

Parabens

BMF 64 - PARABENS

Parabens are a class of chemicals widely used as preservatives in personal care, cosmetic, pharmaceutical and food products since the 1930s. Parabens are esters of *para*-hydroxybenzoic acid (Fig.1) with methylparaben, ethylparaben, propylparaben, and butylparaben being most commonly used. Parabens and their salts are used for antimicrobial properties. They are detected in waste water, rivers, soil and house dust, hence human exposure is ubiquitous throughout life. Due to their omnipresent nature parabens are usually detected in human tissues and fluid samples although they are excreted relatively quickly. Although parabens are still widely considered to be safe, health concerns have been raised since studies have shown that parabens are found in breast tissue from patients with breast cancer.^{1,2}

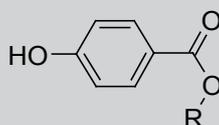


Fig. 1 Parabens (R=Alkyl, Aryl)

Parabens- commonplace in consumables

Among other consumer products, many hand soaps, body lotions, lipsticks, toothpastes and sunscreens contain parabens in concentrations of up to 1%. However, not all parabens are used in such high concentrations. Within the European Union, the following parabens are allowed as food additives: methylparaben (E number E218), ethylparaben (E214), propylparaben (E216), butylparaben and heptylparaben (E209). Jam and other foodstuffs contain parabens in amounts up to 0,1%.^{1,2}

Natural and synthetic parabens in the environment

Some living organisms (plants and microbes) produce parabens. Among these are blueberries, carrots and olives which principally contain methylparaben for its antimicrobial activity. Concentrations of parabens in the environment are low, but vary a lot e.g. soil and house-dust (mainly derived from synthetic sources) with concentrations of 6ng/g and 2400ng/g, respectively.²



Metabolism

Parabens are mainly metabolized in human beings by hydrolysis catalyzed by esterases or glucuronidation followed by hydrolysis. Sulfonations of the 4-hydroxygroup by sulfotransferase and formation of an amide from the carboxylic group by amino acid transferase have also been found (Fig 2).³

