Research Article

Phthalates consumed from milk: safety assessment for the population

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Abstract

Phthalates, or phthalic acid ethers, are hazardous for human health as they produce negative effects on the endocrine system and liver when entering a body. Alimentary introduction into a body with food products is a priority for phthalates. Phthalates contents in milk are of particular interest since milk is the most popular food product among the population. It is vital to assess whether phthalates consumption from milk is safe for people due to their potential contents in this product and their potential hazards for human health. Research results indicate that when phthalates are introduced with milk it creates unacceptable non-carcinogenic risks for the examined children. Assessment of hazards caused by phthalates introduction allowed revealing that calculated phthalates doses were not safe as per adherence to the reference dose both for children and examined adults. The carcinogenic risk was also estimated as unacceptable both for children and adults.

Keywords: *phthalates, safety, polymer package, milk, migration.*

1. INTRODUCTION

Issues related to food product safety are becoming more and more vital every year since providing proper quality of food raw materials and food products is a basic factor that determines them not being hazardous for human health when consumed by people. Nowadays, food products can contain various contaminants, phthalates being among them.

Phthalates, or phthalic acid ethers, are oily fluids without any smell and with a yellowish tint. They are not soluble in water but are easily dissolved in organic solvents. Phthalates are inert substances and do not enter chemical reactions. Phthalates were first produced in the 1920s last century; they started to be actively used in plastic production in the 1930s to make plastic products more durable and flexible. Starting from the 2nd half of the 20th century, phthalates have been widely used in many spheres, not only as plasticizers but also as additives to many plastic products [1].

The most widely spread phthalates that are used in industry worldwide are dibutyl phthalate (DBP), benzyl butyl phthalate (BBP), di-2-ethyl hexyl phthalate (DEHP), diisononyl phthalate (DINP), diisodecyl phthalate (DIDP), di-octyl phthalate (DOP), and diethyl phthalate (DEP). DBP, BBP, and DEHP are the most hazardous [2]. According to REACH (Registration, Evaluation, Authorization and Restriction of Chemical substances) classification that is valid within the European Union legislation, these phthalates are considered to be short-chained and

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are the most hazardous for human health [2] as they produce negative effects on the endocrine system and liver when entering a body.

Phthalates are compounds that have weak bonds with a matrix. Their migration into the environment is observed both due to impacts exerted by external physical factors and without such impacts. Phthalates can enter a human body from plastic bags, swimming accessories, clothing, toys, and personal hygiene items and they can be found in the air inside rooms with plastic windows and floors made of polymer materials [3]. However, a priority way for phthalates to enter a body is an alimentary introduction [3] when they enter a body with food products.

Several researched works focus on phthalates migration. Thus, it was established that plasticizers migrated into food products from the ink used to print data on a package (research objects were snacks). DBP, DEHP, as well as dicyclohexyl phthalate (DCHP) were detected in examined food products in concentrations up to 18.6 mg/kg [4]. Packaging films are another source of phthalates introduction into food products. At present several films made of various materials are used in packaging including polyvinyl chloride (PVC), polyethylene (PE), polyvinylidene chloride (PVDC), reduced cellulose (RCF), cellulose acetate, etc. All the said materials contain various plasticizers to a certain extent, DEHP included [4]. The authors note that phthalates migrate into the environment, including food products, due to their weak bonds with polymer matrixes.

In the EU countries, it is prohibited to use phthalates (DEHP in particular) in the food industry to make caps or lids, but they can be used to make polymer package for food products provided that this package does not enter any contacts with fatty foods [5]. There are no legal restrictions in Russia imposed on the use of phthalates in package manufacturing.

When studying plasticizers migration into various model media, experts established that on the 10th day of exposure phthalates contents that migrated from food package reached 16.3 mg/kg for distilled water; 12.5 mg/kg for 3% acetate solution [6-7]. A lot of studies on assessing phthalates migration have been accomplished on model media. According to the Council Directive 85/572/EEC issued in 1985 and still valid at present, model media should be distilled water for milk and 3% acetic acid solution for milk products [8]. When studying phthalates migration from polymer packages into model media, experts established that polymer film made of low-density polyethylene "excreted" DBP into a model medium in a quantity equal to 30 ± 8 ng/L. Combined Tetrapak package "excreted" DMP into a model medium in a quantity equal to 12 ± 5 ng/L as well as DBP (40 ± 15 ng/L) [7].

