Apau et al., *Cogent Chemistry* (2018), 4: 1506601
https://doi.org/10.1080/23312009.2018.1506601

cogent chemistry

MEDICINAL CHEMISTRY | REVIEW ARTICLE

Exposure to bisphenol A, bisphenol F, and bisphenol S can result in obesity in human body

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Received: 05 June 2018
Accepted: 26 July 2018
First Published: 07 September 2018

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Reviewing editor:
Bryan M. Wong, University of California, Riverside, USA

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Abstract: Exposure to endocrine disruptors such as bisphenols (BPs), for example, bisphenol A, bisphenol S and bisphenol F in early life may contribute to obesity.

BPs are man-made chemicals found in lots of household products including food packaging, drink containers, lotions, toys, plastic PVC flooring and water pipes. Human exposure to these chemicals has been linked to serious adverse health outcomes including cardiovascular disease, abnormal sperm morphology/sperm DNA damage, miscarriage, early puberty, diabetes and obesity.

Subjects: Chemistry; Health & Society; Health Conditions

Keywords: bisphenols; household products; adverse health outcomes; man-made chemicals; obesity

1. Introduction

Bisphenols (BPs) are produced in large amounts worldwide and it is estimated that 2 million tons are used for production of goods each year. Their use has increased over the last few decades and as a result they are found throughout the environment and in human tissue (Bonefeld-Jorgensen, Long, Hofmeister, & Vinggaard, 2007). BPs are known endocrine disrupting chemicals (EDCs) that imitate or block the action of natural hormone or alter the amount of hormone synthesized (Diamanti-Kandarakis et al., 2009). EDCs are also known as obesogens. Obesogens promote adiposity by changing programming of fat cell development (adipogenesis) raising energy storage in fat tissue and interfering with neuroendocrine control of appetite and satiety (Heindel et al., 2005). EDCs are

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PUBLIC INTEREST STATEMENT

Bisphenol A (BPA) is one bisphenol that is widely use as monomer in the industry to manufacture plastics and other household goods that human use. Because of health concerns due to adverse health effect on human, an attempt is made to replace BPA with bisphenol F (BPF), and bisphenol S. BPA, BPF and bisphenol S are produced in large amount every year as are used to manufacture plenty industrial products. Consequently, they are present everywhere in the environment. BPF and BPS are not safe substitute for BPA as they have same adverse health effect to human. The three bisphenols are known as endocrine disrupting chemicals (EDCs); that imitate or block the action of natural hormone or alter the amount of hormone synthesized. EDCs are called obesogens as they promote adiposity in the human body and cause the body to gain weight. This can lead to being severely overweight or obese.

synthetic chemicals, found in various consumer products and building materials including furniture, electronics, personal care and cleaning products (Casals-Casas and Desvergne, 2011).

Bisphenol A (BPA) is one of the BPs that is widely used as a monomer in the industry to manufacture polycarbonate plastics; however, because of health concerns, it has largely been replaced by BPF, bisphenol S (BPS), and this has resulted in an increase in the production of BPF and BPS over the last few decades (Fürhacker, 2000). Research shows that BPS and BPF being employed to replace BPA have metabolism, potencies and mechanism of action close to BPA. BPS and BPF appear to be endocrine disruptors with hormonal actions exceeding that of BPA (Vinas and Watson, 2013a). BPA-free containers like baby bottles made of materials such as glass, stainless steel and Tritan copolyester are at the market whereas, polypropylene is in reusable food storage containers, baby bottles, food packaging, plastic parts and laboratory equipment all available at the market (Oregon Environmental Council., 2013). Other BPA-free materials are acrylic resin, phenolic resin and polyester resin which are used in metal cans of food liners (LaKind, 2013)

BPs, however, are not stable and over time can migrate from cans coated with epoxy or other plastics in contact with food or beverages (Koch et al., 2006).

Children because of their behaviour are often vulnerable to contaminants, harmful chemicals and this is also true with respect to BPs. The exposure of children to BPs has been linked with obesity (Grun et al, 2006). Obesity increases the risk of several weakening and killer diseases including diabetes, heart diseases and some cancers (US National Heart, Lung and Blood Institute, 1998). Obesity decreases the quality and length of life of a person, the healthcare costs of an individual increases and also increases the health costs of a country with prevalence obesity (US National Heart, Lung and Blood Institute, 1998).