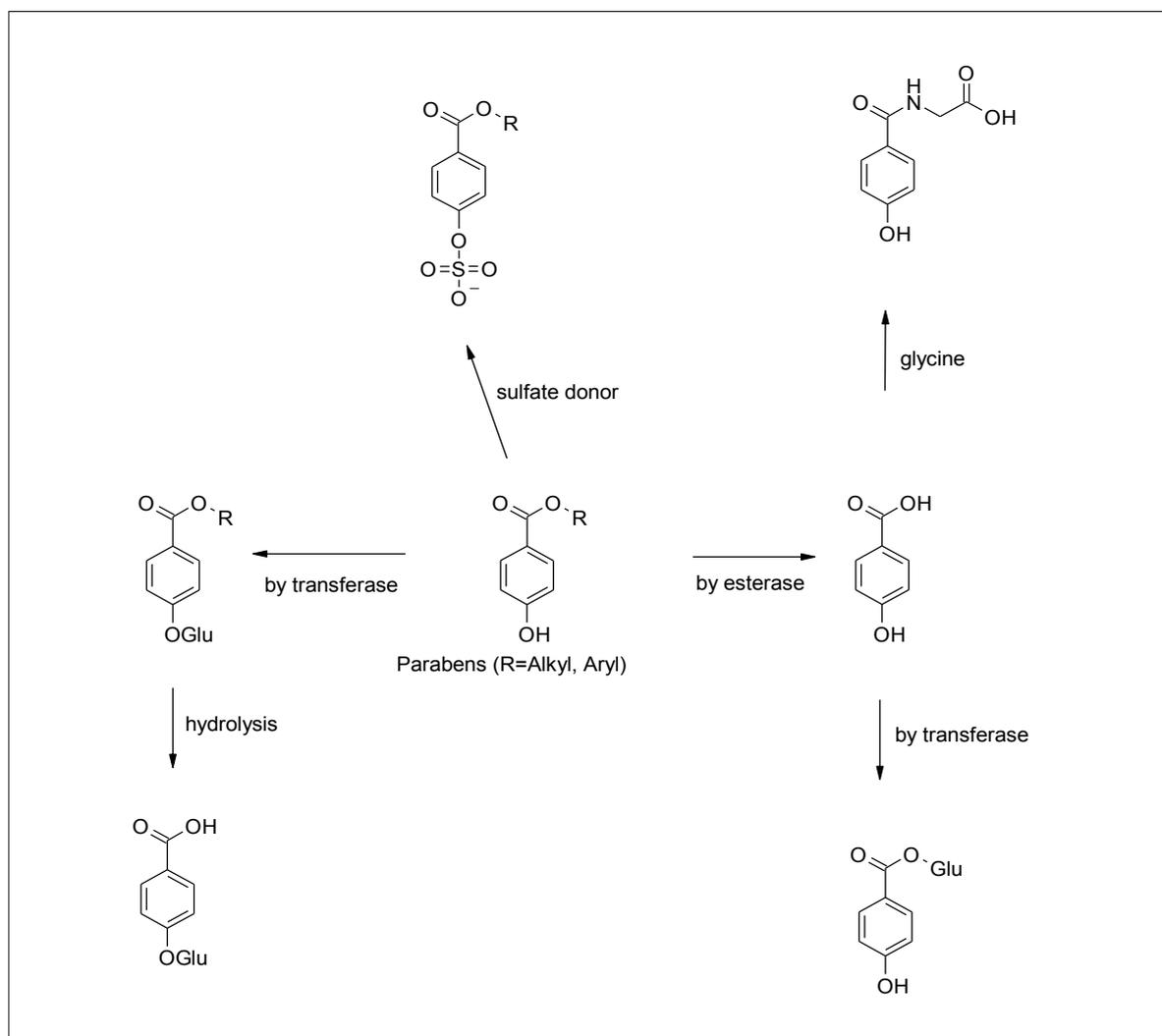


Fig. 2 Different routes of metabolism

Acute toxicology and chronic effects

No acute toxicity has been observed for parabens human or animal studies so far. They are absorbed, metabolized, and quickly excreted by humans. However, parabens are known to cause allergic reactions incl. skin irritation and contact dermatitis on sensitive or already damaged skin. Total paraben concentration has a strong influence on the intensity of these allergic effects.^{4,5}

Parabens are also known for their estrogenic activity, which was validated *in vitro* and *in vivo* by several studies. Binding activities to human estrogen receptors are relatively low compared to estradiol (10,000 to 1,000,000 lower times). Health risks were highlighted when several studies showed high concentrations of parabens in both healthy breast tissue and breast tumors. It has been hypothesized that the mimicking of estrogen and higher concentrations in breast tissue may promote breast cancer development. Another source of controversy is the possible effect of parabens on the male reproductive system.^{1,6}

Regulatory control of parabens

In 2006, the Scientific Committee on Consumer Product (SCCP) of the EU considered the continued use of propyl-, isopropyl-, butyl- and isobutylparaben in a concentration up to the existing 0.4% weight/weight individually or 0.8% when used in combination in cosmetic products to be safe for the consumer.⁷



Controversy

Consumables are subject to expectations of long life-times and being microbacterial-free environments which leads to the need for preservatives. The ideal preservative should be effective in low concentrations against a large variety of microorganisms without affecting the potential of the specific consumable; they should be cheap, available in large amounts and non-toxic.

The mainstream cosmetic industry believes that parabens are safe based on their long term use (for more than 80 years). Public interest organizations which raise awareness about cosmetic ingredients believe that further research is necessary to determine the safety of parabens. The challenge to find preservatives with the fewest side effects as possible will continue.