Phthalates contents in milk are of particular interest since milk is the most popular product among the population. Thus, in the Vietnam Socialist Republic, milk consumption grew from 1,027.9 million liters in 2015 to 1,305.6 million liters in 2019 [9]. In the Russian Federation approximately 65% of men and 75% of women aged 14 and older as well as approximately 80% of children aged 3 - 13 consume milk and milk products daily or several times a week. Milk consumption (including butter) amounted to 305.4 kg on average per year for men and to 276.5 kg for women [10].

Krejčíková et al. established that plasticizers (and phthalates in particular) introduction into milk can occur at various stages in milk production starting from hand milking (provided that workers wear gloves) or with a milking machine with its parts made of polymer materials. Their concentration depends on milking type (by hand or with a machine). It was established that DBP and DEHP contents as well as their sum was two times lower in case milking was done by hand than with a machine [11].

In the Russian Federation, maximum permissible migration level (SML) for phthalates is fixed in the Customs Union Technical Regulations (CU TR) 005/2011 “On package safety”. According to the document, SML from food package into a food product is fixed only for dioctyl phthalate and is equal to 2 mg/L [12]. And there has been no research establishing that this migration level provides safety for human health when phthalates enter a body with food products.

The literature analysis performed here allowed revealing that phthalates could occur in food products including milk as the most widely spread food product which, when being manufactured, often enters contact with polymer materials; it was also established that phthalates were hazardous when entering a human body with food products. Given that, it is vital to assess safety of phthalates introduction into a body with milk since they potentially can enter milk products and create threats for human health.

2. MATERIALS AND METHODS

2.1. Research objects

Our research objects were phthalates contained in liquid milk that was packed in polymer package as well as health risks for people caused by their introduction into a body.

2.2. Methods

Phthalates contents in milk were determined according to the methodical guidelines developed in the RF MG 4.1.3160-14 “Measuring mass concentrations of phthalates (dimethyl phthalate, diethyl phthalate, dibutyl phthalate, benzyl butyl phthalate, and di-(2-ethylhexyl)-phthalate) in milk with high performance liquid chromatography”. Determination of phthalate concentrations in milk samples was carried out by high performance liquid chromatography with a UV detector on a column with a reversed phase in a gradient elution mode. The extraction of phthalates from milk was carried out by liquid extraction with a mixture of organic solvents: methanol, hexane, and isopropanol in a ratio of 1.5 : 2 : 0.1. The extraction efficiency was 61 - 110%. The lower limit of detection of phthalates in milk was 0.1 mg/L, the measurement error was 31%. An important point in the analysis of phthalates was the quantitative assessment of the "background concentrations" of the analyzed compounds, without taking into account which you can get false-positive results. "Background concentration" was formed due to contamination of glassware, organic solvents, and laboratory air. The background concentration of phthalates was experimentally established, which was zero for DMP, DEP, and BBP, 0.09 mg/L for DBP, and 0.03 mg/L for DEHP. To take into account the "background concentration" when making measurements of phthalates in milk, a blank analysis was performed for each batch of milk samples. The obtained values were used in calculating the concentration of phthalates in milk [13]. 25 samples of milk contained phthalates were investigated. Five phthalates were determined in total: DMP, DBP, BBP, DEHP, and DEP. The concentrations of determined phthalates are listed in Table 1.

