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Research article

ASSESSMENT OF PUBLIC HEALTH RISKS CAUSED BY PHTHALATES MIGRATING FROM POLYMER MATERIAL TO BOTTLED WATER

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At present, consumption of packaged drinking water is growing worldwide. In this regard, ensuring packaged drinking water safety, which directly depends on the composition and quality of used polymer materials, is becoming especially relevant. Bottles made of polymer materials, i.e. polyethylene terephthalate and polycarbonate, is the most common packaging for drinking water.

The aim of this study was to assess population health risks caused by exposure to phthalates migrating from polymer bottles into drinking water.

The study was carried out according to the requirements of the Customs Union Technical Regulation… on packaging and Instruction... on sanitary-chemical study of goods. Bottles and model media were analyzed using gas chromatography with mass-spectrometric detection. Risk assessment was performed according to the current guidelines.

The study findings allow to report the following phthalate levels in bottle samples: di(2-ethylhexyl)phthalate (DEHP), 1.7–4.2 mg/kg; di-n-butyl phthalate (DnBP), <2.4–31.3 mg/kg; diisobutyl phthalate (DiBP), 2.2–10.2 mg/kg. Phthalate migration into model media occurred from all analyzed samples: DEHP and DiBP migrated from Polyethylene terephthalate in quantities equal to 8.6–71.0 µg/l and from < 2.6 to 19.2 µg/l respectively; DEHP, DnBP, and DiBP migrated from polycarbonate, 31.5–43.5 µg/l, 4.8–6.2 µg/l, and 17.0–54.0 µg/l, respectively.

The identified phthalate levels are safe according to the performed assessment of health risks associated with chronic intake of harmful substances with drinking water. The values of the estrogenicity equivalent calculated for the analyzed phthalates in model samples of bottled water were seen at a minimum level in Russian Federation as compared to other countries.

The results of this study can be used in safety assessment of polymer bottles for drinking water.

Keywords: *packaged drinking water, bottled water, model medium, phthalate migration, di(2-ethylhexyl) phthalate (DEHP), di-n-Butylphtalate (DnBP), diisobutylphthalate (DiBP), safety, health risk assessment.*

Packaged (bottled) water production has been growing steadily worldwide and the output reached $6.6 \cdot 10^{10}$ liters in 2020 [1]. People tend to think that bottled water is tastier than tapped one, more tolerable and safer as well [2]. However, some studies accomplished in several countries have reported organic compounds in bottled water; among such compounds, phthalates are given more and more attention due to their potential hazardous effects on human health [3–5]

Exposure to phthalates can cause some adverse health outcomes including endocrine disruptions, diseases of the nervous, cardiovascular, and reproductive systems [6, 7]. Di(2-ethylhexyl)phthalate (DEHP), di-n-butyl phthalate (DnBP), diisobutyl phthalate (DiBP), and benzyl butyl phthalate (BBP) are

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included into the SVHC list (Substances of Very High Concern) of the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), a European Union regulation. Certain limitations are imposed on their production and use considering their cumulative effects and co-exposure to all four phthalates [8, 9].

According to A. Pradhan et al. and V.R. Kay et al., DEHP and other phthalates produced negative effects on male and female reproductive systems in animal experiments and also on development of estrogen-sensitive tissues [10, 11]. Perinatal exposure to phthalates had certain adverse effects on animal offspring including stillbirth, increased prenatal fetus death rate, and congenital malformations including reproductive ones [12]. Phthalates are known to modulate gene expression, cell maturation, and apoptosis in mammal tissues due to their genomic, non-genomic and epigenetic mechanisms of action [13].

A study accomplished on a group of children with detected premature breast development revealed significantly high levels of phthalates and their metabolites in blood serum samples. The study results indicate a potential association between plasticizers with known estrogenic and anti-androgenic activity (dimethyl, diethyl, dibutyl and di-(2-ethylhexyl) phthalates) and the cause of premature breast development in a female population [14].

Upon oral exposure, phthalates are initially metabolized in the saliva and gastrointestinal tract into monoester metabolites. Importantly, toxicological effects of phthalates are caused by these monoester metabolites, not the original parent compounds. Several previous studies have detected phthalates in different human matrices, including urine, blood, breast milk, semen, ovarian follicular fluid, and saliva. In addition to that, phthalate metabolites have been found in maternal and cord blood, placenta tissues, and amniotic fluid [15].

Studies accomplished in the USA and Germany have identified a tentative daily exposure to phthalates within the following ranges: DEHP, between ~ 3 and 30 μg/kg/day; DnBP, between 0.84 and 5.22 μg/kg/day; and DiBP, between 0.12 and 1.4 μg/kg/day [16, 17].

