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Chapter- 18

An Environmental Pollutant: Bisphenol A (BPA), Posing a Risk to Human Health

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Keywords: Bisphenol A, environmental pollutant, endocrine disrupter, multisystem toxicity.

Abstract:

Every day, we come into contact with various chemicals produced by humans and found in the natural world. These substances are referred to as environmental pollutants. Even while certain chemicals are not dangerous, they might pose a risk if handled or misused. We can absorb harmful substances through our skin or breathe them in, ingest, or drink them. Bisphenol A (BPA) is one of the most significant substances we eat regularly. One synthetic organic chemical is BPA. It belongs to the group of phenol derivatives chemically. Commercial uses include the production of polycarbonate plastics for water and infant bottles, among other things, and epoxy resins for the inner coating of food and drink cans (soft and heavy). Studies have shown that consuming foods, beverages, and water tainted with BPA exposes people to the chemical. BPA's potential health risks have been investigated in humans and animals. Since it exhibits estrogenic effects in a variety of animal models, it is regarded as an endocrine disruptor. Nevertheless, BPA also causes different forms of neuromuscular, behavioral, developmental, and reproductive toxicity in laboratory animals. One could argue that ingesting BPA daily increases the risk of disease development in all people. Because of this, such substances constantly endanger our lives, both directly and indirectly. To ensure that our society is safe for future generations, we should aim to limit BPA exposure through reduced consumption, even though we are unable to stop BPA exposure from the environment at this time.

Introduction:

Both naturally occurring and artificially created chemicals have made a significant contribution to prosperity. Some of these chemicals, nevertheless, have also been shown to seriously harm both the environment and people (Samal et al., 2017; Mondal et al., 2022). While not all chemicals are dangerous, they can still be dangerous if handled or used improperly. To cause illness, our bodies need to absorb a specific quantity of a dangerous substance. Inhaled, eaten, drunk, or absorbed through the skin are all ways that harmful chemicals can enter our bodies. Individuals react differently to exposure to these chemicals. Sometimes illness happens only if we are exposed to a harmful substance for a long time. Several factors play a role in whether we get sick from contact with chemicals, such as the kind of chemical we are exposed to, how much of the chemicals we were in contact with, how long the contact lasted, how often we were exposed, how it entered our body, and finally our health

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risk. This brief review of BPA explains some of the connections between chemicals and potential health risks. We will undoubtedly learn about BPA from this article and the potential health risks that come with being exposed to it daily at home and work.

BPA is a synthetic organic compound. Many plastics and plastic additives are made of it as their building block (Biedermann et al., 1998; NTP, 1982; Vom Saal and Meyers, 2008). It is utilized in the manufacturing of epoxy resins and polycarbonate plastics. Plastic products of all kinds, including water bottles, bottles for nursing babies, soft and hard drink containers, etc., are mostly made of polycarbonate plastics. Moreover, BPA is frequently utilized in the production of various plastic goods, including dental sealants, optical lenses, medical equipment, CDs, DVDs, electrical equipment, sports safety equipment, and a host of other household appliances (Burridge, 2003; NTP, 1982). When BPA-contaminated food, drink, or water is consumed, humans are exposed to BPA. According to Biles et al., 1997 and NTP, 1982, certain dental sealants and composites may also be significant sources of BPA exposure for people (Figure 1). Both humans and certain animal models have been used to study the potential health risks of BPA.

