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Review

Parabens. From environmental studies to human health

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ABSTRACT

Parabens are a group of substances commonly employed as preservatives, mainly in personal care products, pharmaceuticals and food. Scientific reports concerning their endocrine disrupting potential and the possible link with breast cancer raised wide discussion about parabens' impact and safety. This paper provides holistic overview of paraben usage, occurrence in the environment, methods of their degradation and removal from aqueous solution, as well as hazards related to their endocrine disrupting potential and possible involvement in carcinogenesis.

Contents

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1. Introduction

1.1. Properties

In terms of chemical structure, parabens (PBs) are esters of *p*-hydroxybenzoic acid (pHBA), with alkyl substituents ranging from methyl to butyl or benzyl groups (Jonkers et al., 2010). Namely, we can distinguish methylparaben (MePB), ethylparaben (EtPB), propylparaben (PrPB), isopropylparaben (iPrPB), butylparaben (BuPB), isobutylparaben (iBuPB) and benzylparaben (BePB). Among them, methylparaben and propylparaben are the most commonly used and often present in the products together (Núñez et al., 2008). Main physicochemical properties of parabens are shown in Table 1.

Commercially, parabens are produced by esterification of *p*-hydroxybenzoic acid with an appropriate alcohol in the presence of a catalyst (e.g. concentrated sulfuric acid or *p*-toluenesulfonic acid) (Liao et al., 2002).

In acidic aqueous solutions parabens are stable. In alkaline solutions parabens are hydrolyzed to *p*-hydroxybenzoic acid and the corresponding alcohol. In general, with the increase in the alkyl chain length, the resistance of aqueous solutions of parabens to hydrolysis increases (Masten, 2005). PB antibacterial properties are directly proportional to the chain length of the ester group, and so, for example, butylparaben has 4-fold greater ability to inhibit microbial growth than ethylparaben. However, simultaneously with the increase of the length of the alkyl chain, the value of octanol–water partition coefficient rises, which results in decrease of water solubility (Table 1; Jewell et al., 2007; Soni et al., 2005). At concentrations as low as those used for water treatment, chlorine reacts with parabens to produce chlorinated derivatives (Canosa et al., 2006b). Canosa et al. (2006b) observed that even a few minutes of contact between cosmetics containing PB (e.g. bath gel) and chlorinated tap water results in the formation of chlorinated and brominated by-products. The reaction rate increases with temperature. This phenomenon is alarming due to the high stability of the resulting di-chlorinated derivatives and unknown estrogenic potential (Canosa et al., 2006b; Terasaki and Makino, 2008). Moreover, chlorinated derivatives are considerably more toxic to aquatic organisms than the respective parent compounds (Terasaki et al., 2009).

The numerous properties predisposing parabens for usage as preserving agents have contributed to their considerable popularity. The features determining PB high utility include, among others (Aguilar-Bernier et al., 2012; Guadarrama et al., 2008; Rastogi et al., 1995; Soni et al., 2001, 2005; Terasaki et al., 2012):

- broad spectrum of activity against yeasts, molds and bacteria,
- chemical stability (for a wide temperature interval and pHs ranging from 4.5 to 7.5),
- inertness,
- low degree of systemic toxicity,
- low frequency of sensitization,
- sufficient water solubility (enabling to obtain effective concentration),
- relatively safe use,
- low costs of production,
- no perceptible odor or taste,
- not causing changes in consistency or coloration of products.

The combination of these properties makes it relatively difficult to find a preservative, which will be a satisfactory replacement for parabens.

Parabens are classified as "generally regarded as safe" (GRAS) compounds and approved for use in foods by the US Food and Drug Administration (FDA) and the European Union (EU) regulations (Soni et al., 2001).

1.2. Usage of parabens

Parabens were first introduced in mid 1920s as preservatives in drug products (Liebert, 1984). Currently, they are widely used preservatives, mainly in cosmetics and pharmaceuticals, but also in food commodities and industrial products. Besides water, they are regarded as the most common ingredient of cosmetics (Cashman and Warshaw, 2005; Janjua et al., 2007). Parabens are present in approximately 80% of personal care products (Pouillot et al., 2006). In a 1995 study, parabens were found in 77% of rinse-off and 99% of leave-on cosmetics (Rastogi et al., 1995). However, in a report from the Danish market, 36% of the considered 751 commodities contained parabens. A Norwegian study revealed that parabens were present in 32% of 117 baby care products (Eriksson et al., 2008). Other estimation shows that butylparaben is present in 13%, while propylparaben and/or methylparaben in 48% of cosmetics and personal care products (Masten, 2005).

At the turn of the millennium, several studies were published suggesting PB estrogenic activity (Oishi, 2001; Routledge et al., 1998) and carcinogenic potential (Darbre et al., 2004). As a result, some manufacturers altered composition of their cosmetic products by replacing parabens with other preservative system and introducing so called "paraben free" formulae. Even though, the Cosmetic Ingredient Review Expert Panel (CIR, 2008) reported, on the basis of USA Food and Drug Administration (FDA) database, that the number of cosmetic formulations in which PB was used was 1.7 times higher in 2006 compared to 1981. Namely, the use in 1981 was equal to 13,200 (Liebert, 1984), whereas in 2006 it was as high as 22,000 (CIR, 2008). However, the PB content in cosmetics seems to decrease. According to the industry's voluntary submission to the FDA in 1981, the concentration for a single paraben was up to 25% for MePB and PrPB, 5% for BuPB and 1% for EtPB. The usual content of parabens was up to 1% (Liebert, 1984). About 14 years later, the content of PBs in 215 tested products from the Danish market ranged from 0.01% to 0.87% (Rastogi et al., 1995). Nevertheless, the difference may also arise from regional disparities between United States and Europe.

1.3. Legislation

In European Union (EU) countries, the allowable content of PB in cosmetic products is 0.4% for single ester and 0.8% for mixtures of all parabens (Official Journal of the European Union, 2009). The governmental units of the United States (Food and Drug Administration, FDA) and Canada (Health Canada) have recommended the same threshold for PB as that of EU. However, there is no legislation regulating concentrations of parabens in cosmetics in any of those countries

Table 1
Physical and chemical characteristics of parabens.

Characteristic	MePB	EtPB	PrPB	BuPB	BePB	References
Chemical formula	$C_8H_8O_3$	$C_9H_{10}O_3$	$C_{10}H_{12}O_3$	$C_{11}H_{14}O_3$	$C_{14}H_{12}O_3$	–
Molecular weight (g/mol)	152.16	166.18	180.21	194.23	228.25	CIR (2008)
pK_a	8.17	8.22	8.35	8.37	–	Soni et al. (2005)
Log octanol–water partition coefficients (log k_{OW})	1.66	2.19	2.71	3.24	3.56	Golden et al. (2005)
Solubility in water at 25 °C (g/100 ml)	2.00	0.86	0.30	0.15	0.05	Jewell et al. (2007)