Considering toxic effects of phthalates as well as population exposure to them, we can state it is necessary to assess their levels in bottled water as a source of their intake into the body.

Bottles made of polymer materials, i.e. polyethylene terephthalate (PET) and polycarbonate are the most common packages for drinking water [18].

These materials contain plasticizing additives, which are usually DEHP, DiBP, and DnBP. As a rule, phthalates do not form any strong bonds within a polymer and are easily released from ready-made goods [19].

Initial water, production processes and package materials can be potential sources of phthalates in bottled water [2]. However, a study identified significantly high levels of phthalates in materials plastic bottles were made of. Identified di-ethyl-hexyl phthalate levels were within 393–1499 mg/kg; levels of diethyl phthalate and dimethyl phthalates were 3.1 and 14.8 mg/kg respectively [20]. This indicates that package is the most likely source of phthalates in drinking water.

Some studies focused in identifying DEHP in bottled water; as a result, in 2012 13.9 % of 379 brands were established to fail to conform to the WHO recommendations (8 μg/l). Generalized results of studies accomplished all over the world have established frequency of five target phthalates in more than three hundred samples of bottled water from 21 countries, which is 67.6 % for dibutyl phthalate (DBP), 61.7 % for DEHP, 47.1 % for diethyl phthalate (DEP), 36.9 % for BBP, and 30.1 % for dimethyl phthalate (DMP). Maximum levels of these phthalates are 222.0; 94.1; 34.2; 109.0 and 61.3 μg/l respectively [21–23].

Therefore, the composition and quality of package polymer materials have direct influence on food safety. To protect population health, a relevant task is to study quality and safety of polymer packages that contact various food products, drinking water included.

The EU Commission Regulation on plastic materials and articles intended to come into contact with food[1] stipulates special standards for DEHP, BBP, and DBP, which regulate introduction of these components into food.

In the Russian Federation, requirements to safety of package drinking water[2] and package[3] do not cover these chemicals in the stipulated lists of sanitary-hygienic indicators.

The aim of this study was to assess population health risks caused by exposure to phthalates migrating from polymer package into drinking water.

Several tasks needed to be accomplished to reach it:

♦ Hazard identification. It was necessary to identify residual quantities of phthalates (DEHP, DnBP, and DiBP) in two package materials and determine levels of their migration for polyethylene terephthalate (PET) and polycarbonate (PC) produced in the RF by six manufacturers in conformity with the CU TR 005/2011[3];

♦ Assessment of health risks (carcinogenic and non-carcinogenic ones) for people who consume bottled drinking water every day;

♦ Assessment of potential estrogenic effects of phthalates due to bottled drinking water consumption based on toxicological examinations.

Materials and methods. To identify hazards, laboratory tests were planned and accomplished relaying on the requirements of the Customs Union Technical Regulations[3] and the Instruction on sanitary-chemical study of articles made of polymers and other synthetic materials[4].

Nine samples of polymer bottles for drinking water made of PETP and PC were examined within this study; they were all produced in the Russian Federation by six different manufacturers. Of them, seven were PETP bottles of 0.6, 6 and 19 liters in volume; the remaining two were PC bottles of 19 liters in volume. The samples were taken at production facilities and were new products ready to be filled with water. Twenty-seven samples of polymers (3 for each sample bottle) were prepared to laboratory tests.

Phthalate migration was estimated by simulating a contact between a medium (drinking water) and polymer materials. Polymer samples (4 × 5 cm, square of 40 cm^2) were submerged into the model medium (distilled water, pH = 7) and put into a thermostat for 30 days under 20 °C. Isotopic labeled analogues or analyte isomers were employed as internal standards: DBP-D4 to measure DBP and DiBP; DEHP-D4 to measure DEHP. They had been added to the model medium prior to the beginning of the experiment. Upon test completion, phthalates were extracted from the model medium by liquid-liquid extraction in hexane (5 cm^3). Analyte extracts were analyzed by gas chromatography-mass spectrome-

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try (GC-MS)[5] [23, 24]. Limit of quantification equaled 0.0040; 0.0026; 0.0026 mg/dm^3 for DEHP, DnBP, and DiBP respectively. Experiment data were statistically analyzed using Microsoft Excel 2010.

To quantify phthalates in a polymer, fragments were cut out of package samples, then ground and homogenized. The analyzed samples were put into retorts; internal standards and extracting agent (methanol) were added. Analytes were extracted by using an US-field under heating. Extracts were analyzed by GC-MS in selected ion registration mode. The LOQ equaled 0.56; 1.5; 1.5 mg/kg for DEHP, DnBP, and DiBP respectively[5].

