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Bisphenol-A

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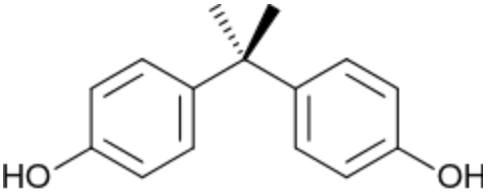
Overview



Bisphenol-A (BPA) was created in the late-nineteenth century by the Russian Aleksandr Dianin, who coined it "Dianin's Compound." BPA is now ubiquitous and used primarily as a strengthener in polycarbonate plastics. It is widely used, but has been shown to cause many developmental disorders and thyroid problems in laboratory settings. Concerns over BPA's adverse effects on human health have recently led Health Canada to deem it potentially harmful and to ban the sale of plastic baby bottles containing the compound. The United States is poised to issue a ruling on steps to take concerning the chemical as well. A few large retailers, including Wal-Mart, have begun phasing out products that contain BPA.

Chemical Background

BPA has two large phenyl groups, as well as two electron-rich hydroxyl (or alcohol) groups and two methyl groups. BPA in its free form is somewhat lipophilic, the nomenclature used when a substance tends to associate with lipids. However, through conjugation, a biochemical process that makes a substance more water-soluble, BPA is slightly more hydrophilic. The free form is typically found in adipose tissue or reserves and in breast milk. The hydrophilic form is usually seen in urine and excrement.

BPA has moderately high water solubility, about 120 mg/liter. In addition, this chemical has a low vapor pressure of about 5.32 to 5 Pascals (Groshart C Okkerman P and Pinjenburg A 2001). A standard coefficient for various environmental substances is the octanol-water partition coefficient (Kow). This ratio is the concentration of a chemical in octanol, commonly used as an organic solvent, and water at equilibrium (United States Geological Survey 2008). The log Kow value for BPA varies from 2.2 to 3.4 (see figure A:3 for additional properties). Consequently, these characteristics of bisphenol-A give it the propensity to partition in water, and the rate of evaporation from soil and water is low. Given this information, it is certain that bisphenol-A has a moderate potential of Bioaccumulation. Furthermore, BPA was found not to readily biodegrade (Groshart et al, 2001).

Adverse Health Effects

Long-Standing Historical Research

BPA has long been documented for its perils and potentially harmful effects. The first studies were conducted in the 1930s. At that time, studies indicated BPA to be a "weakly" estrogenic molecule, but the data were largely dismissed. During this age, a lot of the attention was being directed to the remarkable feat of creating synthetic human estrogen within national laboratories. Additionally, the extremely potent synthetic compound diethylstilbestrol, an oral estrogenic drug, was developed. BPA's studies were unscientifically compared to diethylstilbestrol, a very strong estrogenic compound. Thus, bisphenol-A was overlooked. Nonetheless, studies conducted by Dodds and Lawson (1936) confirmed the estrogenicity of bisphenol-A. Their archaic experiments were conducted on ovariectomized female rats, which had their ovaries removed. Afterward, each rat was directly fed BPA. The results published from this primitive research show over-activation of estrogen receptors through agonist activity. Agonists such as BPA mimic the original substrate molecule, eliciting a response similar or identical to that of the original chemical. The two researchers were particularly interested in the molecular component that triggered the increased concentration of the estrogen hormone, and not so interested in the effects of the increase. Through many years of research, it is unclear why it took so many years for this chemical to resurface in popular media. Recent research has been exhaustive and much more conclusive.