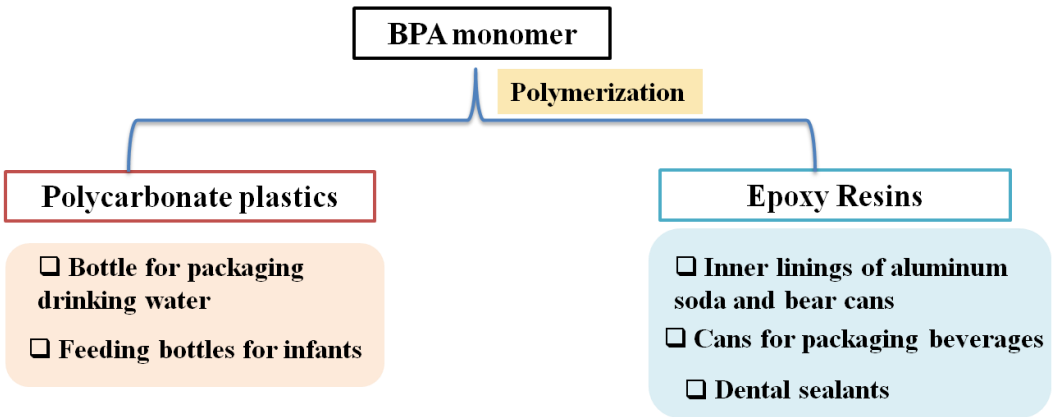

Figure 1. Industrial applications of bisphenol A (BPA).

In animal models, it exhibits multisystem toxicity (Della et al., 2023) (Figure 2). The mode of action of BPA appears to mimic that of the female hormone estrogen (Krishnan et al., 1993; Matsumoto et al., 2005; Rudel et al., 2001). As a result, BPA can be regarded as a synthetic chemical that disrupts hormones. It causes a variety of reproductive and behavioral toxicities as a result of its estrogenic activities (Chitra et al., 2003; Krishnan et al., 1993; Patisaul et al., 2006; Patisaul et al., 2009; Savabieasfahani et al., 2006). Additionally, it has harmful effects on the liver (Inoue et al., 2003; Bindhumol et al., 2003). According to reports, BPA affects the function of coronary smooth muscle in addition to its estrogenic properties (Asano et al., 2010). Rats' intestinal and atrial contractility are both decreased by BPA (Pant et al., 2011; Sarkar et al., 2016).

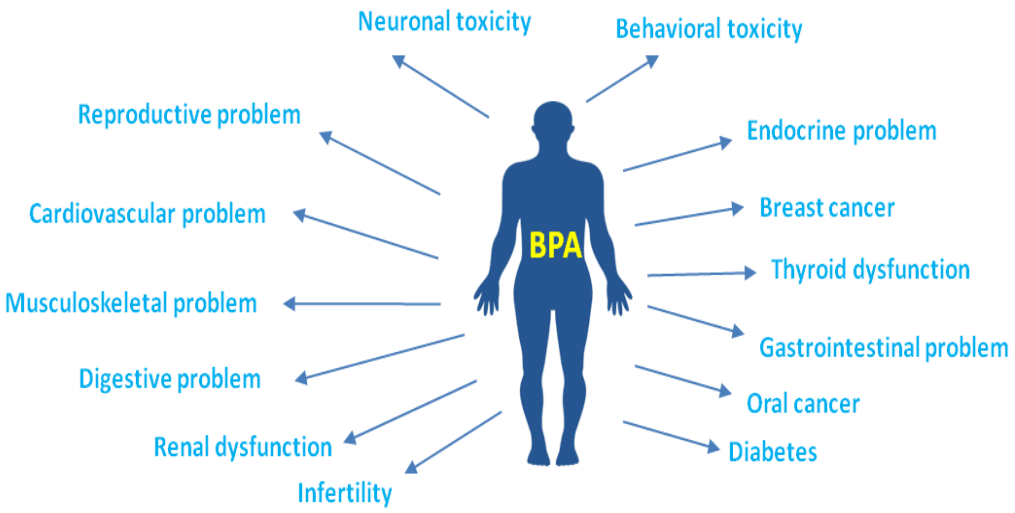

Figure 2. Adverse effect of BPA on human health.