Table 1. *Concentrations of phthalates determined in milk, mg/L*

No.	*Type of packing*	*DMP*	*DEP*	*DBP*	*BBP*	*DEHP*
1	***PE**-film***	0.1 (LOD*)	0.1 (LOD)	0.2 (LOD)	0.2 (LOD)	0.2 (LOD)
2	***PE-film***	0.1 (LOD)	0.1 (LOD)	0.2 (LOD)	0.2 (LOD)	0.2 (LOD)
3	***PE-film***	0.1 (LOD)	0.1 (LOD)	0.2 (LOD)	0.2 (LOD)	1.16
4	***PE-film***	0.1 (LOD)	0.1 (LOD)	0.2 (LOD)	0.2 (LOD)	0.2 (LOD)
5	***PE-film***	0.1 (LOD)	0.1 (LOD)	0.2 (LOD)	0.2 (LOD)	0.2 (LOD)
6	***PE-film***	0.1 (LOD)	0.1 (LOD)	0.2 (LOD)	0,2 (LOD)	3.57
7	***PE-film***	0.1 (LOD)	0.1 (LOD)	0.2 (LOD)	0.2 (LOD)	3.35
8	***PE-film***	0.1 (LOD)	0.1 (LOD)	0.2 (LOD)	0.2 (LOD)	3.43
9	***PE-film***	0.1 (LOD)	0.1 (LOD)	0.2 (LOD)	0.2 (LOD)	3.71
10	***PE-film***	0.1 (LOD)	0.25	0.2 (LOD)	0.2 (LOD)	1.29
11	***PE-film***	0.16	0.232	0.2 (LOD)	0.2 (LOD)	0.2 (LOD)
12	***PE-film***	0.1 (LOD)	0.1 (LOD)	0.55	0.2 (LOD)	0.2 (LOD)
13	***PE-film***	0.1 (LOD)	0.1 (LOD)	0.86	0.072	0.83
14	***PE-film***	0.1 (LOD)	0.1 (LOD)	0.2 (LOD)	0.2 (LOD)	0.2 (LOD)
15	***PE-film***	0.1 (LOD)	0.1 (LOD)	1.06	0.2 (LOD)	1.37
16	***PE-film***	0.1 (LOD)	0.1 (LOD)	1.43	0.2 (LOD)	1.32
17	***PE-film***	0.1 (LOD)	0.036	1.69	0.2 (LOD)	1.58
18	***PE-film***	0.1 (LOD)	0.1 (LOD)	29.81	0.2 (LOD)	8.18
19	***PE-film***	0.1 (LOD)	0.1 (LOD)	22.32	0.2 (LOD)	12.54
20	***PET***-bottle***	0.15	0.783	2.84	0.2 (LOD)	1.58
21	***PET-bottle***	0.1 (LOD)	0.1 (LOD)	0.2 (LOD)	0.2 (LOD)	0.2 (LOD)
22	***PET-bottle***	0.1 (LOD)	0.1 (LOD)	0.2 (LOD)	0.2 (LOD)	0.2 (LOD)
23	***PET-bottle***	0.1 (LOD)	0.1 (LOD)	0.2 (LOD)	0.2 (LOD)	0.2 (LOD)
24	***PET-bottle***	0.1 (LOD)	0.1 (LOD)	0.2 (LOD)	0.2 (LOD)	2.71
25	***PET-bottle***	0.1 (LOD)	0.1 (LOD)	0.2 (LOD)	0.2 (LOD)	3.35

*LOD - limit of detection

**PE - polyethylene

***PET - polyethylene terephthalate

According to Table 1, the most spread phthalate in milk packed in polyethylene film is DEHP which was determined in 60% of samples. At the same time, the maximum concentration is set for DBP (29.81 mg/L). In this research, we used data of maximal phthalates' concentrations to calculate doses for further risk assessment. Safety assessment involved assessing population health risks according to the methodical guidelines MG 2.1.10.0062-12 "Quantitative assessment of non-carcinogenic risks caused by exposure to chemicals based on building up evolution models" [14].

Health risk assessment was accomplished in four stages:

+ At the hazard identification stages, we assessed the completeness and authenticity of available data on hazards crated by phthalates under oral introduction.

+ At the stage that involved analyzing "dose-response" dependence, we considered a possibility that an adverse effect might occur due to exposure to phthalates that entered a body. Besides, we determined reference doses and critical organs and systems under the oral introduction of phthalates with milk products; it was done using data from relevant sources (ATSDR toxicological profiles).

+ Exposure assessment included calculating milk consumption volumes and phthalate doses introduced with milk as per the following formula (1):

$$I = (A \times m)/BW \qquad (1)$$

where:

I is an introduced dose (a chemical quantity at exchange boundary), mg/kg of a body mass per day;

A is chemical concentration in milk, mg/L of a product;

m is milk consumption per day, L;

BW is body weight, kg.

