



Reply to comment on construction of simplified models to simulate estrogenic disruptions by esters of 4-hydroxy benzoic acid (Parabens) by D. Godfrey

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In response to this comment we should firstly point out that the level of theory used in our calculations [1] is robust, validated with experimental data, and not challenged here. Following review of the literature on parabens, we decided to include the work of Darbre et al. since we considered that it was comprehensive and well intended. It is commonly stated, even by Darbre's group, that estrogenic activity generally increases with the length of the alkyl chain. But it is also mentioned that the fact that methylparaben was found at the highest levels (approximately 62% of the total parabens) in human breast tumours not only reflects the greater ability of methylparaben to be absorbed into body tissues and to resist hydrolysis by esterases of human skin and subcutaneous fat tissue [2], but also it may be able to accumulate in fatty components of body tissues in a similar manner to that of other lipophilic pollutants that are known to bioaccumulate [3–6]. And subcutaneous administration of methylparaben has been reported to cause mammary adenocarcinomas in rats [7]. Earlier studies have identified other environmental estrogenic chemicals that can accumulate in fatty tissue of the breast [8–11]. It is therefore not inconceivable that the levels of parabens measured in the Darbre study [12] could exert estrogenic effects on epithelial cells in the human breast.

Consequently, a major issue in current studies of accumulation of environmental pollutants in body tissues is whether the levels reached could be sufficiently high to exert any biological action like estrogenicity, and there will be opinions both in favor of or against such a relationship. This remains an open question that must be addressed at several levels. The theoretical results that we obtained [1] stand unchanged, exactly as reported after peer review, and are intended to be a constructive contribution to this ongoing debate.

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