Estrogenic activities of BPA:

Endocrine disrupting chemical (EDC) is an external substance that tampers with the body's natural hormone production, release, transport, metabolism, binding, action, or elimination. These hormones are in charge of preserving homeostasis and controlling developmental processes (Wetherill et al., 2007). Based on conventional bioassays, BPA has been deemed a weak environmental estrogen because of its ability to bind to α and β estrogen receptors (Gould et al., 1998; Kuiper et al., 1998; Pennie et al., 1998). According to certain earlier studies, low levels of BPA exposure cause disruptions in tissues that respond to androgen or estrogen, as well as in the thyroid, immune system, and developing nervous system (Richter et al., 2007; Vandenberg et al., 2008; Wetherill et al., 2007) (Figure 3). In a variety of target tissues, including the pancreas, BPA has also been demonstrated to interfere with the normal function of the estrogen nuclear hormone receptors (Adachi et al., 2005). According to Steinmetz et al., 1998, there is also evidence that ovariectomized rats' uterine and vaginal epithelial cells proliferate when exposed to single, high doses of BPA (up to 150 mg/kg BW). In response to BPA exposure, other organs such as the pituitary and mammary glands also showed estrogenic responses (Colerangle et al., 1997). Therefore, it is likely that the description of BPA as a weak oestrogen will understate the effects of BPA exposure on various target organs.

Toxicokinetics of BPA:

Toxicological studies of BPA have determined that the maximum tolerated dose for BPA is 1000 mg/kg body weight (BW)/day (Morrissey et al., 1987; Welshons et al., 2003). The US-EPA used a safety factor of 1000 to determine a reference dose of 50µg/kg/day. Usually, the NOAEL is used to calculate a reference dose; however, in the case of BPA, the LOAEL was used since no NOAEL was well known and adverse reactions were observed even at the lowest dose that was given (Soto et al., 2006). The toxicity profile thus indicates that the proper level

to use in risk assessment of human exposures is 50 mg/kg/day. The US-EPA chose this value to serve as the foundation for determining a reference dose of BPA (US EPA 1984a, 1984b, 1984c, 1987; NTP 1982, 1985a, 1986a).

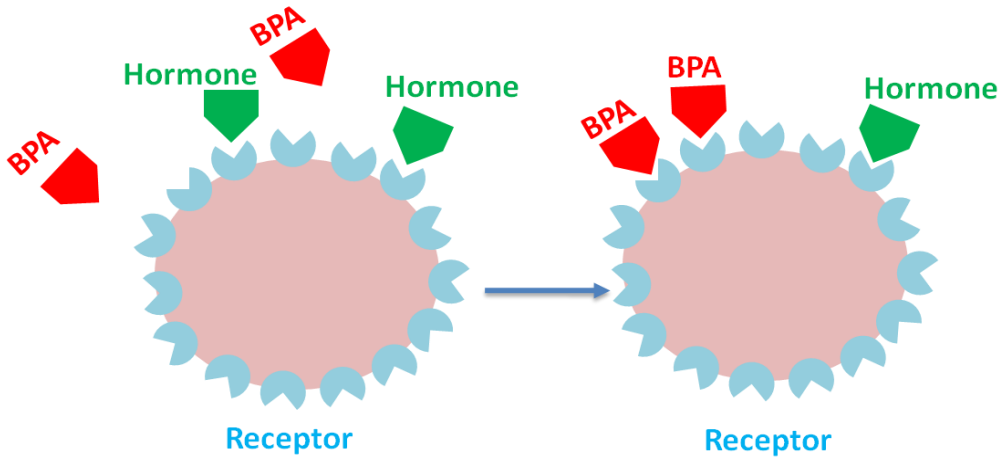

Figure 3. Endocrine disrupting effect of bisphenol A (BPA).

