BPS and BPF

Date: July 28, 2020

Source: Johns Hopkins University Bloomberg School of Public Health

Summary: Children in low-income neighborhoods in Baltimore tended to have more asthma symptoms when levels of the synthetic chemical BPA (Bisphenol A) in their urine were elevated, according to a new study.

FULL STORY

Children in low-income neighborhoods in Baltimore tended to have more asthma symptoms when levels of the synthetic chemical BPA (Bisphenol A) in their urine were elevated, according to a study from researchers at the Johns Hopkins Bloomberg School of Public Health and School of Medicine.

While some products, including baby bottles, no longer contain BPA, exposures to BPA remain almost universal, and there are still concerns that, especially in childhood, those exposures might have a health impact.

Boys with elevated BPA were found to be at higher risk for having more asthma symptoms, the study found. The researchers found no statistically significant link between BPA levels and asthma symptoms among the girls in the study. The researchers also found that higher levels of two common chemicals closely related to BPA -- BPS and BPF -- were not consistently associated with more asthma symptoms. Like BPA, BPS and BPF are found in many consumer products, including food cans and beverage bottles.

For their analysis, the researchers examined clinical data and urine samples, taken at three-month intervals over a year, from 148 predominantly Black children in Baltimore. They found consistent links between higher BPA levels in urine and measures of recent asthma severity.

The study, published July 28 in the *Journal of Allergy and Clinical Immunology*, is thought to be the first to examine children's environmental exposures to BPA, BPS, and BPF and their associations with asthma severity.

"Our findings suggest that additional studies are needed to examine this BPA-asthma link, given the high burden of pediatric asthma and widespread exposure to BPA in the United States," says lead author Lesliam Quirós-Alcalá, PhD, assistant professor in the Department of Environmental Health and Engineering at the Bloomberg School. "This is especially important given that Black Americans have higher asthma rates than whites and also, according to CDC data, have higher exposure to these chemicals than whites."

BPA is a chemical building block used to make polycarbonate plastic as well as some epoxies. Produced at the rate of about 7 million tons per year worldwide, it can leach from polycarbonate bottles into the liquids they contain, and from epoxies that line cans of soup and other food items. A 2011 study published found that eating soup from cans lined with BPA-containing epoxy caused study participants' BPA levels to rise by a factor of almost 20.

BPA can activate estrogen receptors on cells, which suggests that it may have hormone-like effects -- disrupting human biology even at very small exposure levels. Animal studies have found evidence that the chemical can have pro-inflammatory effects. Epidemiological studies have found that people with higher BPA levels in their urine are more likely to have cardiovascular disease, diabetes, asthma, and some other conditions. Children are in principle more vulnerable, to the extent that they use BPA-containing products more often than adults do. Due to consumer concerns, companies stopped making BPA-containing baby bottles and sippy cups more than a decade ago, and have largely switched to non-BPA can epoxies.

BPS and BPF are close chemical relatives, or analogs, of BPA, and are found, for example, in can-linings and thermal-printer receipts -- often as replacements for BPA. They too can interact with estrogen receptors, although very little is known about their health impacts at current exposure levels.

In the new study, Quirós-Alcalá and colleagues examined the link between BPA and asthma. More than 25 million Americans, including about one out of twelve children, have this airway inflammatory disorder.

While prior studies in children have linked higher BPA levels to a greater likelihood of developing asthma, the researchers here looked for a link between BPA exposure and the extent of symptoms in established asthma -- or asthma "morbidity," as epidemiologists call it.

To do this, they analyzed clinical data, as well as stored urine samples, from the Mouse Allergen and Asthma Cohort Study (MAACS), which was conducted from 2007 to 2010 in Baltimore and covered 148 asthmatic children between 5 and 17. The study included 85 boys and 63 girls. Most of the children (91 percent) were Black, and most (69 percent) came from households with annual incomes below $35,000. Each child in the study was evaluated by doctors every three months for a year, and at these visits the child's caregiver filled out a questionnaire about the child's recent asthma symptoms and medical care.

Quirós-Alcalá and her colleagues found BPA in every urine sample taken during the study, with a mean concentration of 3.6 nanograms per milliliter -- consistent with one study of low-income minority children in the U.S., but several times higher than levels measured in other groups.

The children in the study varied greatly in their urine BPS levels, and the researchers found that a ten-times-greater level of BPS was associated with a 40 percent increased chance of having had "coughing, wheezing, or chest tightness" in the prior two weeks, along with an 84 percent and 112 percent increased chance of reporting an acute care or an emergency-room visit in the prior three months.

When the researchers analyzed the children by sex, they found that these associations remained statistically significant only for the boys.

The analysis also showed that BPS and BPF levels in urine of the 148 children were much lower on average than those for BPA, and in some urine samples were not found at all. Higher BPS or BPF levels were not consistently associated with more asthma morbidity.

