Migration of Phthalates from Plastic Products to Model Solutions

Jasna Bošnir¹, Dinko Puntarić¹, Ivo Škes¹, Maja Klarić², Spomenka Šimić³ and Ivan Zorić⁴

¹ Department of Health Ecology, Public Health Institute, Zagreb, Croatia
² Public Health Institute of Osijek-Baranja County, Osijek, Croatia
³ University Hospital »Osijek«, Osijek, Croatia
⁴ School of Medicine, University of Split, Split, Croatia

A B S T R A C T

The aim of this investigation was to determine the level and rate of migration of phthalates, compounds used as plastic softeners, from various plastic products into model solutions and to assess the possible adverse effects of the phthalate amounts released on human health, thus to contribute to harmonization of the opinions on the maximal allowed human exposure to these compounds through environmental factors. Nine specimens of plastic toys, 16 specimens of plastic food containers and 10 specimens of other plastic consumer goods were analyzed. The specimens of plastic products were submitted to 10-day action of model solutions. Three model solutions were used: distilled water, 10% ethyl alcohol, and 3% acetic acid. Identification and quantification of the phthalates released were performed by the method of gas chromatography on days 1, 5 and 10 of exposure, at a detection limit of 0.005 μg/kg. On day 10, the highest level of released phthalates (54.5 mg/kg) was measured in distilled water, followed by 44.4 mg/kg in 3% acetic acid and 32.3 mg/kg in 10% ethyl alcohol. According to plastic product categories, the highest pooled level of phthalates released to all three solutions was recorded for plastic toys (66.2 mg/kg), followed by food containers (37.6 mg/kg) and other consumer goods (27.4 mg/kg). According to plastic product categories, toys showed the most rapid phthalate release, with 65.4% (43.3 of 66.2 mg/kg) of the pooled level of phthalates released to all three solutions recorded on day 1. As indicated by the study results, the levels of phthalates released would not present a hazard for human health, not even over a prolonged period of time. However, data on the highest and fastest pooled phthalate release from plastic toys, and this especially to distilled water simulating salivary action, point to the need of continuous evaluation and amendments of the legislation on phthalates in consumer goods.

Key words: phthalates, toys, containers, consumer goods, solution model, Croatia.
Introduction

Plastic products intended for some specific purposes have to meet the requirements of elasticity and flexibility, in addition to other conditions required for plastic products in general. The properties of elasticity and flexibility are required in a great variety of plastic products used, for example, in medicine\textsuperscript{1–4}. The so-called consumer goods are a very large and varied category of plastic products where these properties are desirable. By definition, consumer goods include: (a) vessels, equipment and devices for the production of food and consumer goods, and containers for food and consumer goods; (b) children’s toys; (c) toiletries, face and body care accessories, and beauty products; (d) cleaning agents; (e) tobacco, tobacco products and smoking accessories; and (f) some objects and agents coming in direct contact with the skin or mucosa on their usage\textsuperscript{5}.

Phthalates, phthalic acid esters, have for decades been most widely used as plastic softeners (plasticizers). Among them, diethylhexyl phthalate (DEHP) has been most commonly used\textsuperscript{6–11}. Extensive production of phthalates, which exceeds 25 million tons per year, and the fact that plastic products are utilized in virtually every human activity, have imposed the need of continuous investigations conducted all over the world on the possible harmful effects of plastic products and phthalates used in their manufacture on human health\textsuperscript{7,12–16}.

The studies performed to date have provided evidence for the mutagenic, teratogenic, carcinogenic and many other adverse effects in experimental animals exposed to high doses of phthalates\textsuperscript{17–22}. The opinions on the possible harmful effect of phthalates on human health are contradictory, irrespective of the mode and level of exposure, e.g., occupational (manufacture of phthalates or plastic products)\textsuperscript{11,23–25}, extensive and occasionally continuous utilization of such products (dialysis)\textsuperscript{26,27}, or average usage and exposure to these products\textsuperscript{28–31}. On the one hand, according to the World Health Organization (WHO) conclusions and recommendations, exposure to phthalates represents a risk and caution is advised, this being a strong argument for those advocating such an attitude to propose reduction in the number and types (purposes) of plastic products\textsuperscript{10,31–34}. Other researchers, on the other hand, emphasize that the doses administered to experimental animals are several dozen to several hundred times greater than those received by the people at highest level of exposure, and that this exposure is protracted over a long period of time (years or even decades)\textsuperscript{11,35}.