Impact of BPA on the functions of various organ systems:

The toxicological profile of BPA has revealed that it may have an impact on human and laboratory animal organ systemic functions. However, the way the scientists presented their research on the toxicity of BPA was contentious. While some research groups have found significant health effects from BPA, others have not mentioned it. In the majority of instances, BPA exhibits mild estrogenic activity along with primarily producing reproductive and developmental toxicity in laboratory test animals. It has also been reported that some "free" BPA is absorbed in the intestine following oral ingestion. BPA causes gastrointestinal problems in both humans and test animals because of these factors. However, an outline of the toxicity of BPA on several organ systems is provided in this section; these are detailed below.

Role of BPA on the reproductive system:

The toxic effects of BPA on male and female reproductive systems have been reported by various scientists controversially. Findings suggest that high levels of BPA reduced sperm count, motility, sperm mobility, and vitality, anomalies in spermatogenesis, etc. (Li et al., 2010a; Li et al., 2010b; Li et al., 2009, Salian et al., 2009c). Moreover, BPA has been shown to affect the levels of estradiol, LH, FSH, and testosterone in the serum (Watanabe et al., 2003; Salian et al., 2009c; Della et al., 2006; Herath et al., 2004; Zeng et al., 2022). Research carried out in 2006 by Kato et al., demonstrated that BPA alters the expression of certain genes in the testis. After oral exposure to BPA for five weeks, a study by Chitra et al., 2003, revealed a significant increase in the relative weight of the ventral prostate and a significant decrease in the number of epididymal sperm and the relative weight of the testis and epididymis. Furthermore, research conducted in 2011 by Mendoza-Rodriguez et al., indicates that oral BPA

exposure in rats during lactation and pregnancy may cause abnormalities in the estrus cycle in addition to increasing the thickness of the uterine stroma and epithelium in the offspring. Additionally, according to certain studies, BPA changes the expression of ERα and PR and impairs DNA synthesis in the uterine epithelium (Markey et al., 2005; Mendoza-Rodriguez et al., 2011; Signorile et al., 2010; Newbold et al., 2007; Fernandez et al., 2010; Berger et al., 2010). It lowers fertility, ovarian dysfunction, puberty at a younger age, and uterine weight (Adewale et al., 2009; Rubin et al., 2001; Cabaton et al., 2011; Zoeller et al., 2005; Tachibana et al., 2007). Also, it has been documented that BPA exposure in the neonatal period alters hypothalamic-pituitary hormone secretion, reduces the number of oocytes in each ovarian cycle, degrades oocyte quality, and other effects (Savabieasfahani et al., 2006; Mok-Lin et al., 2010; Fujimoto et al., 2011; Takeuchi et al., 2004).

Role of BPA on brain and behaviour:

According to certain studies, BPA causes neurotoxicity during development, anxiety, changes in sexual behavior, and other side effects (Stump et al., 2010; Cox et al., 2010; Poimenova et al., 2010; Tian et al., 2010). Scientific evidence suggests that during utero exposure BPA changes maternal, exploratory, and emotional behavior (Poimenova et al., 2010). Additionally, BPA also inhibits the growth of neuronal stem cells, decreases the amount of dopamine transporter (DAT) in the putamen, increases serotonin (5-HT) levels in the hippocampus, and increases the number of oxytocin neurons in the paraventricular nucleus (Kim et al., 2009; Tian et al., 2010; Matsuda et al., 2010; Adewale et al., 2011; Xu et al., 2010b; Xu et al., 2010c). Several studies indicate that oral exposure to BPA alters maternal behavior, and inhibits the miniature inhibiting postsynaptic currents in brain neurosynapse in a concentration-dependent manner through GABA(A) receptors (Palanza et al., 2008; Choi et al., 2007). Serotonin metabolites and dopaminergic neurotransmission are dynamically altered when low doses of BPA are introduced into neurons (Miyatake et al., 2006; Honma et al., 2006). On the other hand, long-term BPA exposure causes memory impairment linked to decreased acetylcholine (ACh) and choline acetyltransferase (CAT) production (Miyagawa et al., 2007). BPA acts as a xenoestrogen and blocks sodium currents through postsynaptic neuronal membranes by binding to nicotinic ACh receptors, according to research by Nakazawa and Ohno (Nakazawa et al., 2001).