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Available from Chiron AS

Chiron is happy to offer a variety of parabens including internal standards. Native reference materials are available as neat material, or as a solution in methanol. Internal standards are available as a solution in methanol. Please enquire for more information and prices.

Pr. No.	Name	CAS	Synonym
	Parabens		
10203.8	Methyl 4-hydroxybenzoate	99-76-3	Methylparaben, E218
10204.9	Ethyl 4-hydroxybenzoate	120-47-8	Ethylparaben, E214
10205.10	<i>n</i> -Propyl 4-hydroxybenzoate	94-13-3	Propylparaben, E216
10206.10	Isopropyl 4-hydroxybenzoate	4191-73-5	Isopropylparaben
10207.11	<i>n</i> -Butyl 4-hydroxybenzoate	94-26-8	Butylparaben
10208.11	Isobutyl 4-hydroxybenzoate	4247-02-3	Isobutylparaben
10209.12	<i>n</i> -Pentyl 4-hydroxybenzoate	6521-29-5	Pentylparaben
10210.13	<i>n</i> -Hexyl 4-hydroxybenzoate	1083-27-8	Hexylparaben
8776.13	Phenyl 4-hydroxybenzoate	17696-62-7	Phenylparaben
10223.14	<i>n</i> -Heptyl 4-hydroxybenzote	1085-12-7	Heptylparaben, E209
10211.14	Benzyl 4-hydroxybenzoate	94-18-8	Benzylparaben
	Metabolite		
2514.7	4-Hydroxybenzoic acid	99-96-7	pHBA
	Internal standards		
10212.8	Methyl 4-hydroxybenzoate-2,3,5,6-d4	362049-51-2	Methylparaben-d4
10214.9	Ethyl 4-hydroxybenzoate-2,3,5,6-d4	1219795-53-5	Ethylparaben-d4
10216.10	<i>n</i> -Propyl 4-hydroxybenzoate-2,3,5,6-d4	1219802-67-1	<i>n</i> -Propylparaben-d4
10225.10	Isopropyl 4-hydroxybenzoate-2,3,5,6-d4	1219798-72-7	Isopropylparaben-d4
10226.11	Isobutyl 4-hydroxybenzoate-2,3,5,6-d4	121-9805-33-0	Isobutylparaben-d4
10218.11	<i>n</i> -Butyl 4-hydroxybenzoate-2,3,5,6-d4	1219798-67-0	<i>n</i> -Butylparaben-d4
10220.12	<i>n</i> -Pentyl 4-hydroxybenzoate-2,3,5,6-d4	1219798-66-9	<i>n</i> -Pentylparaben-d4
10230.13	<i>n</i> -Hexyl 4-hydroxybenzoate-2,3,5,6-d4	1083-27-8 (unlabeled compound)	<i>n</i> -Hexylparaben-d4
10227.14	<i>n</i> -Heptyl 4-hydroxybenzoate-2,3,5,6-d4	1085-12-7 (unlabeled compound)	<i>n</i> -Heptylparaben-d4
10229.14	Benzyl 4-hydroxybenzoate-2,3,5,6-d4	1219805-81-8	Benzylparaben-d4

Please note: All details are without guarantee.

¹Kirchhof M. G., de Gannes G. C. *Skin Therapy Letter*. 2013, 18 (2).

²K. W. Smith et al. *Environmental Health Perspectives*. 2013; <http://dx.doi.org/10.1289/ehp.1205350>.

³S. Abbas et al. *Drug Metab. Pharmacokin.* 2010, 25 (6), 568-577.

⁴M.G. Soni et al. *Food and Chem. Tox.* 2005, 43, 985-1015.

⁵J. E. Nagel et al. *JAMA* 1977, 237 (15), 1594-1595.

⁶P.W. Harvey, D. J. Everett; *Journal of Applied Toxicology*. 2004, 24 (1), 1-4.

⁷SCCP: Opinion on Parabens. Colipa No P82 10 Oct 2006.



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