These contradictions have resulted in quite generalized legislation in the field, especially in Croatia, merely defining the total allowed amount of phthalates in plastic products, which should not exceed 35%, without considering the purpose of the product, the length of its usage, and the age of the user\textsuperscript{36}. At the same time, paradoxically, consumer goods made from other materials have to stand very strict simulation of the conditions in which they may be used in daily routine. So, there are legal regulations on the consumer goods to be submitted to the action of so-called model solutions (10% ethyl alcohol, distilled water, and 3% acetic acid) to determine the possible release of heavy metals (Pb, Cd, Cr, etc.), and low-molecular organic and inorganic substances. The latter is termed global migration and includes release of compounds such as primary aromatic amines expressed as aniline, secondary aromatic amines expressed as diphenylamine, and residual peroxides expressed as active oxygen. Also, consumer goods are expected not to lose stain. The objects are immersed in model solutions for at least 24 hours, then the
type and amount of the compounds and elements released to the solution are determined with the aim to approximately predict the release of these substances in contact with the skin and mucosa, human secretions and excreta, and with food intended for human use, including alcohol and non-alcohol beverages.

Taking the requirements stated in the act on safety of foods and consumer goods not made from plastics, the aim and purpose of the present study were to determine whether and to what extent and dynamics phthalates were released to model solutions, and whether the amount of phthalates thus released could pose a risk for human health at long run. The endpoint was to hopefully contribute to the harmonization of opinions on the maximal allowed amount of phthalates to which humans can be safely exposed during lifetime through daily usage of consumer goods and total environmental phthalate exposure.

**Material and Methods**

Plastic consumer goods, domestic and imported, referred to the Institute of Public Health, Zagreb, Croatia, for assessment of their safety, were classified into three groups. Group 1 included 9 specimens of plastic toys, group 2 had 16 specimens of plastic food containers, and group 3 had 10 specimens of other plastic products (disposable saucers, glasses and cutlery) intended for common usage. The specimens of plastic products were submitted to 10-day action of model solutions. Three model solutions were used: distilled water, 10% ethyl alcohol, and 3% acetic acid. The method of gas chromatography was employed for identification and quantification of released phthalates. The level of phthalates released was measured on days 1, 5 and 10 of exposure, and as a pool. The values obtained were processed according to the type of model solution, group of plastic products, and dynamics of phthalate release. Phthalate identification was performed by the method of gas chromatography with a specific electron capture detector (ECD) on a Perkin Elmer PE AutoSystem XL supplied with ECD with 63 Ni (Norwalk, USA) gas chromatograph. Under standard gas chromatography conditions, detection limits of 0.005 and 0.040 μg/l for butyl benzyl phthalate (BBP) and dioctyl phthalate (DOP), respectively, were achieved.

**Results**

On day 10 of exposure, the highest level of released phthalates (54.4 mg/kg) was found in distilled water. According to groups of products, the highest pooled level of phthalates released to all three solutions was recorded for toys (66.2 mg/kg), whereas the levels of phthalates released from food containers and other consumer goods were considerably lower (37.6 and 27.4 mg/kg, respectively) (Table 1). The highest rate of phthalate release was recorded in 3% acetic acid, whereas as much as 62.2% of the total amount of phthalate release was found on day 1. A similar pattern of phthalate release was observed in distilled water, with 58.1% of total phthalate release recorded on day 1. The rate of phthalate release in 10% ethyl alcohol was considerably lower (Table 1).

According to the group of products, the highest rate of phthalate release was recorded for toys, with 65.4% (43.3 of 66.2 mg/kg) of the pooled level of phthalates released to all three model solutions recorded on day 1. A similar pattern of phthalate release was observed in distilled water, with 58.1% of total phthalate release recorded on day 1. The rate of phthalate release in 10% ethyl alcohol was considerably lower (Table 1).
**TABLE 1**

PHTHALATE RELEASE FROM SPECIMENS OF PLASTIC CONSUMER PRODUCTS UPON EXPOSURE TO MODEL SOLUTIONS (MG/KG)