Developmental and Reproductive Concerns

Those most vulnerable to problems resulting from BPA exposure are pregnant mothers and newborns. According to Ramakrishnan and Wayne (2007), BPA has been detected in various fluids such as amniotic fluid, maternal and fetal plasma, placenta, and breast milk. Their research shows significant data about the harmful effects of bisphenol-A on many developing fetuses. Testing on Japanese medaka fish (*Oryzias latipes*), which have a transparent embryo allowing for analysis of organ development, led researchers to conclude that BPA, at chronic and subchronic levels, would alter several variables: embryonic development, hatching, body growth, and reproductive maturation (see figure 3). An "increased rate of development observed upon chronic exposure to BPA was an effect on the whole organism and not just specific organs" (#Ramakrishnan and Wayne, 2007). Growth patterns of the organisms consistently show undersized patterns when compared to control groups. Furthermore, researchers observed changes in the onset of puberty and in reproductive functioning, which is consistent with many previous studies. Lastly, the article states that BPA may affect sexual maturation and reproductive function through an alteration in endocrine homeostasis.

Common Uses of BPA

With more than six million pounds produced in the U.S. each year, BPA is a widely used component in many products including these
below:

- baby bottles and nursing products
- dental sealants and orthodontic products
- water bottles and other food and beverage containers
- the liners of food cans
- CDs and DVDs

- eyeglasses
- water pipes
- sports safety equipment
- medical equipment and tubing
- consumer electronics
- PVC
- plasticizers From (#AP, 2008), (#Vandenberg, et al., 2007), Groshart C Okkerman P and Pijnenburg A (2001).

Nalgene Bottles

One of BPA's most infamous uses was as a component in the wildly popular Nalgene water bottles. The company that produces Nalgene, Nalge Nunc International (a division of Waltham, Mass.-based Thermo Fisher Scientific Inc.), stated in April 2007 that it will substitute its "Nalgene Outdoor" line of polycarbonate plastic containers with BPA-free alternatives (#Gillies, 2008).

Additional Uses

#Groshart et al, 2001 states that bisphenol-A is used for unsaturated polyester, polysulfone, polyetherimide, and that nonpolymer BPA is used as an additive in flame retardants, brake fluids, and thermal papers. (see figure A:1 for flow chart of polymers).

Opportunities for Exposure

This chemical is ubiquitous and can be found aquatically, terrestrially, and aerobically (#vom Saal et al, 2007). Bisphenol-A is currently produced by well-known companies including General Electric, Dow Industries, Shell Corporation, Mitsubishi, and Bayer (#Groshart et al, 2001). Some claim that exposures are higher in highly industrialized countries, but developing nations are equally at risk, if not at greater risk, due to the comparative lack of regulatory agencies.

BPA is known to have leaching capabilities, which is of particular concern due to BPA's use in food and beverage containers and common disposal in landfills. Many scientists cite the biggest source of exposure as consumption of food and beverages enclosed in plastic containers containing BPA.

Regulation

There are several cities and countries implementing bans on BPA. In Ottawa, Canada, many stores have banned popular products which contain bisphenol-A. "Church and environmental groups in Canada have mounted campaigns against bottled water because of concerns about the huge amount of plastic used in containers" (#Austen, 2007). This trend can be seen throughout North America and Western Europe. Scandinavian countries have yet to implement a national policy, but some nations like Norway have designed a better waste management system for products containing a significant amount of BPA. The Netherlands, one of the most environmentally progressive nations in the world, plans to establish a policy regarding this chemical, and many others, by 2010.

Health Canada Decision

See the Health Canada report from April 2008

The Canadian Departments of Health and the Environment announced on Friday, April 17, 2008 that they considered BPA to be potentially harmful and moved to ban polycarbonate bottles used to feed infants (#Gillies, 2006 and #Austen, 2008). They banned only the sale of bottles used for feeding infants because they concluded that BPA posed the greatest risk for newborns and children up to the age of 18 months (#Austen, 2008). Children are more vulberable to exposure to BPA, and the regular cleaning of infant bottles causes BPA to leach from the plastic (#Austen, 2008). Some major retailers, including Wal-Mart, are phasing out infant bottles that contain BPA (#Pooter, 2008).