Since levels of the quantified chemicals were statistically significantly not distributed normally, medians and interquartile range (25–75 percentiles) were used to describe the results and maximum and minimum values were calculated as well. Minimum and maximum values and median were calculated for to PC bottles (4 samples).

Calculation methods. Average daily intake of phthalates with drinking water was calculated for humans in conformity with the valid Guide Human Health Risk Assessment from Environmental Chemicals[6]. Variables in the formula are set in conformity with the recommended standard values of exposure factors stipulated in the Guide. Water consumption by children younger than 18 years was identified relying on the Methodical Guidelines on Physiological Needs of various population groups[7] which stipulates 1.5–1.6 liters for boys and 1.4–1.5 liters for girls (aged 14–17 years).

Average daily intake was calculated for children younger than 6 years (body mass is 15 kg, water consumption is 1 l/day), for children aged between 6 and 18 years (body mass is 42 kg, water consumption is 1.5 l/day) and for adults (body mass is 70 kg, water consumption is 2 l/day). Exposure frequency was 350 days/year.

To comparatively analyze estrogenic potential, the estrogenicity equivalent (*EEQ*) was calculated and the results were compared with those provided in other studies [9]:

$$EEQ = \Sigma EP_i \cdot C,$$

where *EP* is an estrogenic potential of a specific phthalate identified in vitro; *C* is a level of a specific phthalate.

Estrogenic activity of 17b-estradiol (E2) is established to equal 1 [22]. In case a compound has stronger estrogenic activity than (E2), its *EP* value is above 1; in case its estrogenic activity is weaker, below 1.

Results and discussion. Residual phthalate quantities were identified in all samples of polymer package. Phthalate levels were within a wide range: DEHP, 1.7–4.2 mg/kg; DnBP, < 2.4–31.3 mg/kg; DiBP, 2.2–10.2 mg/kg. It is worth noting that DnBP was identified only in three samples out of nine. The experiment results are provided in Tables 1 and 2. Based on the experiment data, phthalate levels (medians) were distributed as follows from high to low in PET package: DiBP > DEHP > DnBP; in PC package: DEHO > DiBP > DnBP.

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Table 1

Phthalate levels in package material (PET) and model medium (distilled water)

Indicator	Research object, level	*Min*	*Max*	*Me*	Q_{25}–Q_{75}
DEHP CAS 117-81-7	Package, mg/kg	1.7	2.8	2.4	2.2–2.5
	Water, µg/l	8.6	71.0	14.5	13.0–18.8
DnBP CAS 84-74-2	Package, mg/kg	< 2.4	31.3	1.2	3.5–10.2
	Water, µg/l	< 2.6	< 2.6	< 2.6	–
DiBP CAS 84-69-5	Package, mg/kg	3.5	10.2	5.6	3.4–6.4
	Water, µg/l	< 2.6	19.2	9.3	5.6–11.0

Table 2

Phthalate levels in package material (PC) and model medium (distilled water)

Indicator	Research object, level	*Min*	*Max*	*Me*
DEHP CAS 117-81-7	Package, mg/kg	3.4	4.2	3.8
	Water, µg/l	31.5	43.5	37.5
DnBP CAS 84-74-2	Package, mg/kg	< 2.4	2.4	1.8
	Water, µg/l	4.8	6.2	4.8
DiBP CAS 84-69-5	Package, mg/kg	2.2	4.6	3.4
	Water, µg/l	17.0	54.0	18.0

Phthalates were detected in all water extracts that contacted PET. DEHP levels were within 8.6–71.0 µg/l range; DiBP, between < 2.6 and 19.2 µg/l. DnBP was not identified.

Three phthalates were identified in analyzed samples of model media that contacted PC. However, maximum levels were detected for DEHP and DiBP, respectively 31.5–43.5 µg/l; 17.0–54.0 µg/l. DnBP levels were within 4.8–6.2 µg/l range.

Migration of two phthalates, namely DEHP and DiBP, occurs from both analyzed polymer materials judging by these experimental results; it is worth noting that phthalate migration was much faster from PC than PET as evidenced by estimated total contents of phthalates.

Phthalate occurrence in a material and in water medium means it is quite possible for polymer package components to migrate from polymer package into drinking water. Therefore, it is necessary to assess potential effects on health of people who consume packaged drinking water.

Health risks were assessed based on the obtained experimental data. We calculated daily intake, chronic carcinogenic and non-carcinogenic risks caused by consuming dirking water in package made of PET and PC. The results are provided in Tables 3 and 4.

Levels of non-carcinogenic risks caused by consuming drinking water from bottles made of PET and PC are ranked as permissible for all age groups; the highest HQ values were identified for children younger than 6 years. Levels of carcinogenic risk fall within the second risk range, which means risk is permissible. Such levels do not require any activities aimed at risk mitigation and are only subject to permanent control. The highest risk levels were identified for consumption of drinking water in PC package.