<table>
<thead>
<tr>
<th>Products (N)</th>
<th>Distilled water</th>
<th>10% Ethyl alcohol</th>
<th>3% Acetic acid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 5</td>
<td>Day 10</td>
</tr>
<tr>
<td>Plastic toys (N=9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>17.6±3.1</td>
<td>5.2±1.8</td>
<td>4.9±1.3</td>
</tr>
<tr>
<td>(N=9)</td>
<td>(63.6%)</td>
<td>(18.7%)</td>
<td>(17.7%)</td>
</tr>
<tr>
<td>Plastic food containers (N=16)</td>
<td>9.6±2.4</td>
<td>2.6±0.3</td>
<td>4.1±0.9</td>
</tr>
<tr>
<td>(N=16)</td>
<td>(59.0%)</td>
<td>(16.0%)</td>
<td>(25.0%)</td>
</tr>
<tr>
<td>Other plastic products (N=10)</td>
<td>4.4±2.0</td>
<td>4.0±1.4</td>
<td>2.1±0.2</td>
</tr>
<tr>
<td>(N=10)</td>
<td>(42.3%)</td>
<td>(37.9%)</td>
<td>(19.8%)</td>
</tr>
<tr>
<td>Total (N=35)</td>
<td>31.6±2.6</td>
<td>11.7±1.2</td>
<td>11.1±0.8</td>
</tr>
</tbody>
</table>
Discussion

Analysis of the results revealed the highest level of phthalates to be released to distilled water, which is used as a model solution to imitate the action of chemically similar saliva. Accordingly, the action of sweat, blood, gastric acid and other media in and on the human body on plastic products should be expected to be less aggressive. This is by no means negligible considering the common and wide usage of plastic products in medicine.

Toys were definitely found to be by far least resistant to the action of body secretions and excreta, for at least two reasons. First, toys showed quantitatively highest phthalate release. Second, about two thirds of total phthalates were released from toys in all three model solutions, i.e. under the action of all body fluids simulated by the solutions, on the very first day of exposure. Neither this information should be underestimated, knowing that plastic toys are intended for children of various age and grade of maturity, and that toys are mostly put into the mouth by children under the age of 2 years, yet fully unaware of the hygienic and other aspects of this motion. After all, the European Union recommendations on the use of plastic toys have resulted from similar studies30–34.

One of the aims of the present study was to assess the presence and effect of the phthalates thus released on human health. According to the literature reports available, phthalates undoubtly have adverse effects on experimental animals17–22. These effects vary in severity and impact on animal general health, and as a rule depend on the level, mode (oral, percutaneous, inhalatory, etc.) and length of phthalate exposure. Mild alterations manifested as body weight loss and insignificant reduction of life expectancy in exposed animals as compared with the control group11,35. An increased prevalence of spontaneous abortion17, stillbirth, low birth weight, and fetal malformations, i.e. teratogenic effects, has also been reported19,39,40. Changes in the activities of particular liver enzymes42, a mild estrogenic effect, and an adverse gonadal effect in male experimental animals18,21,42 have been described. Carcinogenic43 and mutagenic44,45 effects of phthalates are a 'classic' finding. However, common to all these studies irrespective of the duration and mode of exposure is that marked health impact in experimental animals occurred at doses exceeding 500 mg/kg body weight39,40,42–44.

No detrimental effects of phthalates have to date been definitely demonstrated in humans. Some authors describe some mild discomforts such as headache and neurovegetative system disturbances (sleep disturbance, increased sweating) in individuals occupationally exposed to phthalates in the manufacture of phthalates or plastic products with phthalates used as plasticizers23–25.

There is still much controversy on the issue, which has resulted in recommendations on the limited amounts of phthalates in particular media. For example, the amount of DEHP, the most widely used phthalate, has been limited to 6 μg/L drinking water and 5 mg/cubic meter air per 8-hour work time or 10 mg/cubic meter air per 15-minute exposure10.

Other authors performed mega-analysis of all studies on the issue to demonstrate that the phthalate exposure in humans is several times lower than the levels used in animal experiments, and therefore cannot have any major effect on human health. They found the doses in case of highest human exposure and under worst conditions to be dozens to hundreds times lower as compared with animal experiments. The highest and most unfavorable variant of exposure is exemplified by infants on life sustaining extracorporeal oxygenation or patients of other
age groups treated at intensive care units for a variable period of time, all with phthalate exposure expressed as body weight percentage as a common denominator\textsuperscript{11,35}. According to these studies, daily animal exposure to phthalates at a level of 0.025\% of their body weight for several years will definitely have no adverse effects on their health. In some but not all animals, impairments occurred on phthalate exposure at a level of 0.09\% of their body weight, however, only when applied for most of their life span\textsuperscript{11,35}.