+ Risk characteristics included calculating hazard quotients (HQ) and were performed according to [15]. Besides, we assessed whether phthalates doses introduced with milk were higher than previously fixed reference doses and treated the results as safety criteria for assessing whether phthalates introduction into a body was safe for health.

Hazard quotient being equal to 1 or lower was considered to be the acceptable risk level. Safety criterion for phthalates introduction was adherence to reference doses. Should a substance be carcinogenic, it is necessary to assess carcinogenic risks as per the following formula (2):

$$CR = (Vcons \times Cpr)/BW \times SFo \qquad (2)$$

where:

CR is carcinogenic risk;

V_{cons} is average daily consumption of a product, kg;

C_{pr} is substance concentration in a product, mg/kg of a product;

BW is body weight, kg;

SF is slope factor.

Carcinogenic risk equal to 0.0001 (one case of a cancer per 10,000 people) was considered acceptable.

Health risks associated with phthalates introduction into a body were assessed both for children and adults. Reference doses published in relevant sources were used as risk assessment criteria; when hazards were assessed, we took reference phthalates concentrations established via our research as hazard assessment criteria. Children aged 4 - 17 took part in our research;

overall, we examined 49 children aged 4 - 17 and 49 adults aged 18 - 70. The children and the adults selected for this investigation were the patients of preventive treatment in the hospital of Federal Scientific Center for Medical and Preventive Health Risk Management Technologies.

We applied a questionnaire to establish a share of the population who consumed milk as well as daily milk consumption. To assess health risks, we took data on maximum daily milk consumption and then calculated chemical doses and characterized health risks. This approach could result in risk overestimation but at the same time, it allowed performing the most comprehensive assessment.

3. RESULTS AND DISCUSSION

The results are presented according to the guidelines from one stage to others.

The hazard identification stage is theoretical and dedicated to detailed literature analysis of phthalates' hazard and critical points. At this stage, we established that phthalates produced several toxic effects on a body. Their influence on the endocrine system and liver is well known as well as certain phthalates being able to produce carcinogenic effects. Besides, there are data on impacts exerted by these substances on lipid metabolism as well as on insulin resistance occurrence and type II pancreatic diabetes among elderly people [16-17]. There is an authentic correlation between phthalates concentration in urine and attention deficit hyperactive disorder in children aged 6 - 15 [18].

Basic effects detected in experiments in animals were produced on the endocrine system and liver [19-21]. There is a hypothesis regarding the effects produced by phthalates on the liver. It states that effects produced by phthalates are related to interaction with receptors activated by the Peroxisome proliferator (PPAR). To assess the interaction between phthalates and various types of these receptors, relevant studies were accomplished. They revealed that phthalates interacted with three different PPAR isoforms (α, β, or γ) and were able to damage anti-oxidant protection, including that of the liver [22-23].

There are data on the effects produced by phthalates on the endocrine system in adults [24-26]. A study on children performed in Denmark revealed that phthalates metabolites concentrations in urine were related to the thyroid gland functioning, insulin-like growth factor I (IGF-I), and growth parameters. Phthalate metabolites in girls were negatively related to free and overall T_3 levels in blood serum whereas DEHP and di-iso-nonyl phthalate (DINP) metabolites were negatively related to IGF-I in boys [27].

When describing "dose-response" dependence, we established reference doses as well as basic critical organs and systems under oral phthalates introduction. Thus, according to toxicological profiles developed by IRIS EPA, basic critical organs under chronic oral introduction are the liver and endocrine system (BBP, reference dose is equal to 0.2 mg/kg of body weight; DEHP, reference dose is equal to 0.02 mg/kg of body weight), as well as kidneys (DBP, reference dose is equal to 0.1 mg/kg of body weight; DMP, reference dose is equal to 10 mg/kg of body weight), and overall systemic effects (produced on body weight) (DEP, reference dose is equal to 0.8 mg/kg of body weight) [28-32]. We should note that reference doses were established when contaminants were introduced with water and they can be used as reference ones in risk assessment consequently.