This was an associational study and does not prove that BPA exposures caused health effects, but it suggests that more conclusive studies of cause and effect should be done, the researchers say.

"If these findings are confirmed in future studies, then avoiding or limiting contact with BPA sources may be advisable for families who have children with asthma," Quirós-Alcalá says.

Story Source:

Materials provided by **Johns Hopkins University Bloomberg School of Public Health**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Lesliam Quirós-Alcalá, Nadia N. Hansel, Meredith McCormack, Antonia M. Calafat, Xiaoyun Ye, Roger D. Peng, Elizabeth C. Matsui. **Exposure to bisphenols and asthma morbidity among low-income urban children with asthma**. *Journal of Allergy and Clinical Immunology*, 2020; DOI: 10.1016/j.jaci.2020.05.031

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Annexure 5

BPA, chemical used to make plastics, found to leach from polycarbonate drinking bottles Into humans

https://www.hsph.harvard.edu/news/press-releases/bpa-chemical-plastics-leach-polycarbonate-drinking-bottles-humans/

News

BPA, chemical used to make plastics, found to leach from polycarbonate drinking bottles Into humans

Exposure to BPA May Have Harmful Health Effects

For immediate release: Thursday, May 21, 2009

Boston, MA — A new study from Harvard School of Public Health (HSPH) researchers found that participants who drank for a week from polycarbonate bottles, the popular, hard-plastic drinking bottles and baby bottles, showed a two-thirds increase in their urine of the chemical bisphenol A (BPA). Exposure to BPA, used in the manufacture of polycarbonate and other plastics, has been shown to interfere with reproductive development in animals and has been linked with cardiovascular disease and diabetes in humans. The study is the first to show that drinking from polycarbonate bottles increased the level of urinary BPA, and thus suggests that drinking containers made with BPA release the chemical into the liquid that people drink in sufficient amounts to increase the level of BPA excreted in human urine.

The study appears on the website of the journal *Environmental Health Perspectives* and is freely available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2737011/.

In addition to polycarbonate bottles, which are refillable and a popular container among students, campers and others and are also used as baby bottles, BPA is also found in dentistry composites and sealants and in the lining of aluminum food and beverage cans. (In bottles, polycarbonate can be identified by the recycling number 7.) Numerous studies have shown that it acts as an endocrine-disruptor in animals, including early onset of sexual maturation, altered development and tissue organization of the mammary gland and decreased sperm production in offspring. It may be most harmful in the stages of early development.

“We found that drinking cold liquids from polycarbonate bottles for just one week increased urinary BPA levels by more than two-thirds. If you heat those bottles, as is the case with baby bottles, we would expect the levels to be considerably higher. This would be of concern since

infants may be particularly susceptible to BPA's endocrine-disrupting potential," said Karin B. Michels, associate professor of epidemiology at HSPH and Harvard Medical School and senior author of the study.

The researchers, led by first author Jenny Carwile, a doctoral student in the department of epidemiology at HSPH, and Michels, recruited Harvard College students for the study in April 2008. The 77 participants began the study with a seven-day "washout" phase in which they drank all cold beverages from stainless steel bottles in order to minimize BPA exposure. Participants provided urine samples during the washout period. They were then given two polycarbonate bottles and asked to drink all cold beverages from the bottles during the next week; urine samples were also provided during that time.

The results showed that the participants' urinary BPA concentrations increased 69% after drinking from the polycarbonate bottles. (The study authors noted that BPA concentrations in the college population were similar to those reported for the U.S. general population.) Previous studies had found that BPA could leach from polycarbonate bottles into their contents; this study is the first to show a corresponding increase in urinary BPA concentrations in humans.

One of the study's strengths, the authors note, is that the students drank from the bottles in a normal use setting. Additionally, the students did not wash their bottles in dishwashers nor put hot liquids in them; heating has been shown to increase the leaching of BPA from polycarbonate, so BPA levels might have been higher had students drunk hot liquids from the bottles.

Canada banned the use of BPA in polycarbonate baby bottles in 2008 and some polycarbonate bottle manufacturers have voluntarily eliminated BPA from their products. With increasing evidence of the potential harmful effects of BPA in humans, the authors believe further research is needed on the effect of BPA on infants and on reproductive disorders and on breast cancer in adults.

"This study is coming at an important time because many states are deciding whether to ban the use of BPA in baby bottles and sippy cups. While previous studies have demonstrated that BPA is linked to adverse health effects, this study fills in a missing piece of the puzzle- whether or not polycarbonate plastic bottles are an important contributor to the amount of BPA in the body," said Carwile.

The study was supported by the Harvard University Center for the Environment and the National Institute of Environmental Health Sciences Biological Analysis Core, Department of

Environmental Health, HSPH. Carwile was also supported by the Training Program in Environmental Epidemiology.

