What contributes to human body burdens of phthalate esters?

An experimental approach

Georgios Giovanoulis

Academic dissertation for the Degree of Doctor of Philosophy in Applied Environmental Science at Stockholm University to be publicly defended on Friday 1 September 2017 at 10.00 in Nordenskiöldsalen, Geovetenskapens hus, Svante Arrhenius väg 12.

Abstract

Phthalate esters (PEs) and alternative plasticizers used as additives in numerous consumer products are continuously released into the environment leading to subsequent human exposure. The ubiquitous presence and potential adverse health effects (e.g. endocrine disruption and reproductive toxicity) of some PEs are responsible for their bans or restrictions. This has led to increasing use of alternative plasticizers, especially cyclohexane-1,2-dicarboxylic acid diisononyl ester (DINCH). Human exposure data on alternative plasticizers are lacking and clear evidence for human exposure has previously only been found for di(2-ethylhexyl) terephthalate (DEHTP) and DINCH, with increasing trends in body burdens. In this thesis, a study population of 61 adults (age: 20–66; gender: 16 males and 45 females) living in the Oslo area (Norway) was studied for their exposure to plasticizers. Information on sociodemographic and lifestyle characteristics that potentially affect the concentrations of PE and DINCH metabolites in adults was collected by questionnaires. Using the human biomonitoring approach, we evaluated the internal exposure to PEs and DINCH by measuring concentrations of their metabolites in urine (where metabolism and excretion are well understood) and using these data to back-calculate daily intakes. Metabolite levels in finger nails were also determined. Since reference standards of human metabolites for other important alternative plasticizers apart from DINCH (e.g. DEHTP, di(2-propylheptyl) phthalate (DPHP), di(2-ethylhexyl) adipate (DEHA) and acetyl tributyl citrate (ATBC)) are not commercially available, we further investigated the urine and finger nail samples by Q Exactive Orbitrap LC-MS to identify specific metabolites, which can be used as appropriate biomarkers of human exposure. Many metabolites of alternative plasticizers that were present in in vitro extracts were further identified in vivo in urine and finger nail samples. Hence, we concluded that in vitro assays can reliably mimic the in vivo processes. Also, finger nails may be a useful non-invasive matrix for human biomonitoring of specific organic contaminants, but further validation is needed. Concentrations of PEs and DINCH were also measured in duplicate diet, air, dust and hand wipes. External exposure, estimated based on dietary intake, air inhalation, dust ingestion and dermal uptake, was higher or equal to the back-calculated internal intake. By comparing these, we were able to explain the relative importance of different exposure pathways for the Norwegian study population. Dietary intake was the predominant exposure route for all analyzed substances. Inhalation was important only for lower molecular weight PEs, while dust ingestion was important for higher molecular weight PEs and DINCH. Dermal uptake based on hand wipes was much lower than the total dermal uptake calculated via air, dust and personal care products, but still several research gaps remain for this exposure pathway. Based on calculated intakes, the exposure risk for the Norwegian participants to the PEs and DINCH did not exceed the established tolerable daily intake and reference doses, and the cumulative risk assessment for combined exposure to plasticizers with similar toxic endpoints indicated no health concerns for the selected population. Nevertheless, exposure to alternative plasticizers, such as DPHP and DINCH, is expected to increase in the future and continuous monitoring is required. Findings through uni- and multivariate analysis suggested that age, smoking, use of personal care products and many other everyday habits, such as washing hands or eating food from plastic packages are possible contributors to plasticizer exposure.

Keywords: *Phthalates, Alternative plasticizers, DINCH, In vivo screening, Urine, Nails, Air, Dust, Hand wipes, Duplicate diet, Predictors of exposure.*

Stockholm 2017
http://urn.kb.se/resolve?urn=urn:nbn:se:su:diva-143147

ISBN 978-91-7649-874-3
ISBN 978-91-7649-875-0

Department of Environmental Science and Analytical Chemistry

Stockholm University

Stockholm University, 106 91 Stockholm