We should also note that according to IARC classification DEHP belongs to the 2B category as per carcinogenic properties, that is, it can be a carcinogen for people [33]. Carcinogenic potential factor under oral exposure (SFo) is equal to 0.14 for the substance.

European Food Safety Authority (EFSA) expert panel established NOAEL for BBP in experiments on rats and LOAEL for phthalates as well; they were equal to 20 mg/kg of body weight and 100 mg/kg of body weight per day accordingly [34]. But still, no modifying factor was taken into account when LOAEL and NOAEL were established.

Research performed at the Federal Scientific Center for Medical and Preventive Health Risk Management Technologies allowed establishing a reference dose that was equal to 0.001 mg/kg per day (1×10^{-3} mg/kg per day) for a sum of phthalates; 0.0002 mg/kg per day (2×10^{-4} mg/kg per day) for DMP and DEP; 0.0004 mg/kg per day (4×10^{-4} mg/kg per day) for DBP and DEHP. An increase in malonic dialdehyde in blood plasma was considered a limiting parameter in establishing a reference dose. When developing reference levels, we used modifying factors that took into account the fact that the study was performed on an overall population without selecting the most sensitive groups (the factor was equal to 2), and a factor that took into account intraspecific sensitivity (equal to 1); a factor that took into account transition from high doses to low ones (equal to 1).

At the exposure assessment stage, we established that five phthalates were detected in milk that was sold on the Russian market; they were dibutyl phthalate (DBP), dimethyl phthalate (DMP), diethyl phthalate (DEP), di-2-ethyl hexyl phthalate (DEHP), and butyl benzyl phthalate (BBP). We detected that 58% of samples of milk that were packed in polyethylene film and 40% of milk bottled samples in PET bottles contained phthalates. DEHP makes the greatest contribution to total phthalates concentration in milk packed in polyethylene film (70%); DBP, for milk bottled in PET bottles (65%).

At this stage, we determined maximum phthalates doses introduced with milk for each population group. When calculating doses, we took body weight into account. We established that 75% of children aged 4 - 6 years consumed milk. Their parents bought only milk packed in polyethylene film. The daily consumption was ranged from 0 to 0.2 L/day. 80% of children aged 7 - 17 consumed milk. Their parents bought milk packed in polyethylene film (68%), PET bottles (16%), or both (16%). The daily consumption was ranged from 0.1 to 0.3 L/day. 57% examined adults consumed milk, they all bought and consumed milk packed in polyethylene film. The daily consumption was ranged from 0.1 to 0.6 L/day. In this research, we used data of maximal daily milk consumption to calculate and characterize risk (Table 2).

At the risk characterization stage, we established that hazard quotient (HQ) was acceptable for children 4 - 6 years old for all compounds except DEHP (0.0002 for DMP, 0.3 for DBP, 0.005 for BBP). At the same time, HQ was unacceptable for DEHP consumed with milk contained phthalates (HQ = 2.5) (Table 3). Taking into account that risk is going to be acceptable if HQ ≤ 1, we may conclude that the consumption of DEHP with milk among children 4 - 6 years old is going to be a risk factor of liver and endocrine diseases.

Table 2. *Maximum phthalates doses introduced into a body with packed in polymer package for different age groups (mg/kg of body weight per day)*

Age group	*Maximum daily milk consumption, L/day*	*Compound*	*Package type*	*Dose, mg/kg/day*
Children aged 4 - 6	0.2	DMP	PE-film	2.44×10^{-3}
		DBP		2.55×10^{-2}
		BBP		1.06×10^{-3}
		DEHP		5.61×10^{-2}
		DEP		3.78×10^{-3}
Children aged 7 - 17	0.3	DMP	PE-film	1.43×10^{-3}
		DBP		1.49×10^{-2}
		BBP		6.21×10^{-4}
		DEHP		3.29×10^{-2}
		DEP		2.22×10^{-3}
		DMP	PET-bottle	0
		DBP		1.50×10^{-1}
		BBP		0
		DEHP		6.32×10^{-2}
		DEP		0
Adults	0.6	DMP	PET-bottle	1.82×10^{-3}
		DBP		2.83×10^{-3}
		BBP		1.19×10^{-2}
		DEHP		8.15×10^{-4}
		DEP		4.2×10^{-2}