2. Chemical structures of BPs and uses

BPA, BPF and BPS are group of chemical compounds that have similar structure. Bisphenol A, bis(4-hydroxyphenyl) propane, (BPA), is an organic compound made of two benzene rings, two methyl groups and two hydroxide groups ($C_{15}H_6O_2$) (Danzl, Sei, Soda, Ike, & Fujita, 2009). The chemical structures of BPA, BPF and BPS are shown in Figure 1(A). BPA is one of the most widely used chemicals with nearly 2 million tons used in the industry every year. Normally, BPA appears as white crystals and it is derived from acetone and phenol as shown in Figure 2.

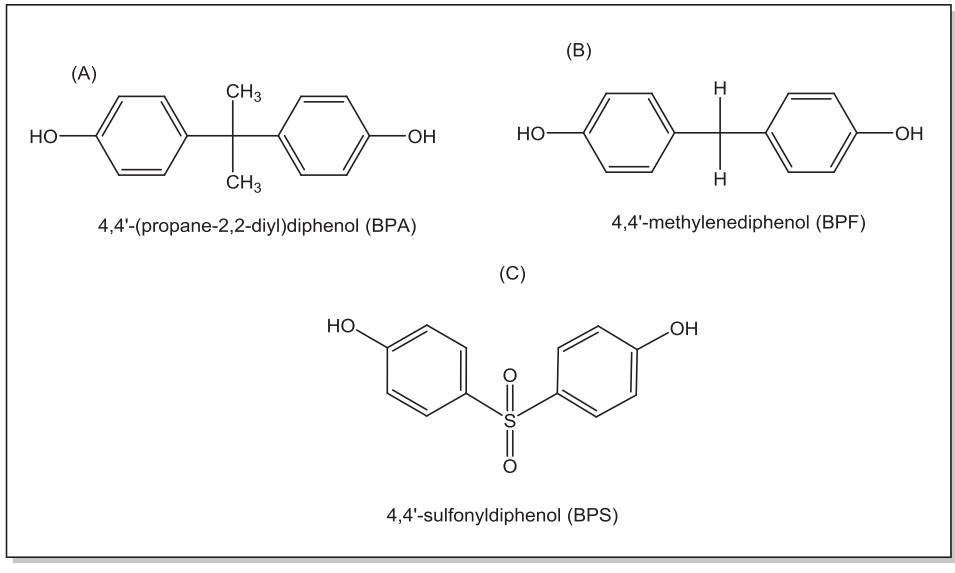


Figure 1. Chemical structures of BPA, BPF and BPS.

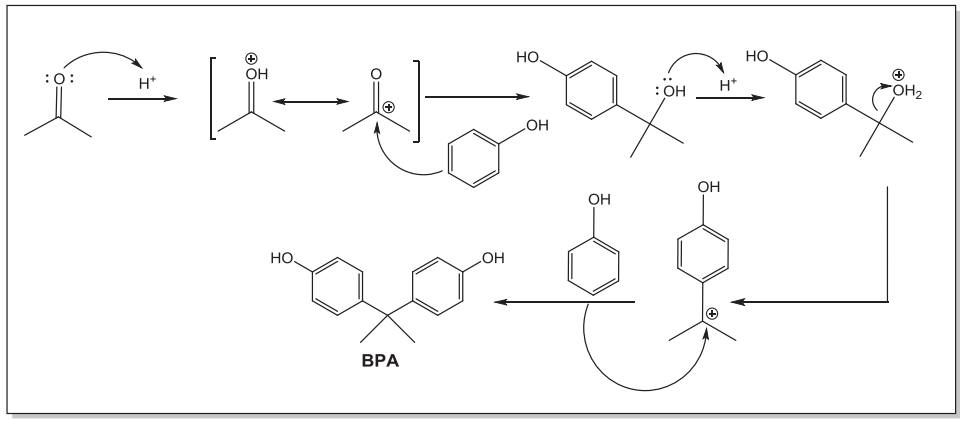


Figure 2. Friedel–Crafts hydroxyalkylation for the manufacture of BPA.

Currently there are two known analogues of BPA, and these are BPF also called bis(4-hydroxyphenyl) methane and BPS called bis(4-hydroxyphenyl) sulphone (Rochester & Bolden, 2015) (Figure 1B,C).

BPA and the analogues BPS and BPF are used in the manufacture of plastics, the paper on which receipts are printed, food packaging (Bonefeld-Jorgensen et al., 2007; Rochester, 2013), fastening agents in cleaning products, an electroplating solvent, a constituent of phenolic resin and as a developer in thermal paper (Clark, 2012), and coatings (Rochester & Bolden, 2015). Epoxy resins made from BPs are used for making lacquers, varnishes, adhesives, plastics, water pipes, dental sealants and food packaging (McKenzie et al., 2012). Additionally, BPs are used in compact disc, cell phones and bicycles. BPA is manufactured from acetone and phenol at the industry by the Friedel–Crafts hydroxyalkylation process.

