The Health Controversies of Parabens

Mark G. Kirchhof, MD, PhD, Gillian C. de Gannes, MD, MSc, FRCPC

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Abstract and Introduction

Abstract

Parabens are preservatives used in a variety of personal care, cosmetic, pharmaceutical and food products. Studies have confirmed the ubiquitous presence of parabens, with levels detected in wastewater, rivers, soil and house dust. Parabens have also been detected in human tissues and bodily fluids, but it is the discovery of these chemical compounds in the breast tissue of patients with breast cancer that has raised public concern over their use. It is hypothesized that the estrogenic properties of parabens may play a role in breast cancer development. However, studies investigating the health effects of parabens are conflicting. At this point, there is an insufficient amount of data suggesting serious consequences from paraben use and exposure to warrant drastic avoidance measures or government regulations.

Introduction

Parabens are preservatives that are used in a wide range of cosmetic, pharmaceutical and some food products. Parabens are esters of para-hydroxybenzoic acid and commonly include methylparaben, ethylparaben, propylparaben and butylparaben.[1] The recent health concerns regarding parabens stem from a study published in 2004 that detected parabens in breast tissue from patients with breast cancer.[2] Public pressure has persuaded several governments to introduce regulations on the use of parabens in consumer products. In this review, we examine the data regarding the health effects of parabens to provide physicians and patients with a better understanding of this issue.

Consumer Products and Parabens

Parabens have been used in food, cosmetic and pharmaceutical products since the 1930s. Their use in cosmetic consumer products is more prevalent than their utility elsewhere. Products found to contain parabens include hand soap, body lotion, shampoo, conditioner, face lotion, facial cleansers, foundation, lipstick, mascara, hair spray/mousse/gel, toothpaste and sunscreen.[1,3,4] One study identified parabens in 44% of cosmetics tested.[3] In personal care products tested in the US, concentrations of methylparaben up to 1.0% were found, with lipsticks containing the highest concentration ranging from 0.15% to 1.0%.[1] The other parabens are used at concentrations lower than methylparaben in personal care products. Methylparaben and propylparaben are the most commonly used parabens in pharmaceutical products at concentrations of up to 20%;[1] both of these preservatives are also used in food products such as jams, jellies, fillings and toppings at concentrations of up to 0.1%.[1,5]

Parabens in the Environment

Parabens have been found in urban streams into which treated or untreated effluent from wastewater treatment plants flows.[6,7] Consequently, these chemical compounds have been identified in rivers and drinking water sources.[6,8] Parabens have been detected in soil from agricultural fields, possibly from irrigation or fertilization practices.[9,10] The dust in houses has also been found to contain parabens.[11,12] Although commercially used parabens are of synthetic origin, some parabens are produced by living organisms, specifically by plants and microbes, e.g., a marine bacterial strain belonging to the genus Microbulbifer.[13] Plants such as blueberries, carrots, olives, strawberries and others produce parabens (mainly methylparaben) for its presumed antimicrobial activity.[14–16] Overall, the concentrations of parabens within the environment are low with water concentrations around 7 ng/L and effluent concentrations up to 6 µg/L, soil concentrations range from 0.5 to 8 ng/g while house dust contained up to 2400 ng/g.7–11

Parabens in the Human Body

Parabens can enter the human body through the skin and parenterally. The average daily total personal paraben exposure is estimated to be 76 mg, with cosmetics and personal care products accounting for 50 mg, 25 mg from pharmaceutical products, and 1 mg from food.[17–19] Parabens applied to the skin are metabolized by keratinocyte carboxylesterases and the conjugated metabolites are excreted in urine and bile.[20,21] Oral or intravenous parabens are metabolized by esterases within the intestine and liver.[1] Parabens have been detected in urine, serum, breast milk and seminal fluid, but most worrisome has been the detection in breast tissue from patients with breast cancer.[2,22–26] Some have hypothesized that the higher concentration in the upper lateral breast near the axilla correlates with exposure from underarm deodorant and an increased incidence of breast cancer development in the area.[27,28] Still absolute concentrations indicate that levels of paraben within human fluids and tissue are low with average urine concentrations reported in the US ranging from 0.5 to 680 ng/mL and breast tissue concentrations ranging from 0 to 5100 ng/g of breast tissue (the median being 85.5 ng/g).[25,26] These low concentrations should be interpreted in the context of known estrogenic effects of parabens, which are discussed in the next section.

Toxicity and Adverse Effects of Parabens

Human and animal studies have failed to show that parabens have any acute toxicity by various routes of administration. As such, many of the studies examining paraben toxicity have focused on the long-term effects of chronic exposure.

