



Story of Bisphenol S – Steps from Bad to Worse

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BISFENOL S – PŘÍBĚH POLITOVÁNÍHODNÉ SUBSTITUCE

ABSTRAKT Žijeme v „době plastové“. Obrovské množství plastů vstupuje do životního prostředí a z tohoto materiálu se uvolňuje řada chemikálií s endokrinně disruptivními účinky. Bisfenol A (BPA) je znám jako jeden z takových účinných endokrinních disruptorů uvolňovaných z plastů. Tato látka vykazuje široké spektrum negativních efektů na zdraví zvířat i lidí. Proto bylo používání BPA v řadě lidských oborů omezeno a u mnoha výrobků je garantováno, že BPA neobsahují. BPA může v plastech chybět, jen pokud je nahrazen jinými látkami. Jako náhrada za BPA se často používá bisfenol S (BPS), i když jeho endokrinně disruptivní účinky jsou prozkoumány jen velmi málo. Jako chemikálie, jejíž používání podléhá mnohem slabší legislativní regulaci než její předchůdce, je nyní BPS používán v mnoha materiálech. Nově získávané poznatky ale stále jasněji ukazují, že BPS není zdaleka bezpečná látka. Nenápadná náhrada BPA za BPS může být vnímána jako zlepšení. Ale zdá se, že tomu přesně naopak. S tím, jak se BPS šíří naším „do plastu zabaleným“ světem, jsme se jen dostali z bláta do louže.

KLÍČOVÁ SLOVA antropocén; endokrinní disruptory; bisfenol A; bisfenol S; politováníhodná náhrada

ABSTRACT We are living in the “Age of Plastics”. A vast amount of this material enters the environment, with chemicals released from the bulk of this matter often exhibiting endocrine-disrupting effects. Bisphenol A (BPA), originating from plastics, is well-known as such a potent endocrine disruptor. This compound exhibits wide spectra of detrimental effects on animal and human health. For these reasons, the use of BPA has been limited in many human activities and bisphenol A-free products are now guaranteed. As a key compound of many plastics, BPA could not be omitted from plastics without being replaced by other chemicals. Bisphenol S (BPS) is often chosen as a substitute for BPA, although its endocrine-disruptive effects are poorly known. As a chemical facing much less stringent legislation than BPA, its forerunner, BPS is now widely used in many materials. However, an increasing volume of new knowledge indicates that BPS is far from safe. The “silent” substitution of BPA with BPS could be perceived as an improvement. However, the converse appears to be true. With BPS spreading through our “plastic-encased” world, we are going from bad to worse.

KEY WORDS anthropocene; endocrine disruptors; bisphenol A; bisphenol S; regrettable substitution

INTRODUCTION

For several past centuries, mankind and its activities have become such an important factor shaping the environment of our planet that the term ‘Anthropocene’ is starting to be

used for the present period of human history (Monastersky, 2015). Besides other phenomena, the excessive use of plastics and their quick integration into the environment, including the seas and oceans, has become characteristic of the current stage of development of human civilisation (Jambeck et al.,



Figure 1. Bisphenol A is primarily used to make plastics, such as this polycarbonate water bottle. (Source Wikimedia)

https://upload.wikimedia.org/wikipedia/commons/d/d7/Polycarbonate_water_bottle.JPG

2015). Microplastic – plastic particles smaller than 5 mm – accumulate in the oceans (Rochman et al., 2013), are trapped in the polar ice (Obbart et al., 2014) and integrate into living organisms (Wright et al., 2013; Watts et al., 2014). In some cases, plastics become part rocks which are known as plastiglomerates (Corcoran et al., 2013).

Hormonally active substances are released from plastics into the environment (Vandenberg et al., 2012). These chemicals are known as endocrine disruptors (Colborn, 2004). They are defined as „any chemical that can interact directly or indirectly with the endocrine system, and subsequently result in an effect on the endocrine system, target organs and tissues“ (EFSA, 2012). It is estimated that exposure to endocrine disruptors in inhabitants of the European Union results in annual damages amounting to at least €157 billion, both in healthcare costs, as well as in lost earning potential. The upper limit for these estimates of the damages is around €270 billion, representing 2 % of the gross domestic product of European Union countries (Trasande et al., 2015).

Bisphenol A (BPA), which was used as an important component in many materials including various plastics, represents one of the substances which completely fulfils the definition of endocrine disruptor. Due to fear of the endocrine-disrupting effects of BPA, this chemical has been replaced in some

materials with other substances. Products made from these materials are guaranteed as BPA-free.

But we have to ask what chemicals have replaced BPA in BPA-free products? One of the substitutes for BPA is bisphenol S (BPS). Despite there being only limited data on the endocrine-disrupting properties of BPS, this chemical is not subjected to such strict regulation as BPA. Today BPS is used in bulk and its presence has been demonstrated both in the environment and in the human body. This begs the question whether this substitution of bisphenol S is a step in the right direction.

