Bisphenol-A: A Powerful Endocrine Disrupting Chemical

Marco Pupo and Marcello Maggiolini

Department of Pharmacy and Health and Nutritional Sciences, University of Calabria, Rende, Italy

Corresponding author: Marcello Maggiolini, Department of Pharmacy and Health and Nutritional Sciences, University of Calabria, Rende, Italy, Tel: +39 0984 493076; Fax: +39 0984 493107; E-mail: marcellomaggiolini@yahoo.it

Rec date: May 14, 2014, Acc date: May 15, 2014, Pub date: May 19, 2014

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Editorial

Over the last decades, numerous synthetic compounds, including pesticides and industrial chemicals, have been introduced into the environment under the premise that they would improve standards of living without any negative consequences for humans. However, several of these compounds have produced deleterious effects on both wildlife and human health. For instance, since 1990s it became evident that many environmental chemicals exert hormone-like activity and interfere with the function of endogenous hormones by disrupting their synthesis, release, transport, metabolism, binding, action or elimination. These compounds were then named endocrine disrupting chemicals (EDCs) [1]. A large body of data has shown that bisphenol A (BPA), which is largely used in the manufacture of polycarbonate plastics and epoxy resins, may act as an EDC. Polycarbonate is currently used to produce materials intended to come into contact with food such as reusable plastic bottles, feeding-bottles, plates, goblets, cups, microwave ovens, storage containers and others, whereas the epoxy resins are used for internal coating of food and beverage cans [2]. Moreover, BPA is also used for the manufacture of products like sunglasses, building materials, CD-ROM, medical devices, dental materials and thermal paper [3]. As the use of this plastic products has strongly increased in the last years, BPA is today one of the highest volume EDCs produced worldwide with a total of 2.8 million metric tons manufactured in 2002 that increased to 5.5 million metric tons in 2011 [4]. Additionally, it has been estimated that every year over 100 tons of BPA are released into the atmosphere [5]. Therefore, BPA is ubiquitously found in the environment throughout the world and the human exposure occurs mainly through the diet due to leaching of BPA from packaging materials into food items. However, other possible routes of exposure, due to the contamination of soil, water and air, are inhalation and dermal contact [6]. The interaction between humans and BPA has consequently increased so much in recent years as confirmed by the observation that in more than 80% of the general population this contaminants may be detectable in urine [7,8]. BPA has also been detected in human blood, amniotic fluid, placenta, cord blood and human breast milk [9]. In the 1980s, the lowest-observable-adverse effect-level (LOAEL) for BPA was determined at 50 mg/kg bw/day, and the Environmental Protection Agency (EPA) calculated a “reference dose” of 50 lg/kg bw [10]. Since that time, abundant scientific evidence have suggested that BPA can interfere with the endocrine signaling pathways at doses below the calculated safe dose after fetal, neonatal, perinatal and adult exposure. Acting as an endocrine disruptor, BPA may interfere with endocrine transduction mechanisms at very low doses and the exposure to this contaminant has been correlated with a wide variety of adverse health effects in both male and female including birth defects, reproductive, developmental, metabolic, immune, and neurobehavioral disorders [4]. Epidemiological studies have highlighted the correlation between the increased levels of BPA in the environment and the incidence of hormone-related cancers including breast, prostate, ovarian and endometrium malignancies [11]. Since 1993 several studies have reported that BPA has estrogenic activity both in vitro and in vivo, hence the estrogen-like action was connected with its adverse effects on human health and the onset of hormone-dependent tumors. BPA has two benzene rings and two (4,4’)-OH substituents which fitting in the estrogen receptor (ER) binding pocket activate both ER isoforms (ERα and ERβ) [5]. Although the estrogen action was accepted from the early beginning, BPA is a weak estrogen as its binding affinity to ER is 1000-10,000-fold lower than the natural steroid 17β-estradiol (E2) [12,13]. Therefore, the effects exerted by BPA at low doses can be explained at least partially by the fact that this endocrine disruptor may bind differently than E2 within the ER ligand domain or recruit different ER co-activators [14]. Besides, BPA is able to bind the membrane-bound form of ER (mER) and the G protein coupled estrogen receptor GPR30/GPER [15]. In particular, the estrogen-like activity of BPA has been recently shown to occur through GPER in both normal and neoplastic cells [16,17]. Although the action of BPA in cancer mainly mimics estrogen-like mechanisms, it may also act via the androgen receptor, the thyroid receptor, the peroxisome proliferator-activated receptor-y and other estrogen signaling pathways [18]. Therefore, it has become increasingly evident that BPA activates transduction signals in a cell context dependent manner. Cumulatively, the adverse biological responses involve a network of effectors and arise from both rapid and late mechanisms that lead to gene expression changes. The further characterization of the action of BPA elicited at the molecular level towards tumor progression should bring a better understanding of the risks connected to the BPA exposure. In the meantime, a shift towards a green chemistry research, aimed at identifying and developing alternatives that do not display endocrine-disrupting activity, should be taken into account in order to avoid any potential risk that BPA poses to human health.

References