Similar studies were accomplished in China with their aim to identify phthalates in packaged drinking water and to assess health risks. The highest levels were typical for such phthalates as DEHP, DnBP, and DiBP. Their levels were identified within a range from the limit of detection to 0.041 mg/l (DEHP), 0.016 mg/l (DiBP), and 0.0049 mg/l (DnBP). Assessed health risks were ranked as permissible considering their mean values [25].

The estrogenicity equivalent was calculated in order to compare likely estrogenic effects caused by consuming packaged drinking water (Table 5).

Table 3

Health risk assessment for consumption of bottled drinking water packaged in PET

CAS	Phthalate	*C*	*RfD*	*SFo*	*I* younger than 6 years	*I* aged 6–18 years	*I* adults	*HQ* younger than 6 years	*HQ* aged 6–18 years	*HQ* adults	*CR*
117-81-7	DEHP	0.0145	0.02	0.014	9.27E-04	4.97E-04	3.97E-04	4.63E-02	2.48E-02	1.99E-02	5.56E-06
84-74-2	DnBP	0.0013	0.1	-	8.31E-05	4.45E-05	3.56E-05	8.31E-04	4.45E-04	3.56E-04	-
84-69-5	DiBP	0.0093	-	-	5.95E-04	3.18E-04	2.55E-04	-	-	-	-

Table 4

Health risk assessment for consumption of bottled drinking water packaged in PC

CAS	Phthalate	*C*	*RfD*	*SFo*	*I* younger than 6 years	*I* aged 6–18 years	*I* adults	*HQ* younger than 6 years	*HQ* aged 6–18 years	*HQ* adults	*CR*
117-81-7	DEHP	0.0375	0.02	0.014	2.40E-03	1.28E-03	1.03E-03	1.20E-01	6.42E-02	5.14E-02	3.36E-05
84-74-2	DnBP	0.00475	0.1	-	3.04E-04	1.63E-04	1.30E-04	3.04E-03	1.63E-03	1.30E-03	
84-69-5	DiBP	0.018	-	-	1.15E-03	6.16E-04	4.93E-04	-	-	-	

Table 5

The estrogenicity equivalent calculation

Country	Phthalates	Rank among countries	Average level (µg/l)	Estrogenic potential	Estrogenicity equivalent
Thailand	DEHP	2	61.1	3.00E-07	0.018
	DBP		31.8	4.10E-05	1.304
	Total phthalates				1.322
Saudi Arabia	DEHP	4	6.2	3.00E-07	0.002
	DBP		3.1	4.10E-05	0.127
	Total phthalates				0.129
Mexico	DEHP	1	-	3.00E-07	-
	DBP		45.1	4.10E-05	1.849
	Total phthalates				1.849
Pakistan	DEHP	3	3.8	3.00E-07	0.001
	DBP		17.8	4.10E-05	0.730
	Total phthalates				0.731
Russian Federation (PETP)	DEHP	6	14.5	3.00E-07	4.35E-06
	DBP		1.3	4.10E-05	5.33E-05
	Total phthalates				5.77E-05
Russian Federation (PC)	DEHP	5	37.5	3.00E-07	1.13E-05
	DBP		4.8	4.10E-05	1.95E-04
	Total phthalates				2.06E-04

The lowest possible ranks of the estrogenicity equivalent in packaged drinking water (5 and 6) were calculated for the Russian Federation among all countries where similar studies were accomplished. Nevertheless, some authors report levels of phthalates in packaged drinking water that can still have adverse estrogenic effects. This calls for further systemic studies of bottled water safety related to phthalates.

Attention should also be paid to the fact that the data in our experiments were obtained for 30-day exposure under 20 °C; quality of most packaged drinking water is guaranteed for a period up to 24 months and this may require additional long-term experiments on phthalates migration.

Conclusions. The results of hazard identification allowed estimating levels of target phthalates in a limited sample of two polymer materials and their migration into drinking water.

The study established that daily intake of drinking water packaged in up-to-date polymer bottles did not created impermissible health risks due to exposure to phthalates. The highest HQ values were obtained for children younger by 6 years due to exposure to DEHP migrating from PET samples where they equaled 4.63E-02 and for PC samples where they equaled 1.20E-01. Both values corresponded to permissible risk levels. Identified carcinogenic risks reached their maximum permissible levels ($1 \cdot 10^{-4}$–$1 \cdot 10^{-6}$): they equaled 5.56E-06 for PET samples and 3.36E-05 for PC samples.

The results of this study can be used in estimating safety of new polymer packages for drinking water.

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