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Alternative Toxicity of Phthalates

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Phthalic acid ester plasticizers are widely used in flexible polyvinyl chloride products including vinyl flooring and wall covering, food containers, medical devices, and infant toys. Exposure of the general populations to phthalates is ubiquitous [1,2] and occurs due to the use and/or contact of above mentioned artificial structures. Previously, phthalates were reported to have toxic potential against liver [3], kidney [4,5], and lung [6-8]. Especially, liver toxicity of phthalates is widely implicated, since phthalates including DEHP are regulators of important transcriptional factors in homeostasis in the liver, i.e. Peroxisome Proliferator-Activated Receptors (PPARs) [9]. As for carcinogenicity and/or mutagenicity, the human database includes researches that infer possible correlation between exposure to phthalates or other chemicals present in polyvinyl chloride-containing products and excess mortality from malignant tumors derived from pancreas [10,11], testicular [12], respiratory tract [13,14], and breast [15]. On the other hand, the primary human health concern of exposure to phthalates is placed on earlier life exposures and associated risks of reproductive and developmental impacts, in particular in males [16]. Nonetheless, there is a pitfall about their possible potential in toxicity.

The prevalence of allergic disorders has rapidly increased, in particular in developed countries throughout the past several decades [17] Alternation in environmental factors such as allergen load, infectious disease profile, vaccination, and the environmental adjuvants such as diesel engine-derived particles and so on, rather than genetic factors, is likely to be regarded as the cause of this increase [18,19]. Epidemiologically, environmental risk factors for immunotoxicity on allergy are, at least in part, attributable to environmental pollutants including endocrine disruptors. On the other hand, we and others have experimentally demonstrated that several environmental chemical components such as diesel engine-derived particles (diesel exhaust particles: DEP: they have vast numbers of chemicals around the particles) and nano-leveled particles exacerbate murine atopic allergy models including asthma and dermatitis ones [20-25].

Besides, recently, causal relationship between phthalate exposure and induction, increase, and/or exacerbation of allergic diseases including asthma, dermatitis, and eczema has been implicated, in particular in children [26,28]. Also, we have reported that di-(2-ethylhexyl) phthalate (DEHP), widely used [1.8 million metric tons/year] among phthalates, potentiates atopic dermatitis-like skin lesions in NC/Nga mice [29]. Further, reportedly, phthalates have been connected to autoimmune disorders such as systemic lupus erythematosus [28,30]. Also, Larsen et al. have shown that DEHP facilitates allergic asthma in BALB/c mice [31,32]. Our present study added the biological evidence that DEHP deteriorate allergen-related inflammation in ICR mice [33], which had been reported to correlate in epidemiological studies [2]. Also, we provided evidence that this aggravation was concomitant with local production/release of inflammation- and allergy-related molecules such as IL-5, eotaxin, and KC.

In sum, phthaletes have potential to exacerbate allergic pathophysiology, whose adverse impact should list up as alternative toxicity of these chemicals. As well, toxicologists should expand investigation to other environmental chemicals.

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