Table 3. *Risk assessment results for consumption of milk packed in polymer packaged, children aged 4 - 6*

Compound	*Hazard quotient (HQ)*
DMP	0.0002
DBP	0.3
BBP	0.005
DEHP	2.5*
DEP	0.005

Note: *means risk is unacceptable

As for reference dose determined in the research of the Federal Scientific Center for Medical and Preventive Health Risk Management Technologies, it was established that doses of phthalates consumed with milk among children 4 - 6 years old were higher than reference ones: the consumed dose of DMP was ten times higher; the consumed dose of DEP was 20 times higher; the consumed dose of DBP was 75 times higher; the consumed dose of DEHP was 125 times higher (Table 4). Taking into account that risk is going to be acceptable if there's no excess of reference dose, we may conclude that the consumption of phthalates with milk among children 4 - 6 years old is going to be a risk factor of target organs and systems' diseases.

Table 4. *Assessment of hazards caused by consumption of milk packed in polymer package, taking into account phthalates reference doses, children aged 4 - 6*

Compound	Exceeding the reference dose, times
DMP	10
DBP	75
DEHP	125
DEP	20

During the risk assessment among children 7 - 17 years old it was determined that HQ was acceptable for DMP (HQ = 0.0001 for PE-film and no consumption from PET-bottle), DBP for PE-film (HQ = 0.1), BBP (HQ = 0.003 for PE-film and no consumption from PET-bottle), and DEP (HQ = 0.03 for PE-film and no consumption from PET-bottle). At the same time there was an unacceptable risk calculated for children 7 - 17 years old caused by consuming DEHP with milk packed in polyethylene film (HQ = 1.5), and caused by consuming DBP and DEHP with milk packed in PET-bottles (HQ = 2 and HQ = 3 respectively) (Table 5). Taking into account that risk is going to be acceptable if HQ ≤ 1, we may conclude that the consumption of DEHP with milk packed both in PE-film and PET-bottle as well as the consumption of DBP with milk packed in PET-bottle among children 7 - 17 years old is going to be a risk factor of liver and endocrine diseases (DEHP), and diseases of kidneys (DBP).

Table 5. *Risk assessment results for consumption of milk packed in polymer packaged, children aged 7 - 17*

Compound	Hazard quotient (HQ)	
	PE-film	PET-bottle
DMP	0.0001	0
DBP	0.1	2*
BBP	0.003	0
DEHP	1.5*	3*
DEP	0.03	0

Note: *means risk is unacceptable

As for reference dose determined in the research of the Federal Scientific Center for Medical and Preventive Health Risk Management Technologies, it was established that doses of consumed phthalates were higher than the reference ones: the consumed dose of DMP was five times higher; the consumed dose of DEP was 100 times higher; the consumed dose of DBP was 25 times higher for PE-film as well as 500 times higher for PET-bottle; the consumed dose of DEHP was 75 times higher for PE-film as well as 150 times higher for PET-bottle (Table 6). Taking into account that the risk is going to be acceptable if there's no excess of reference dose, we may conclude that the consumption of phthalates with milk among children 7 - 17 years old is going to be a risk factor of target organs and systems' diseases.

Table 6. *Assessment of hazards caused by consumption of milk packed in polymer package, taking into account phthalates reference doses, children aged 7-17*

Compound	***Exceeding the reference dose, times***	
	PE-film	***PET-bottle***
DMP	**5**	**0**
DBP	25	500
DEHP	75	150
DEP	100	0

During the risk assessment among adults were determined that the hazard quotient was acceptable for all determined phthalates (0.0002 for DMP; 0.03 for DBP; 0.04 for DEHP, and 0.05 for both BBP and DEP) (Table 7). Taking into account that risk is going to be acceptable if HQ ≤ 1, we may conclude that the consumption of milk containing phthalates among adults has no risks associated with these compounds.

