

# Review on Impacts of Bisphenol A

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**Abstract:** Bisphenol A (BPA) is used in industry, especially in polycarbonate plastics manufacturing processes and food packaging. Bisphenol-A (BPA) is a synthetic chemical used in the manufacturing of polycarbonates and epoxy resins. This paper is a review of studies reporting the occurrences and concentrations of BPA in the environment and associated impact on human health. BPA is a proven endocrine disruptor capable of mimicking or blocking the receptors and altering hormone concentrations and its metabolism. Even though it is consumed in a low dose, it can stimulate cellular responses and affect body functions. Biomonitoring studies show that human and animal exposure to BPA is rapid and continuous. In-depth studies are needed to understand the fate of these compounds particularly in the developing nations and the associated adverse health impacts of BPA due to prolonged exposure.

**Keywords:** Bisphenol-A; Endocrine hormones; health impacts

## 1. Introduction

BPA is a crystalline chemical compound with formula  $C_{15}H_{16}O_2$  and a structure made of two hydroxyphenyl groups, which give to it a mild phenolic odour. BPA-based polycarbonate plastics are exceptionally strong and stable as they can endure exposure to high temperatures and sustain high-impact collisions. These characteristics make them valuable as components of safety equipment and food containers as they withstand heating in microwave ovens. Being a component of epoxy resins in protective coatings, such as those lining the inner surfaces of cans, BPA helps to extend the shelf life of food and beverage products. Indeed, one of the first studies aimed at quantifying BPA leaching from food containers showed that the chemical is present at a range of 4-23  $\mu\text{g}$  per can (Brotons, 1994). The resiliency of BPA plastics has led to their use in medical devices such as heart-lung machines, incubators, hemodialyzers, and dental sealants and fillers;

also, their light weight and optical clarity has made them especially useful for eyeglasses. Furthermore, BPA is found in a variety of other products, including compact discs and paper receipts. Due to its widespread applications, the use of BPA has garnered increasing attention over the last decade, especially in terms of human safety. Although scientific data obtained from wildlife and in vivo studies in animal models show the negative effects of BPA on reproductive fitness, there is a growing body of literature investigating the disrupting effects of BPA on male reproductive system, which however presents heterogeneous and sometimes conflicting results between animal and human. This review intends to gather scientific data about the BPA effects on the male reproductive system and the most appropriate analytical strategy. In this review, the effects of BPA on animal and human reproduction and on the hypothalamic-pituitary-gonadal axis will be presented and discussed.

S. No	Year	Title of the Article	Author	Journal
1	2020	Bisphenol A: an emerging threat to female fertility	Claudia Pivonello, <i>et al.</i>	Reproductive Biology and Endocrinology
2	2020	Bisphenol Threaten Male Reproductive Health via Testicular Cells	Elikanah Olusayo Adegoke, <i>et al.</i>	Bisphenols and Testicular Cells
3	2020	Bisphenol A - Induced Epigenetic Changes And Its Effects On The Male Reproductive System	Federica Cariati, <i>et al.</i>	BPA: Epigenetic and Male Reproduction
4	2020	Oxidative Stress and BPA Toxicity: An Antioxidant Approach for Male and Female Reproductive Dysfunction	Rosaria Meli, <i>et al.</i>	Antioxidants
5	2019	Bisphenol a: an emerging threat to male fertility	Federica Cariati, <i>et al.</i>	Reproductive Biology and Endocrinology
6	2019	The Impact of Bisphenol A on Fertility, Reproductive System, and Development: A Review of the Literature	Ewa Matuszczak, <i>et al.</i>	International Journal of Endocrinology
7	2019	Neuro-toxic and Reproductive Effects of BPA	Antonietta Santoro, <i>et al.</i>	Current Neuropharmacology, 2019, Vol. 17, No. 12
8	2018	Effects of bisphenol A on male and couple reproductive health: A review	Lidia Mínguez-Alarcón, <i>et al.</i>	FertilSteril. Author manuscript; available in PMC 2017 January 18
9	2017	The Association between Exposure to Environmental Bisphenol A and Gonadotropic Hormone Levels among Men	Hong Liang, <i>et al.</i>	Environmental Bisphenol A and Male Hormones
10	2016	Evidence for bisphenol A-induced female infertility - Review (2007–2016)	Ayelet Ziv-Gal and Jodi A. Flaws	FertilSteril. 2016 September 15; 106(4): 827–856. doi:10.1016/j.fertnstert.2016.06.027

## 2. Materials and Methods

BPA studies have used various study designs and included a wide range of doses. Based on the definitions in other

studies, we considered a “low dose” of BPA as follows: a dose below the lowest observable adverse effect level (LOAEL) of 50 mg/kg/day in animal models (Peretz, *et al.* 2007-2013) (Vandenberg, *et al.* 2013) (Richter, *et al.* 2007) (Vom Saal *et al.* 2007) 17.2 mg/l for aquatic

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animals,  $1 \times 10^{-7}$  M for cell culture experiments (Vandenberg, *et al.* 2013) and a dose in the range of typical (not occupational) human exposures for epidemiological studies (Vandenberg, *et al.* 2013). The majority of the studies described in this review used doses that are within the category of "low dose". Throughout the text of this review, we indicated if the doses were considered low or high based on the categories above.

### 3. Discussion

This review focused on BPA toxicity on the reproductive system, focusing on its antiestrogenic and antiandrogenic effects. Especially, experimental evidence and conflicting data about the effect of BPA on male reproduction in animal model and in humans were pointed out. Despite some controversial data, it is clear that BPA mediated alteration of endogenous steroids levels occurs at different stages as they enter synthesis, metabolism, distribution or clearance processes. BPA can also interact directly with steroid receptors to either simulate or block steroid actions. The majority animal studies, performed at different developmental stages, showed that BPA estrogenic effect results in testis morphological alteration, testicular steroidogenesis inhibition, leading to hypogonadotropic hypogonadism and compromise, spermatogenesis. On the other hand, discordant data were reported about the role of BPA in humans. Inconsistency of results regarding BPA effects on semen quality could be due to intrinsic differences in population sampling across the various studies. In fact, all studies reviewed in this article have sampling biases as they analyse men exposed to BPA but with no proven fertility (Li, *et al.* 2009; 2011; 2015), young men not exposed to BPA and with no proven fertility and fertile men from the general population exposed to BPA (Mendiola, *et al.* 2010). In addition, differences in concentrations of individual steroids and BPA across human body fluids were shown by several studies explained above. In particular, concentrations were measured with different methods, introducing potential biases in the analysis and consequently affecting clinical significance. In particular, this study found that BPA and steroids concentration differed between seminal fluid and blood plasma. The results of this validation method confirmed that there is a transfer of BPA from blood to seminal plasma through blood–testis barrier, as previously indicated in invitro studies.

The review intended to highlight the mechanisms by which BPA modifies at various levels the reproductive system. In particular, we looked into literature and summarized the studies that analyzed the epigenetic changes leading to impairment of the different aspects of male reproduction, both in animals and in humans. Epigenetics is responsible for the control of many genes implicated in hormonal production, sperm parameters, and inheritable abnormalities.

In conclusion The connection between laboratory data and what actually happens in vivo is always problematic to confirm, but the identification of potentially harmful substances is of utmost importance for future research. One future way to study the impact of BPA would be to create an in vitro implantation model for studies of whether a chemical hampers implantation or disturbs the expression of

endometrial receptivity markers. Such knowledge may also form a good basis for future regulations concerning the handling of BPA

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