BISPHENOL A

Bisphenol A is one of the most mass-produced chemicals in the world. Annually about 4 million tons of BPA is produced and about 100 tons is released into the environment every year (Vandenberg et al., 2010). This substance was first synthesised in the late 19th century. In the 1930s, it was tested as a potential oestrogen, but was not of practical use. The industrial production of plastics with BPA began in the 1940s and 1950s. BPA was quickly used as a component of polycarbonate plastics for food containers and in epoxy resins e.g. in dental fillings. Further widespread use of BPA occurred in recycled paper and in paper for thermal printers. A certain quantity of BPA is released from all these materials and this chemical enters the environment, food chain and human body (Rubin, 2011).

Although BPA was evaluated by EFSA from a toxicological point of view as a substance which does not constitute a serious risk (EFSA, 2015), endocrinologists have classified BPA as an endocrine disruptor with considerable health risks (Vandenberg et al., 2010). Most of the population of developed countries have quantifiable levels of BPA in their organisms. The highest levels were detected in children and youth, lower levels were detected in adults (Calafat et al., 2008). This is an alarming finding, because it is suggested that children have increased sensitivity to the endocrine effects of BPA (Richter et al., 2007). Since BPA has even been detected in the bodies of pregnant women, amniotic fluid, placenta, and in the umbilical cord blood of newborn, there is concern about the effect of this substance on infants during prenatal development (Vandenberg et al., 2007a). Concentrations of BPA detected in the blood of the newborn in intensive care units were of an or-

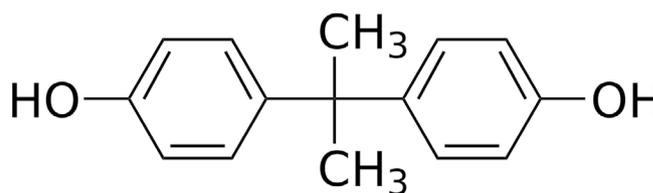


Figure 2. Bisphenol A (Source Wikimedia)
https://upload.wikimedia.org/wikipedia/commons/f/f8/4%2C4%27-%28propane-2%2C2-diy1%29diphenol_200.svg

der of magnitude higher than those in healthy babies. In this case, the source of BPA is medical material made of plastics (Calafat et al., 2009).

Although food and beverages are considered as the major source of BPA, other inputs of BPA into the human body cannot be underestimated, such as the inhalation of contaminated air and the penetration of BPA through the skin. For example, high concentrations of BPA have been demonstrated in supermarket cashiers, who are in contact with the paper for thermal printers and banknote paper containing bisphenol S (Braun et al., 2011). BPA escapes into the air e.g. after the combustion of plastics (Fu-Kawamura, 2010).

THE EFFECTS OF BPA

BPA is known to act as xenoestrogen. Although BPA binds to classic oestrogen receptors much more weakly than estradiol, due to its actions on other target structures of estrogens, the overall estrogenic effects of BPA are comparable to estradiol (Watson et al., 2005). Some metabolites of BPA may even be more effective than BPA alone (Ben-Jonathan – Steinmetz, 1998). Moreover, the influence of BPA is not limited to its estrogenic effects, since it has a wider spectrum of action (Routledge et al., 2000) and acts e.g. as an antiandrogen (Kruger et al., 2008)

BPA acts on a wide variety of tissues and organs. The effect on neural tissue of the brain was clearly demonstrated by distinct effects on behaviour. For example, BPA prevents masculinisation of the brain during the fetal development of males (Patisauel et al., 2006) and interferes with the parental behaviour of males and females (Johnson et al., 2015). BPA disrupts embryonic and fetal development by affecting thyroid hormone signalling pathways (Heimeier – Shi, 2010) and also has a negative impact on the balance of glucocorticoid hormones (Prasanth et al., 2010). A number of effects of BPA, including its multigenerational effects, are apparently caused by BPA-induced epigenetic changes (Dolinoy et al., 2007; Bromer et al., 2010).

BPA AND REPRODUCTION

As an endocrine disruptor, BPA interferes significantly with reproduction in mammals. It has been shown in mice that daughters of mothers exposed to BPA have lower pregnancy rates and lower numbers of pups (Cabaton et al., 2011). The effect of BPA on the reproductive system is complex. BPA affects the whole hypothalamic-pituitary-gonadal axis. In females, it affects the secretion of gonadotropin-releasing hormone in the hypothalamus (Patisauel et al., 2006) and the functions of the pituitary gland (Ramos et al., 2003), ovaries (Hunt et al., 2003), uterus (Markey et al., 2005) and mammary glands (Vandenberg et al., 2007b).

In humans, elevated concentrations of BPA in women are linked to recurrent miscarriages (Sugiura-Ogasawara et al.,

2005) and premature births (Cantonwine et al., 2010). An apparent correlation between levels of BPA in the body and a reduced number of oocytes obtained from patients treated for infertility by assisted reproduction has been observed (Mok-Lin et al., 2010). The levels of BPA also correlate with increased incidence of reproductive system inflammation in post-menopausal women (Yang et al., 2009). There were significant correlations between elevated levels of BPA in the body and reduced sperm quality in men (Li et al., 2011).