Role of BPA on metabolism and cardiovascular system:

There have also been conflicting reports from earlier studies regarding the impact of BPA on the cardiovascular system and metabolism. Studies have evaluated how BPA may interact with the metabolism of fat and carbohydrates. Alonso-Magdalena et al., 2010 reported that exposure to BPA in rats during the gestation period reduces glucose tolerance; and increases insulin resistance, plasma insulin, leptin, triglycerides, and glycerol levels (Alonso-Magdalena et al., 2010). Other findings conclude that BPA increases the female body weight, adipose tissue

weight, etc. (Ryan et al., 2010; Somm et al., 2009; Miyawaki et al., 2007). Rats exposed to BPA during pregnancy have lower glucose tolerance and higher levels of insulin resistance, plasma insulin, leptin, triglycerides, and glycerol were reported by Alonso-Magdalena et al., 2010. Other studies have found that BPA increases body weight, female circumference, adipose tissue weight, and so on (Ryan et al., 2010; Somm et al., 2009; Miyawaki et al., 2007). While there is a positive correlation between fasting glycemia and urine levels of insulin resistance, BPA is also linked to diabetes and modifies alkaline phosphatase activity (Hong et al., 2009; Lang et al., 2008; Melzer et al., 2010). Subsequent investigations revealed a link between human exposure to BPA and an increased risk of cardiovascular disease. According to reports, BPA reduces the activity of acetylcholinesterase (AChE) in cardiac muscle and atrial contractility via the NO-dependent guanylyl cyclase pathway (Pant et al., 2011; Aboul et al., 2015). Although the effects of BPA on Maxi-K potassium channels are unknown, Asano et al. (2010) reported that BPA increased the activity of these channels, which are sensitive to both estrogens and estrogen receptors (Kca 1.1).

Role of BPA on the intestine:

There is an abundance of information on how BPA affects intestinal smooth muscle function in humans and rodents. Nevertheless, a study by Braniste et al., 2010, revealed that BPA causes gastrointestinal inflammation and visceral pain in ovariectomized female rats and reduces intestinal permeability in a dose-dependent manner (Braniste et al., 2010). Other findings suggest that BPA is absorbed into the gut and is primarily eliminated as BPA-glucuronide through the bile system (Inoue et al., 2003). Nonetheless, the primary organs where the BPA-conjugation occurs are the liver and the intestine (Inoue et al., 2001; Pritchett et al., 2002). Additionally, some free BPA is reabsorbed into the intestine after being metabolized by the body (Hanioka et al., 2008). Because of these, BPA may interfere with the intestine's regular function and raise AChE activity in small intestinal smooth muscle (Sarkar et al., 2013). The results of our study indicate that BPA affects both adrenergic and non-adrenergic non-cholinergic signals, which in turn alters small intestinal motility (Sarkar et al., 2016). Thus, it is evident that BPA has a markedly negative impact on several organ systems in both human and animal models. To determine the toxic effects of BPA, this review focuses on a few short of its negative effects on particular organs.

Conclusion:

This review article has made it clear that BPA poses significant health risks to us daily, risks that have been thoroughly investigated by numerous research teams. The fact that BPA functions as an endocrine disruptor, or has a weak estrogenic property, makes it the most effective component of the chemical. So that it can easily cause toxicity to the reproductive system. It impacts the heart, liver, intestines, and other organs in addition to its estrogenic action. Thus, it can be concluded that ingesting these chemicals in the form of foods, drinks, and other liquids increases the risk of disease development in humans. These kinds of

chemicals are a constant threat to our lives. Therefore, although we are unable to completely stop BPA exposure from the environment at this time, we should try to limit our exposure to these harmful chemicals by consuming fewer packaged foods and beverages as well as fast food to ensure the safety of our society for future generations.

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