Scope of BPA Exposure

A recent study measured BPA levels in the urine of nearly 3,000 randomly selected people (6 years old and above), and BPA was found in over 92 percent of the people tested. Statistical analysis showed that females had higher BPA concentrations than males (see table 1). Moreover, BPA concentrations were higher in households with lower incomes, and children had the highest BPA concentrations, followed by adolescents (see figure 2) then adults (#Calafat et al, 2008). Of the three racial groups defined by the researchers, Mexican Americans had the lowest BPA concentrations, as compared to non-Hispanic whites and non-Hispanic blacks.

Calafat et al (2008) state that the data suggest continual exposure to BPA, where a fraction of the absorbed BPA may distribute to fatty tissue sites then be slowly released into the bloodstream, and ultimately into the urine. They hypothesize that the higher concentrations of BPA in children may be due to children's proportionally higher rates of food consumption and air inhalation (compared with adolescents or adults). The differences among the three groups could also be related to varying rates or mechanisms of absorption, distribution, metabolism, or excretion of BPA (#Calafat et al, 2008).

Limiting Exposure

The simplest way to limit exposure is to avoid food and beverage containers containing BPA. Plastics for food use are typically labeled with a recycling code identifying the type of plastic resin used. In the article by Tungend (2008), Professor vom Saal suggests plastic users choose Type 2, made from polyethylene, and Type 5, made from polypropylene. Many agree to stay away from Type 7 plastic, popularly used for thick, resilient plastic products including polycarbonate. However, vom Saal emphasizes not heating any type of plastic in the microwave. The article points out that while conservation is certainly important, people should avoid reusing dented or battered plastic due to increased leaching potential. Reusable bottles made from non-plastic materials are another healthy and environmentally friendly option.

Discrepancies

With so many simultaneous studies being conducted, published, and reviewed, debate revolves around the guidelines and results that allow scientists to deduce the lowest-observable-adverse-effect (LOAEL). This level is the "lowest tested dose of a substance that has been reported to cause harmful (adverse) health effects on people or animals" (Agency for Toxic Substances and Disease Registry2008). In an effort to tackle this problem, a panel was assembled in Chapel Hill, North Carolina, United States. Members of the panel reviewed countless studies and reached the consensus that the currently accepted LOAEL is 50 mg (per kg/day) (#vom Saal et al, 2007).

The panel consisted of researchers from Germany, Italy, Japan, Spain, United Kingdom, and the United States. It affirmed that BPA has other modes of endocrine disruption in addition to binding to estrogen receptors. It also claims that BPA can alter hormone metabolism and concentrations in tissue enzymes and the thyroid hormonal axis. It has been speculated that this modification, specifically with the endocrine functions of the thyroid, is due to antagonist-like properties toward thyroid transcription, but more research is necessary (#vom Saal et al, 2007).

Initial research conducted early in the twentieth century, which dubbed BPA to be a "weak" environmental estrogenic compound, has been debunked. Now, the panel indicates that bisphenol-A is equipotent with moderately strong estradiol, in reference to the ability to activate responses through cellular membrane estrogen receptors (#vom Saal et al, 2007).

Future Research

With an annual production of over six billion pounds, it is no wonder there is so much controversy regarding bisphenol-A's presence in society (#Vadenberg, et al, 2007). While recent studies have been very effective at demonstrating toxicity, many studies show overlap in data and findings. It is clear that the most vulnerable groups are pregnant women (in utero) and children because the effects of BPA are irreversible. During these critical periods in development, possible ailments include increases in prostate and breast cancer, uro-genital abnormalities in male babies, a decline in semen quality in men, early onset of puberty in girls, metabolic disorders including insulin resistant (type 2) diabetes and obesity, and neurobehavioral problems such as attention deficit hyperactivity disorder (#vom Saal et al, 2007). Looking through the literature, it is evident that future research should examine BPA levels within human tissues. And, while most studies hold high ecological validity, the preeminent source of data should be from epidemiology studies of human exposures. Both acute metabolic studies and continuous exposure studies on humans are necessary.

Current Events

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- The Canadian Press, "BPA detected in jarred baby food, water", Telegraph Journal, July 13, 2009.
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