BPA AND OBESITY

BPA belongs to the class of endocrine disrupters called obesogens which operates in the mammalian organism at many levels. As an obesogen, BPA contributes to changes in metabolism and its effects can result in overweight and obesity (Newbold et al., 2008). It also contributes to the disruption of the glucose metabolism (Alonso-Magdalena et al., 2006) and thus could elevate the risks of diabetes. Obesogenic effects of BPA could be involved in the proven correlation between levels of BPA in the body and the risk of cardiovascular disease (Melzer et al., 2010).

BISPHENOL S

Knowledge of the endocrine-disrupting effects of BPA led to the restricted use of this substance in many countries and its substitution with other chemicals. In many cases, bisphenol S is used as a substitute for BPA. This substance is currently not subject to rigorous regulation. At present, BPS is used in a wide range of products (Liao – Kannan, 2011) and its presence has been demonstrated in humans in many populations in economically developed countries (Liao et al., 2012). In many cases, the label “BPA-free” does not mean “bisphenol-free” because BPA is replaced with BPS. This fact is of particular concern (Glausiusz, 2014; Zimmerman – Anastas, 2015). Several studies have shown that BPS has significant endocrine-disrupting effects. Eladak et al. (2015) demonstrated

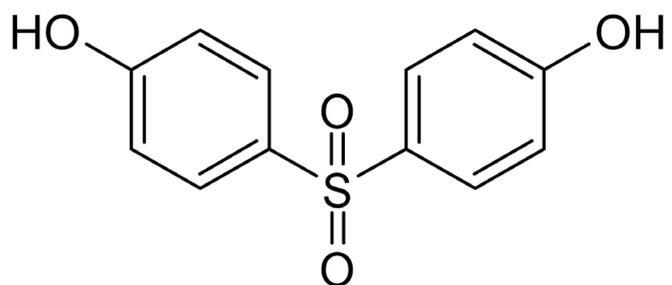


Figure 3. Bisphenol S (Source Wikimedia)
https://upload.wikimedia.org/wikipedia/commons/b/b8/Bisphenol_S.svg

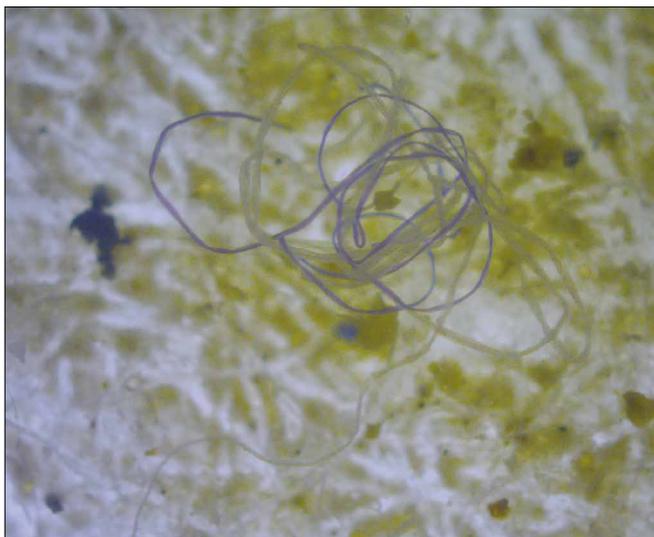


Figure 4. Microplastic fibers identified in the marine environment. (Source Wikimedia)
<https://upload.wikimedia.org/wikipedia/commons/0/0d/Snap-40.jpg>

a negative effect of BPS on mammalian testicular tissue. Vinas and Watson (2013) showed a negative effect of BPS on the function of the mammalian pituitary gland. The negative impact of BPS on reproduction in fish has been clearly demonstrated (Ji et al., 2013). Our preliminary results show that BPS also seriously disrupts the reproduction of mammalian females (Žalmanová et al., 2015).

CONCLUSION

It could appear that we are living the happy-end story in which the dangerous BPA pollutant has been replaced with a safer substance. But the situation is not as rosy as it seems at first glance. The substitution of BPA with BPS is referred to as a “regrettable substitution” (Zimmerman – Anastas, 2015). Unfortunately, this is not an isolated case. There are many similar “regrettable substitutions”. For example, pyrethroids which replaced older insecticides, such as the organochlorines, organophosphates and carbamates, have shown a broad spectrum of undesirable side effects. It now appears that pyrethroids can also have a negative impact on mammals including man. In mammals, pyrethroids affect the functions of the brain (Viel et al, 2015) and reproductive organs (Petr et al., 2013).

There are some “happy-end stories” in the substitution of a detrimental chemical with a harmless one, e.g. the replacement of a wood preservative based on carcinogenic chromate copper arsenate (Landrigan et al., 2004) with the benign wood preservative, alkaline copper quaternary. However, we still face too many substitutions of chemicals which are steps from bad to worse. The story of bisphenol S is just one such example.

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