The estrogenic activity of parabens was first identified in 1998 and has since been validated in vitro and in vivo.[1,29,30] Parabens bind human estrogen receptors, although with affinities 10,000 to 1,000,000 times less than estradiol.[29,31] Butylparaben and propylparaben have higher estrogenic activity than methylparaben or ethylparaben, but butylparaben and propylparaben are detected at concentrations 10 to 1000 times less than methylparaben in humans.[32] The estrogenic effects in vivo have been demonstrated by uterotrophic (uterine growth) assays in mice and rats.[1,33] However, this effect did not prevent implantation of a fertilized egg, which is considered the most sensitive measure of estrogen toxicity.[33,34] As mentioned, it has been hypothesized that the estrogenic activity of parabens may promote breast cancer development. The concentration of estradiol in normal human breast tissue is 55.3 pg/g, suggesting there is a safety margin of 10 to 1000 times for parabens to approximate normal estradiol activity.[1,25,32] The paraben breast cancer data shows no or low parabens in a subset of patients and there are no comparisons with normal controls.[2,25] Hence, having not established a clear correlation, it is difficult to put forth a causal relationship between parabens and breast cancer development.

Another major area of study has been the effect of parabens on the male reproductive system, but findings are conflicting.[35] One in vitro study found that human sperm were not viable when exposed to parabens at concentrations of 1 mg/mL.[36] In vivo studies in mice did not replicate this result, with no spermatotoxic effects at paraben concentrations of 1%.[37] Conflicting results have also been reported in rats, with one study showing decreased sperm number and activity while another study found no adverse reproductive effects.[35,38] In humans, men with fertility problems including low sperm count and decreased motility were assayed for paraben exposure by measuring urine paraben levels.[23] No correlation between sperm count or motility and parabens levels was found.

Parabens, as is the case for many preservatives, can be allergenic in a small subset of the population. This sensitization commonly manifests as an eczematous rash. The rates of reported sensitization to parabens range from 0.5% to 3.5%.[17] These rates of sensitization are amongst the lowest of all preservatives.[17,18] In addition, there are reports of immediate immunoglobulin Emediated allergic reactions to parabens resulting in urticaria and, in one case, bronchospasm.[39,40] However, these immediate allergic reactions are extremely rare.

Government and Regulatory Control of Parabens

Government regulatory boards have examined parabens and most have agreed that current concentrations of parabens are safe for consumer use. The European Union (EU) has set up limits on paraben use that have also been reviewed by the European Scientific Committee on Consumer Products (SCCP). In 2006, the SCCP

concluded that parabens can be safely used in cosmetic products at concentrations of 0.4% for any individual paraben and 0.8% for total paraben concentrations.[1,41] These limits echo the legislative limits put in place by the EU. The Danish government went further in 2011 by banning the use of parabens in personal care products intended for children younger than 3 years of age. This decision is based on the possibility of high systemic absorption from an immature metabolism and skin barrier dysfunction.[42] In the United States, the Cosmetic Ingredient Review (CIR) assesses ingredients for safety and is reviewed by the US Food and Drug Administration (FDA). The CIR has recommended the same maximum paraben concentrations as suggested by the SCCP and as legislated by the EU.[1] However, it should be noted that the CIR recommendations are only guidelines and manufacturers are not required to follow them. Likewise in Canada, there are no laws regulating paraben concentrations, but Health Canada agrees with the FDA and the CIR in regards to the safety of parabens and the adoption of maximum concentration guidelines.[43]

Alternatives to Parabens

There are numerous preservatives that could be used in place of parabens. Some other commonly used preservatives include formaldehyde, quaternium-15, imidazolidinyl urea, diazolidinyl urea and dimethyloldimethyl hydantoin.[18] These preservatives more commonly cause allergic reactions and some pose more serious health implications, such as formaldehyde and its causal link with cancer.[18] The use of "natural" preservatives has been advocated, including grapefruit seed extract (GSE).[44] Unfortunately, GSE can interact with medications due to its ability to inhibit CYP3A4, an important enzyme involved in drug metabolism.[45] Other natural preservatives include thymol, cinnamaldehyde, allyl isothiocyanate, citric acid, ascorbic acid and rosemary extract.[46,47] These natural preservatives inhibit microbial growth in vitro, but the few studies testing antimicrobial activity in food products have provided equivocal results.[46,48,49] Therefore, further studies to determine their efficacy, safety and toxicology are warranted before widespread use.

Conclusion

The expectation of long shelf lives and microorganism-free consumer products mandates the use of preservatives. Ideally, preservatives should be active at low concentrations against a wide variety of microorganisms without interfering with other ingredients in the product, while also remaining nontoxic to humans and available at low cost to manufacturers. Parabens have been used for over 80 years and, despite reports of adverse reactions, they have proven to be amongst the safest and most well tolerated preservatives. Although the possible association of parabens with decreased sperm quality and breast cancer does warrant continued examination, the current data does not support drastic regulations or personal restrictions to exposure. Other recently regulated chemicals, such as phthalates and bisphenol A, may serve as archetypes for continued vigilance and investigation.[50,51]

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