In our study, the levels of phthalates were expressed in mg/kg product. The worst variant was simultaneous exposure per kilogram of all three-product groups and their simultaneous ‘dissolving’ by three body fluids (three model solutions simulating body fluids). In real life, this would be considered a ‘science fiction’, because an average toy is rarely weighing more than 100 g, not to speak of food containers or disposable saucers in kilograms. Furthermore, the worst variant would imply continuous phthalate release at the rate recorded on day 1 (when more than a half of the total phthalate amount was released) and exposure of a newborn weighing 3 kg. Thus, the worst variant, i.e. 0.025\% of 3 kg, theoretical birth weight of a newborn exposed to the effects of phthalates, would yield 0.85 g or 850 mg; and 0.09\% would make 2.7 g or 2,700 mg. By analogy with animals, daily exposure to a dose of 850 mg phthalates should not induce any disturbances, and only a prolonged exposure to a dose of 2,700 mg could entail some effect. Total phthalate release from all three groups of products in all three model solutions on day 1 characterized by highest and fastest phthalate release yielded a maximal daily level of 73.9 mg phthalates, i.e. an amount by far less than those that might have any notable effect on the health of exposed individuals. The more so, in real conditions the amount of phthalates released from the tested products is several times lower and body weight of those exposed is significantly greater. In addition, cutaneous absorption of phthalates from the gastrointestinal tract in humans is by 10\% to 20\% lower than in rodents, and the metabolism of detoxification in humans differs from and is considered more efficient than that in animals\textsuperscript{11,35}.

All these considerations support the opinion that man during his lifetime could theoretically be daily exposed to phthalate doses of several hundreds to even thousands of milligrams without any major adverse effects on his health. It should be remembered, though, that man is exposed to phthalates from various sources, e.g., water, food, air, medicinal products, etc., the doses received being cumulated in the body\textsuperscript{10,11,23–31}. Although phthalate toxicity is obviously low, their maximal levels in environmental factors should be determined, first of all because of possible accidents (e.g., in the plants manufacturing phthalates or plastics), when short-term exposure may increase several times.

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D. Puntarić

Department of Health Ecology, Public Health Institute, Mirogojska c. 16, 10000 Zagreb, Croatia
MIGRACIJA FTALATA IZ PLASTIČNIH PROIZVODA U MODEL OTOPINE

SAŽETAK

Cilj istraživanja bio je utvrditi količinu i brzinu migracije ftalata, spojeva koji se koriste kao omekšivači plastike, iz različitih plastičnih proizvoda, u model otopine. Izlaganje pokusnih životinja ftalatima pokazala su kancerogeno, mutageno i teratogeno djelovanje. Istraživanjem se željelo pokazati mogu li otpuštene količine ftalata štetno djelovati na zdravlje ljudi, te doprinesati usaglašavanju mišljenja o maksimalno dozvoljenoj izloženosti ljudi tim spojevima putem faktora okoliša. Analizirano je 9 uzoraka plastičnih dječjih igračaka, 16 uzoraka plastične ambalaže za prehrambene proizvode i 10 uzoraka drugih plastičnih proizvoda namjenjenih općoj uporabi. Uzorci plastičnih proizvoda bili su podvrgnuti 10-dnevnom djelovanju model otopine. Korištene su 3 model otopine: destilirana voda, 10% etilni alkohol i 3% octena kiselina. Identifikacija i kvantifikacija otpuštanih ftalata rađena je 1., 5. i 10. dan izlaganja metodom plinske kromatografije. Granica detekcije metode bila je 0.005 µg/kg. Nakon 10 dana, najviše otpuštanih ftalata (54.5 mg/kg) nađeno je u destiliranoj vodi, u 3% octenoj kiselini nađeno je 44.4 mg/kg ukupnih ftalata, dok ih je u 10% etilnom alkoholu utvrđeno 32.3 mg/kg. Prema skupinama proizvoda, nakon 10 dana, ukupno najviše otpuštanih ftalata (66.2 mg/kg), u sve tri model otopine zajedno, utvrđeno je iz dječjih igračaka, dok su količine utvrđenih ftalata iz prehrambene ambalaže (37.6 mg/kg) i iz ostalih proizvoda opće uporabe (27.4 mg/kg), bile znatno manje. Prema skupinama proizvoda, najbrže otpuštanje ftalata utvrđeno je kod igračaka, kod kojih je već nakon prvog dana izlaganja u sve tri model otopine ukupno otpušteno 65.4% ftalata (43.3 od 66.2 mg/kg). Utvrđene otpuštene količine ftalata, po svemu sudeći, ne mogu ugroziti zdravlje ljudi, niti kroz dulji vremenski period. Ipak, činjenica da su ukupno najviše količine ftalata otpuštene iz igračaka, da je otpuštanje iz igračaka najbrže, a posebice da je to najnaglašenije u destiliranoj vodi, koja simulira djelovanje sline, govori o potrebi stalnog evaluiranja i dopunjavanja zakonske regulative o ftalatima u predmetima opće uporabe.