Table 7. *Risk assessment results for consumption of milk packed in polymer package, adults*

Compound	***Hazard quotient (HQ)***
DMP	0.0002
DBP	0.03
BBP	0.05
DEHP	0.04
DEP	0.05

As for reference dose determined in the research of the Federal Scientific Center for Medical and Preventive Health Risk Management Technologies, it was established that calculated doses of consumed phthalates were from 2 (DEHP) to 200 (DEP) times higher than the reference ones: the consumed dose of DMP was ten times higher; the consumed dose of DEP was 200 times higher; the consumed dose of DBP was 7.5 times higher; the consumed dose of DEHP was two times higher (Table 8). Taking into account that risk is going to be acceptable if there's no excess of reference dose, we may conclude that the consumption of phthalates with milk among adults is going to be a risk factor of target organs and systems' diseases.

Table 8. *Assessment of hazards caused by consumption of milk packed in polymer package, taking into account phthalates reference doses, adults*

Compound	***Higher than a reference dose, times***
DMP	10
DBP	7.5
DEHP	2
DEP	200

Taking into account that DEHP is a carcinogenic compound we calculated carcinogenic risk (CR) for investigated groups. Criterium of acceptable carcinogenic risk is 0.0001 i.e. One new case of cancer per 10,000 people. We revealed that in case of maximal calculated doses of phthalates consumed with milk carcinogenic risk was unacceptable: CR for children 4 - 6 years old was 0.06 (600 new cases per 10,000 people); CR for children 7 - 17 years old consumed milk from PE-film was 0.1 (1.000 cases per 10,000 people) as well as 0.006 (60 new cases per 10,000 people) for children consuming milk from PET-bottle; CR for adults was 0.04 (400 new cases per 10,000 people) (Table 9).

Table 9. *Carcinogenic risk assessment for diethyl hexyl phthalate (DEHP) introduction with milk packed in polymer package*

Age group	***Package type***	***Carcinogenic risk (CR)***
Children aged 4 - 6	PE-film	0.06
Children aged 7 - 17	PE-film	0.1
	PET-bottle	0.006
Adults	PE-film	0.04

4. CONCLUSION

Risk characterization revealed that hazard quotients related to phthalate introduction exceeded permissible levels for children who consumed milk (up to 2.5 times among children aged 4 - 6, and up to three times for children aged 7 - 17) and it indicates that health risk is unacceptable. At the same time, hazard quotients established for adults did not exceed acceptable levels. Having assessed hazards related to phthalates consumption, we established that calculated phthalates doses did not provide safety as per criterion of adherence to a reference dose. Established doses were up to 125 times higher than reference ones for children aged 4 - 6; up to 500 times higher for children aged 7 - 17; and up to 200 times higher for adults. The calculated carcinogenic risk was unacceptable for all examined age groups (up to 0.1 against the acceptable level equal to 0.0001). Therefore, health risk related to negative effects on the liver and endocrine system is assessed as unacceptable for DMP, DBP, DEHP, and DEP under a scenario that involves phthalates introduction with milk in maximum doses. Besides, there is a hazard of negative effects occur in the liver and endocrine system. To avoid risk over-assessment, it is necessary to specify exposure to phthalates at risk and hazard assessment stage as well as to recommend developing maximum permissible doses as per risk criteria basing on established reference ones.

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Phthalate trong sữa: đánh giá an toàn cho người sử dụng

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Tóm tắt

Các phthalate, hay phthalic acid ether, có nguy cơ gây ảnh hưởng xấu đến sức khỏe người sử dụng do tác động đến hệ nội tiết và gan. Thực phẩm là nguồn phơi nhiễm phthalate chủ yếu đối với con người. Hàm lượng phthalate trong sữa được quan tâm đặc biệt vì sữa là loại thực phẩm phổ biến nhất trong chế độ ăn. Do đó, việc đánh giá phơi nhiễm phthalate từ sữa đối với sức khỏe con người là cần thiết. Kết quả cho thấy, hàm lượng phthlate trong sữa tạo ra rủi ro không thể chấp nhận được đối với nguy cơ không gây ung thư ở trẻ em trong nghiên cứu này. Liều phthalate phơi nhiễm tính được lớn hơn so với liều tham chiếu cho cả trẻ em và người lớn. Nguy cơ gây ung thư cũng được ước tính là không thể chấp nhận được đối với cả trẻ em và người lớn.

***Từ khóa*:** *phthalates, safety, polymer package, milk, migration.*

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