Abstract. Background/Aim: Bisphenol A (BPA) is a ubiquitous substance found in a wide array of consumer products and healthcare consumables, and at low doses in drinking water. Currently, in the UK, it is classed as a low-risk substance with little potential for harm. It has been known to have effects on oestrogen receptors. The implications of this for public safety is currently subject to debate. Materials and Methods: In this study, we review recent literature regarding the effects and safety of BPA, and discuss the potential implications, in particular from the perspective of human breast oncogenesis. Results and Conclusion: Recent evidence suggests that low-doses of endocrine disruptors, such as BPA, could have profound effects in breast development and cancer risk. Recent studies in marine models suggest that BPA could contribute to breast oncogenesis via several pathways. The position of regulators should shift accordingly to safeguard the public interest.

Bisphenol A (BPA) is a near-ubiquitous substance in today’s world. It is widely used for manufacturing epoxy resins, which are found in the protective lining of plastic food containers, healthcare equipment, steel drums and pipes. BPA is a food contact material, and is thus practically ubiquitous in household kitchenware and in canned food items. BPA-based epoxy resins are also widely used for their adhesive properties (1).

BPA is also important in the production of polycarbonate plastics, and is thus found in eye-ware, optical devices and medical equipment. BPA is also an additive in the manufacture of polyvinyl chloride plastics, which have wide applications in healthcare consumables, piping, wire insulation and construction materials (1, 2). The annual world production of BPA in 2009 was at least 2.2 million tonnes, with the USA producing a fifth of the total (1). BPA was discovered on 1891, and has been in mass production since at least the interwar era (3). Consequently, BPA has permeated our ecosystem, making human exposure to BPA near-universal. Calafat et al. have found that 93% of Americans above the age of six had detectable levels of BPA in their urine (4). Arnold et al. have found the maximum quantified BPA concentration in European drinking water to be 0.014 μg/l. They also observed that the exposure levels were well below the stated toxic thresholds for BPA (5). This coincides with the current position of the Food and Safety Agency (FSA) of the UK (6).

Endocrine Disrupting Chemicals

The endocrine effects of BPA have been known since the 1930s. In comparison to other substances studied at the time, the affinity of BPA to oestrogen receptor was relatively weak. Unlike, for instance, diethylstilbestrol (DES). BPA was never found to have a commercial role as a synthetic oestrogen (3). However, since the 1980s, there have been concerns regarding the endocrine effects of BPA, especially since the ban of DES in 1979, after it was implicated in the causation of uterine tumours in young women who were exposed in utero to DES (7). The studies on DES identified molecules with endocrine effects to be of specific interest regarding oncogenesis. BPA has been evaluated as one such endocrine disruptor chemical (EDC) (8). In a commentary on reviews on the effect of BPA at the toxic thresholds recognised at the time, vom Saal et al. observed that the majority of studies they reviewed were showing effects due to BPA at concentrations significantly below the stated safety threshold (9). Furthermore, they noted that there was a discernible effect of funding source on the results of these studies. More than 90% of government-funded
In the absence of adequately powered epidemiological studies, evidence derived from in vitro and in vivo studies and human studies using surrogate markers for breast cancer such as breast density become critical. These findings make the low but ubiquitous ambient exposure to EDCs such as BPA all the more a cause for concern. Additionally, recent studies have posited that BPA may induce oncogenic pathways other than those related to hormone receptors, including those pertaining to stem cell differentiation (19), DNA repair (20), and immunomodulation (21).

Furthermore, it has been found that despite its limited half-life, BPA accumulates in adipose tissue in its active unconjugated form (13, 22). This could serve as a continuous source of exposure in humans, which cannot be effectively modelled for in murine models. It is not unreasonable to expect that exposure to and effects of BPA will be worse than that predicted by murine studies (4).

This accumulation of evidence has led to mounting concerns at the market and regulatory level. BPA-free products are currently being offered (2), and certain regulators have revised their previous rulings regarding BPA. A full ban was considered in France (23). Most recently, the US National Toxicology Programme has concluded its study on the effects of BPA, and shall be publishing their final report in the fall of 2019 (24).

Safer alternatives to BPA have been developed. For example, syringaresinol has been characterised as a renewable and safer alternative to BPA in the manufacturing of epoxy resins. Such alternatives make the phasing out of BPA from consumer goods feasible (25).

**Conclusion**

In view of the developments in our understanding of the effects of low-dose xeno-oestrogens, it is imperative that measures should be taken to curb further cancer risk to our populations. BPA, and indeed other EDCs, should be phased out as soon as feasible. The full extent of their effects is difficult to predict, and what we have determined is highly suggestive of an increased risk of human oncogenesis, including breast cancer. It would be imperative to phase out BPA from use in the manufacture of consumer and healthcare goods in favour of safer alternatives (25).

**Conflicts of Interest**

UW and KM declare that they have no conflicts of interest regarding this study.

**Authors’ Contributions**

KM initiated the project. UW did the literature review and drafted the initial manuscript. KM proof-read and finalised the manuscript.
Appendix

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