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Concentrations of Parabens in Human Breast Tumours

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Abstract

Parabens are used as preservatives in many thousands of cosmetic, food and pharmaceutical products to which the human population is exposed. Although recent reports of the oestrogenic properties of parabens have challenged current concepts of their toxicity in these consumer products, the question remains as to whether any of the parabens can accumulate intact in the body from the long-term, low-dose levels to which humans are exposed. Initial studies reported here show that parabens can be extracted from human breast tissue and detected by thin-layer chromatography. More detailed studies enabled identification and measurement of mean concentrations of individual parabens in samples of 20 human breast tumours by high-pressure liquid chromatography followed by tandem mass spectrometry. The mean concentration of parabens in these 20 human breast tumours was found to be 20.6 +/- 4.2 ng x g(-1) tissue. Comparison of individual parabens showed that methylparaben was present at the highest level (with a mean value of 12.8 +/- 2.2 ng x g(-1) tissue) and represents 62% of the total paraben recovered in the extractions. **These studies demonstrate that parabens can be found intact in the human breast and this should open the way technically for more detailed information to be obtained on body burdens of parabens and in particular whether body burdens are different in cancer from those in normal tissues**.

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Some Alkyl Hydroxy Benzoate Preservatives (Parabens) Are Estrogenic

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Abstract

The inadvertent estrogenicity of certain synthetic chemicals, and their subsequent effects on the endocrine system of humans and wildlife, is of concern. In this paper we report findings fromin vitroandin vivo(uterotrophic) studies which confirm that a range of alkyl hydroxy benzoate preservatives (parabens) are weakly estrogenic. In a receptor-binding assay, butylparaben was able to compete with3H-estradiol for binding to the rat estrogen receptor with an affinity approximately 5 orders of magnitude lower than that of diethylstilboestrol, and between 1 and 2 orders of magnitude less than nonylphenol. In anin vitroyeast-based estrogen assay, the four most widely used parabens (namely methyl-, ethyl-, propyl-, and butylparaben) were all found to be weakly estrogenic with the most potent (butylparaben) being 10,000-fold less potent than 17β-estradiol. The estrogenic activity of parabens was inhibited by 4-hydroxy tamoxifenin vitro,illustrating the requirement of these chemicals to interact with the estrogen receptor in order to activate the yeast. When administered orally to immature rats, the parabens were inactive. **However, subcutaneous administration of butylparaben produced a positive uterotrophic responsein vivo,although it was approximately 100,000 times less potent than 17β-estradiol. Given their use in a wide range of commercially available topical preparations, it is suggested that the safety in use of these chemicals should be reassessed, with particular attention being paid to estimation of the actual levels of systemic exposure of humans exposed to these chemicals**. The acquisition of such data is a prerequisite to the derivation of reliable estimates of the possible human risk of exposure to parabens.

Combined Activation of Methyl Paraben by Light Irradiation and Esterase Metabolism toward Oxidative DNA Damage

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Methyl paraben (MP) is often used as a preservative in foods, drugs, and cosmetics because of its high reliability in safety based on the rapid excretion and nonaccumulation following administration. Light irradiation sometimes produces unexpected activity from chemicals such as MP; furthermore, there is ample opportunity for MP to be exposed to sunlight. Here, we investigated whether MP shows DNA damage after sunlight irradiation. Two major photoproducts, p-hydroxybenzoic acid (PHBA) and 3-hydroxy methyl paraben (MP-3OH), were detected after sunlight irradiation to an aqueous MP solution. Both photoproducts were inactive in the in vitro DNA damage assay that measures oxidized guanine formed in calf thymus DNA in the presence of divalent copper ion, a known mediator of oxidative DNA damage. Simulated MP metabolism using dermal tissues after light irradiation produced these two photoproducts, which reacted with a microsomal fraction (S9) of the skin. A metabolite from MP-3OH, not PHBA, caused distinct DNA damage in the in vitro assay. This active metabolite was identified as protocatechuic acid, a hydrolyzed MP-3OH product. In addition, NADH, a cellular reductant, enhanced DNA damage by approximately five times. These results suggest that reactive oxygen species generated by the redox cycle via metal ion and catechol autoxidation are participating in oxidative DNA damage. **This study reveals that MP might cause skin damage involving carcinogenesis through the combined activation of sunlight irradiation and skin esterases.**

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Methylparaben potentiates UV-induced damage of skin keratinocytes

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Abstract

For many years, methylparaben (MP) has been used as a preservative in cosmetics. In this study, we investigated the effects of ultraviolet-B (UVB) exposure on MP-treated human skin keratinocytes. HaCaT keratinocyte was cultured in MP-containing medium for 24 h, exposed to UVB (15 or 30 mJ/cm2) and further cultured for another 24 h. Subsequent cellular viability was quantified by MTT-based assay and cell death was qualified by fluorescent microscopy and flow cytometry. Oxidative stress, nitric oxide (NO) production and cellular lipid peroxidation were measured using fluorescent probes. In addition, activation of nuclear factor kappa B and activator protein-1 was assessed by electro-mobility gel-shift assay. Practical concentrations of MP (0.003%) had a little or no effect on cellular viability, oxidative stress, NO production, lipid peroxidation and activation of nuclear transcription factors in HaCaT keratinocytes. Low-dose UVB also had little or no effect on these parameters in HaCaT keratinocytes. **However, UVB exposure significantly increased cell death, oxidative stress, NO production, lipid peroxidation and activation of transcription factors in MP-treated HaCaT keratinocytes. These results indicate that MP, which has been considered a safe preservative in cosmetics, may have harmful effects on human skin when exposed to sunlight.**