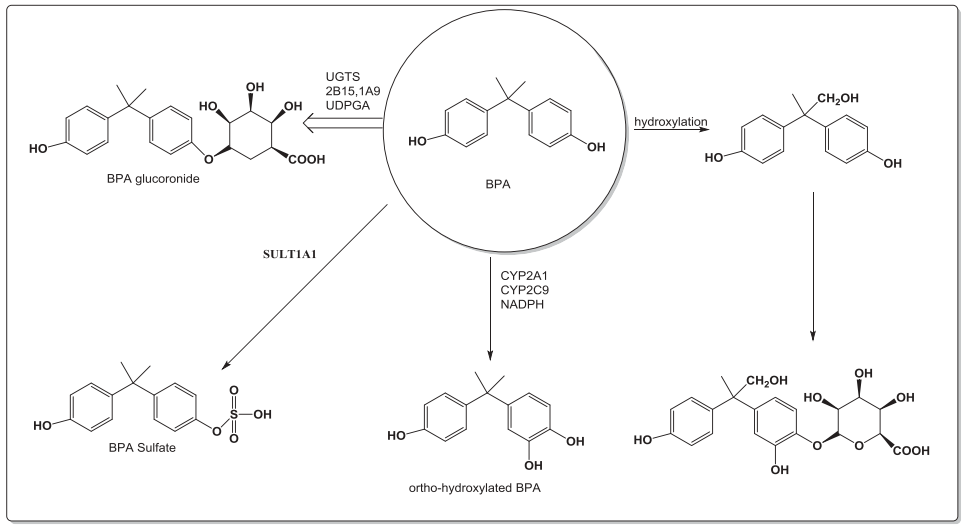
3. Metabolism of BPs in human

Human are exposed to BPA to a large extent via foods contaminated with epoxy resin, and this come from polycarbonated food cans or beverage cans, to a lesser extent through other pathways such as dermal absorption and inhalation of BPA-contaminated air (Geens, Goeyens, & Covaci, 2011). Once in the body, BPA metabolism is by glucuronidation under the catalytic action of two enzymes. While uridine 5-diphospho-glucuronosyltransferase (UGT) catalyses the conversion of BPA to BPA glucuronide, sulfotransferase catalyses the conversion of BPA to the BPA sulphate. Both metabolites are soluble and eliminated from the human body in urine (Nishiyama et al., 2002; Suiko et al., 2000; Yokota et al., 1999). The biotransformation of BPF and BPS is still unclear, but reactions carried out *in vivo* and *in vitro* organisms indicate that BPF metabolism is similar to BPA, while published studies on the biodegradation of BPS are extremely scarce (Cabaton et al., 2008; Dumont et al., 2011; Ji et al., 2013). Figure 3 shows how BPA is metabolised in human body.

4. Effects of exposure to BPs

There is limited information about the adverse effects of non-BPA BPs; however, it is believed that they have similar effects to BPA (Rosenmai et al., 2014). The concentration of BPA in human fluids or tissues including serum, foetal plasma, placental tissue and breast milk has been determined. Several of these studies focused on children and pregnant women where raised BPA levels were linked with chromosomal abnormalities (Vandenberg, Hauser, Marcus, Olea, & Welshons, 2007) and miscarriages (Huang & Leung, 2009; Vandenberg et al., 2007). High levels of BPA have also been linked with infertility in women (Vandenberg et al., 2007) and abnormal karyotypes in foetuses (Vandenberg et al., 2007; Yamada et al., 2002). High BPA levels have also caused increased unilateral or bilateral blood-filled ovarian bursae in women (Markey, Coombs, Sonnenschein, & Soto, 2003).

Figure 3. Metabolism of BPA.



5. Some studies on BPA and obesity

A Serbian study involving 103 women aged 19–50 years measured BPA in first morning urine and a number of anthropometric measures including weight, height and waist circumference (WC) were collected. They reported a positive association between BPA and obesity (Milošević et al., 2017). However, limitations of this study were a cross-sectional sample collection and the number of participants were small. Also, no physical activity data were collected.

