Phthalates—Exposure and Risk to the Human Health

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Introduction

Plastics are important in all walks of life from the cradle to the deathbed. The increasing use of plastics has been accompanied by concerns about the impact of chemical ingredients leaching from plastic containers during use and after disposal on the health of human beings and entire ecosystems. The wide spread use of plastics has been made possible by the development of suitable additives that confer desired properties to plastics. Phthalates like Di-2-ethylexyl phthalate (DEHP) are a group of additives that are used in plastics like Poly vinyl chloride (PVC) and Polyethylene Terephthalate (PET). DEHP is present in plastics used for making medical devices like blood bags, catheters and tubing. In this review author has limited to a discussion of the risks posed by phthalates that have been reported in scientific literature.

Exposure to Phthalates

Phthalates are one of the most abundant man made environmental pollutants. They are diesters of phthalic acid and are used widely in cosmetics, adhesives and as solvents. In plastics, phthalates are used to impart flexibility. They are not chemically bound to the resin and can be released relatively easily (Yuan & Graham, 2008). The leaching of phthalates is affected by several factors like the concentration of free phthalates in the plastics, usage of the container, duration and condition of storage, the characteristics of the polymer resin etc. Human exposure to phthalates can occur from multiple sources and through different routes.

Wilkinson & Lamb (1999) compared the accepted daily intake (ADI) of Di isononyl phthalate (DINP) with estimates of exposure in children through toys. They observed that against an ADI of 1-4 mg/kg/ day the estimated 95th percentile exposure was 94.3 µg/kg/day.

The ADI level for DEHP is 37 µg/kg /day (Koo & Lee, 2004). Shea (2003) reported that the maximum estimated intake of DEHP was 19 µg/kg /day and was observed in children between 6 months to 4 years of age. After 4 years of age, the level of exposure progressively decreased as summarised in the Table 1 below. In all age groups food was the major source of exposure to DEHP, accounting for over 80% of the total exposure.

Blount et al. (2000) measured the monoester metabolites of common phthalates in human urine samples. They expressed concern that the highest levels of the metabolite they measured was found in women of childbearing age. Based on these measurements David (2000) and Kohen et al. (2000) have independently reported the estimated daily intake of different phthalates.

Biological effects of Phthalates

Kluwe et al. (1982) studied the carcinogenic potential of multiple phthalic acid esters on rats and mice. Their study suggested that each ester might have a different mode of action. They also concluded that all phthalic acid esters had a hepatocarcinogenic effect in mice with female mice being more susceptible than males. Ward et al., (1986) studied the tumour initiating and promoting effect of DEHP in mouse and rat animal models in vivo and in mouse epidermis derived JB6 cell lines in vitro. DEHP promoted pre-initiated hyperplastic lesions and neoplastic foci in mice but not in rats. They identified DEHP as a weak complete promoter and a definite second stage promoter. DEHP and its metabolite mono (2-ethylhexyl) phthalate (MEHP) promoted JB6 cells in vitro to anchorage independence (Jobling et al., 1995). In vitro studies by Jobling et al. (1995) have identified BBP and DBP as estrogenic. They also suggest that in the presence of endogenous estrogens the overall effect of these two chemicals would be cumulative. Klaunig et al. (2003) analyzed the bioassay data related to peroxisomal proliferation in vivo and concluded that rodents are more sensitive than primates to

Table 1. Variation in estimated intake of DEHP in different age groups.

	Age (years)				
	0.0 - 0.5	0.5 - 4.0	5.0 -11.0	12.0 -19.0	20.0 - 70.0
Estimated intake (µg/kg/day)	8.9-9.1	19	14	8.2	5.8
Estimated exposure from food (µg/kg/day)	7.9	18	13	7.2	4.9

peroxisomal proliferators. In another study Akingbemi et al. (2004) reported that DEHP increased serum 17 Beta estradiol concentrations by 50%. Shea (2003) concluded that there was disagreement about the exact mechanism by which DEHA and DINP caused cancer and that there were indications that the carcinogenic risk to human beings was lower than that to animals. Rusyn et al. (2006) have supported the hypothesis that DEHP may cause cancer in animal models by peroxisome proliferation.

Recommendations

The leaching of phthalates from medical devices and containers is an area of gravest concern. While one scientific evaluation of the harmful potential of phthalates concludes that DEHP, as used in medical devices, "is unlikely to pose a health risk to even highly exposed humans" (Koop et al., 1999) the other concluded that "the weight of the evidence indicates a significant potential for serious adverse effects on human health from DEHP-containing medical devices" (Tickner et al., 1999). Tickner et al. (2001) have commented on the uncertainty prevailing about the mechanism of action of phthalates and the risk posed by the possibility of inter-individual variability. They recommend a move to safer alternatives to DEHP and PVC in medical devices. Plastics have made an immense contribution to the human society. The current quest is to find safer and environmentally benign products. Given that human beings are likely to be exposed to a cocktail of phthalates, more realistic results would be obtained through studies probing the effect of a mixture of phthalates, mimicking the real life exposure conditions (Kortenkamp & Faust, 2010).

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Table 2. Estimated daily exposure (µg/kg/day) to some phthalates.

	David (2000)			Kohn et al. (2000)		
	Geometric mean	95th percentile	Maximum	Median	95th percentile	Maximum
DEP	12.34	93.33	241.81	12	110	320
DBP	1.56	6.87	116.96	1.5	7.2	110
BBP	0.73	3.34	19.79	0.88	4.0	29
DEHP	0.60	3.05	38.48	0.71	3.6	46
DINP	0.21	1.08	14.35	Below limit of detection	1.7	22

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Water has Vanished in last 32 years

Aral Sea accounts for biggest loss; Iraq loses third of water area; Iran and Afghanistan a half of theirs.

Ninety thousand sq km of water—the equivalent of half of the lakes in the Europe—has vanished from the surface of the Earth since 1984, according to new research.

Google has teamed up with the European Commission's Joint Research Centre to analyse 3 million satellite images, going all the way back to 1984.

The project has been a monumental undertaking and was made possible by new data processing methods, running the analysis of thousands of high performance computers simultaneously.

It took 3 years to download 1.8 petabytes of data from the USGS / NASA Landsat satellite programme and prepare it for analysis. Each pixel in the image was then examined by a computer algorithm developed by the Joint Research Centre running on the Google Earth Engine platform.

More than 10 million hours of computing time was needed for this—roughly equivalent to a modern 2-core computer running day and night for 600 years.

Eventually, Google was able to map changes in the water surface over time with a 30-metre accuracy, month-by-month, over 32 years and the findings are very alarming.

According to the images, the continuing drying up of the Aral Sea in Uzbekistan and Kazakhstan accounts for the biggest water loss in the world.

Iran and Afghanistan have also lost over a half of their water area, and Iraq has lost over a third.

Although the area covered by water in the USA has increased a little, a combination of drought and sustained demand for water have seen six western states—Arizona, California, Idaho, Nevada, Oregon, Utah—account for a third of the loss in US water surface. Meanwhile, more than 13,000 sq km of the Mississippi delta—an area 10 times the size of London—is slowly slipping into the Gulf of Mexico.

These new maps and statistics provide essential information which can aid global water security, agricultural planning, disaster preparedness, and climate understanding, said Noel Gorelick, Chief Extraterrestrial Observer at Google Earth Engine, in a blog post.