"Use of Polycarbonate Bottles and Urinary Bisphenol A Concentrations," Jenny L. Carwile, Henry T. Luu, Laura S. Bassett, Daniel A. Driscoll, Caterina Yuan, Jennifer Y. Chang, Xiaoyun Ye, Antonia M. Calafat, Karin B. Michels, *Environmental Health Perspectives*, online May 12, 2009.

Annexure 6

Leading Edge Erosion

a) Leading Edge Erosion

The following is quoted from “A practical study of the aerodynamic impact of wind turbine blade leading edge erosion” by N Gaudern, Vestas Technology UK Ltd. West Medina Mills, Stag Lane, Newport, Isle of Wight, PO32 5TS

“During operation wind turbine blades are exposed to a wide variety of atmospheric and environmental conditions; inspection reports for blades that have been operating for several years show varying degrees of leading edge erosion. The scale and form of erosion features develop over time, with the observed damage ranging from small pin holes to a substantial loss of leading edge paint. [1-4] The erosion of blade leading edges is considered to be normal wear and tear.”

These images are from the same study.

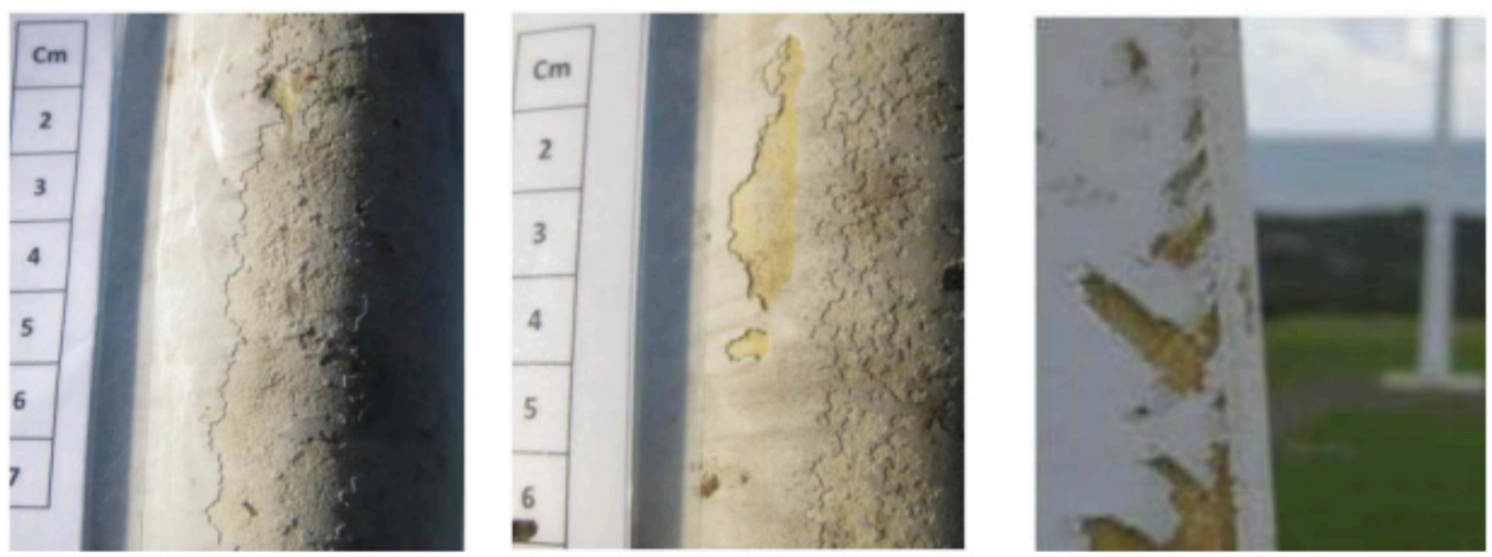

Figure 1. Examples of LE erosion.

A powerpoint presentation by Vestas titled Project 8: Modelling of leading edge erosion patterns provides the following information.

“Leading edge erosion of wind turbine blades is a high priority topic for the wind industry. Degradation of the blade leading edge is caused by continual impacts from airborne particulates (primarily raindrops) during turbine operation. Even minor disturbances to the surface quality can result in premature boundary layer transition which results in lower aerodynamic performance. More severe degradation can result in a significant drop in performance”

An article titled “Leading Edge erosion and pollution from wind turbine blades” Asbjørn Solberg, Bård-Einar Rimereit and Jan Erik Weinbach estimates emissions of microplastics and possible toxic combines from wind turbines based on the report "Rain Erosion Maps for Wind Turbines Based on Geographical Locations: A Case Study in Ireland and Britain" University of Strathclyde, 2021. The authors of this article estimate that the estimated annual emission of microplastics of approximately 62kg per year per turbine. This is based on a turbine that is a significantly smaller than the ones being proposed by Vestas but the rainfall in the example is higher than the rainfall of the project area. However, the Winterbourne area is prone to cold temperatures, creating sleet, hail, snow and ice particles in the air, that would be arguably