Another recent study in the USA involving 977 adult women was conducted, where BPA in urine was monitored, anthropometric measures including weight and height were collected. BPA showed a significant association with modestly faster weight gain (Song et al., 2014). A different recent study in the USA (Hoepner et al., 2016) also determined BPA in urine of children and pregnant women. Of these 408 children were 3 years, 518 children were 5 years monitored until 7 years of age, along with 369 pregnant women who were between the ages 18 and 35. Fat mass index (FMI), body fat (BF) and WC were the anthropometric measures collected. The study was to monitor mothers and their children at different stages of their development.

In this study, BPA concentration of pregnant women had a positive association with FMI, BF and WC of children at age 7 but not associated with birth weight and childhood body mass index *z*-scores (BMIZ) at ages 5 and 7 and change in BMIZ from ages 5 to 7 (Hoepner et al., 2016). A limitation of the study was that the physical activity information of participants was not provided.

A study in China involving 1326 students aged between 9 and 12 also measured BPA in urine where anthropometric measures collected were weight, height, WC, hip circumference and skin-fold thickness (Li et al., 2013). The study showed BPA had positive association with obesity in girls but not in boys

6. Obesity diagnosis

Obesity can be defined using body mass index (BMI) which is accepted by WHO to diagnose obesity in people, less than 18.5 kg/m^2 is underweight, between 18.5 and 24.9 kg/m^2 is normal, between 25 and 29.9 kg/m^2 is overweight, between 30.00 and 34.99 kg/m^2 is class 1 obese, between 35.00 and 39.9 kg/m^2 is class 2 obese and above 40 kg/m^2 is class 3 obese (WHO., 2000). A nomogram is used to assess whether a child is obese. BMI equal to or greater than the age- and gender-specific 95th percentile is considered obese (Centre for disease control (Whitlock et al., 2010). An obese person accumulates excess BF in his or her muscle, bone, fat and water (Ogden et al., 2006). Obese

people are at high risk of many health problems including mortality, high blood pressure (hypertension), high or low-density lipoprotein cholesterol or low high-density lipoprotein cholesterol and high levels of triglycerides (dysilpidemia), type 2 diabetes, coronary heart disease, stroke, gallbladder disease, osteoarthritis and some cancers including endometrial, breast, colon, kidney, and liver cancer and gallbladder (Jensen et al., 2013; Williams et al., 2015).

7. Relevance of the study

Obesity is a global health problem with obesity situation and trends doubled between 1980 and 2008 (WHO, 2014). Ghana is among 73 countries where overweight or obesity has doubled since 1980 (The New York Times Company, 2017). In that period, Ghana's obesity rates have gone up to 650%, from less than 2% of the population to 13.6% (WHO Technical Report Series 894 Geneva: World Health Organization, 2000). Therefore, in order to stop or reduce the trend of rising cases of obesity, it will be necessary to study the EDCs in the human body, which disrupt the work of natural hormone and cause obesity in humans. This will make people worldwide aware of the health threat that these chemicals pose to man. As a result of the adverse health effect of BPA to human; the European Union (EU) in January 2011, placed a ban on the use of BPA in the manufacture of baby bottles and a ban on the marketing and its importation into EU (EU Commission Directive, 2011). On the same adverse health issue of BPA, the US Food and Drugs Administration (FDA) in 2012 banned the use of BPA in baby bottles, sippy cups and infant formular containers (US FDA, 2012). Obesity increases the risk of several, weakening and killer diseases including diabetes, heart diseases and some cancers (US National Heart, Lung and Blood Institute, 1998). Obesity decreases the quality and length of life of a person, the healthcare costs of an individual increases and also increases the health costs of a country with prevalence obesity (US National Heart, Lung and Blood Institute, 1998).

The causes of obesity are plenty, such as lifestyle, genetics, the eating of processed food rich in fat and sugar or carbohydrate; however BPA and analogues when absorb into the human body play a role in promoting adipogensis and cause weight gain resulting in obesity especially in adolescent (Baillie-Hamilton, 2002).

Acknowledgements
The authors highly recognice and appreciate the important role played by Dr Natheniel Owusu Boadi and Mr Joseph Frimpong in the materials processing.

Funding
The authors received no direct funding for this research.

Competing interests
The authors declares no competing interests.

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Citation information
Cite this article as: Exposure to bisphenol A, bisphenol F, and bisphenol S can result in obesity in human body, Joseph Apau, Akwasi Acheampong & Eric Adua, *Cogent Chemistry* (2018), 4: 1506601.

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***Cogent Chemistry* (ISSN: 2331-2009) is published by Cogent OA, part of Taylor & Francis Group.**