Original Article

Release of Phthalate Esters in Pasteurized Milk Samples with Plastic Packaging

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Abstract

Aim: In this study, the presence of four phthalate esters, including diethyl phthalate (DEP), Dibutyl phthalate, benzyl butyl phthalate (BBP), and diethylhexyl phthalate (DEHP) in pasteurized milk with plastic packages was investigated during the time allowed for consumption. **Materials and Methods:** The pasteurized milk samples, including 7 high-consumed brands, were purchased from reputable stores and two factories in Isfahan in 2019. The concentration of phthalate esters was measured by gas chromatography-mass spectroscopy paired with dispersive liquid-liquid microextraction. **Results:** According to the results of this study, among the analyzed samples of stores, DEHP (0.25 µg/l) and BBP (0.25 µg/l) had the highest mean concentrations in pasteurized milk, respectively. The analyzed results of the factories showed a high BBP of 0.1 µg/l. Among the studied brands, the highest concentration of phthalate esters was 0.42 µg/l. The mean concentrations obtained in this study were lower than the international standards set. **Conclusion:** Due to the low average concentration of phthalate esters in pasteurized milk, consumption of these products has no serious risk for humans and the share of pasteurized milk in terms of the presence of phthalate esters is negligible.

Keywords: Gas chromatography-mass spectroscopy, pasteurized milk, phthalate ester, plastic packaging

Introduction

A group of chemicals polluting the environment, which are caused by industrial activity, are a group of phthalic acid esters (PAEs). These compounds are important environmental pollutants that have been used as plasticizers since 1930 and account for about 80% of plasticizers.[1,2] The annual production of PAEs in the world is approximately 4.0 million ton per year.[3] Global consumption of PAEs in the plastics industry is estimated at more than 18 billion pounds each year.[4,5] PAEs include dimethyl phthalate (DMP), diethyl phthalate (DEP), di-n-butyl phthalate (DnBP), benzyl butyl phthalate (BBP), di (2-ethyl hexyl) phthalate (DEHP), and diisononyl phthalate.[6] PAEs are mainly used as emollients and additives in many daily life products such as plastic coatings, food packaging, cosmetics, children's toys, medical equipment, and detergents to increase flexibility.[4,7-9] PAEs are used as additives for polymers in plastics, especially in polyvinyl chloride (PVC) and polyethylene terephthalate (PET).[10] Due to the great progress in the plastics industry, PET polymer coating is used today for food packaging, especially beverages. These materials are widely used due to the nonpenetration of gas and other environmental factors into the packaging, good mechanical strength, good transparency, easy transportation, and reasonable price.[11-14] PVC is also one of the most widely used polymers because it is easy to prepare.[15,16] Due to the wide range of applications and the ability of PAEs to leak from products even after construction, they can be easily found in different environments of water, air, and soil. Human exposure to phthalates occurs in a variety of ways, the most common of which is ingestion. PAEs do not have

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any chemical bonds with the plastics or products used in them and can easily be released into plastic materials and reach food and beverages.[8,17-19]

Prolonged exposure to phthalate esters threatens everyone, especially at-risk groups such as children, pregnant women, and the elderly. These compounds cause damage to the liver, kidneys, abnormalities, and even carcinogenicity in humans. According to researches, phthalates bind to hormonal receptors in the body and cause changes in the structure and function of testicular cells, decreased motility and sperm count in males, changes in the levels of steroid hormones in females, premature puberty, premature birth, and abortion.[17,18,20,21]

The main concern of exposure to PAEs in humans and other organisms is the effect of these compounds on the reproductive system. The presence of these compounds in values greater than the standard value will have, directly and indirectly, a negative impact on human health and other living organisms[10,18] The US Environmental Protection Agency and the European Union (EU) classify PAEs in the list of priority pollutants.[22,23]

Dairy products, especially milk, have a very high nutritional value for infants and the elderly. Since milk contains fats, carbohydrates, proteins, vitamins, and minerals, it has a more complex matrix than other samples of liquid foods.[24-26] Phthalates are lipophilic compounds that have a high potential for the accumulation in fatty foods, and due to the relatively high-fat content of dairy products, they are more likely to contain phthalates than low-fat foods.[24,26-28] Milk contamination with phthalates occurs through a number of different ways, as follows: phthalates that are directly absorbed by the animal from the environment (water, food); substances that are transferred from tankers and storages to milk samples during the process of mechanical milking, and the substances that are transported by various types of plastic packaging and containers. Therefore, monitoring phthalates in milk is very important.[25,26] Ge *et al*. evaluated the phthalates in sheep's milk that were used to prepare dairy products for infants and their results showed that milk products were the main exposure source of the infant to phthalates.[29] Fierens *et al*. studied the transfer of phthalates by the milk chain from farm level to industry. In this study, in addition to the transfer of phthalates in the industry through packaging to dairy products and milk, it was also transferred in farm levels through the food chain.[24] Lin conducted a study on different packages of milk to determine their phthalates, according to which the amount of phthalates in packaged milk samples in glass and metal containers was much lower than in plastic containers.[30] In Iran, Hosseini *et al*. and Rahimi *et al*. conducted the studies for measuring the migration rate of phthalates in rose water and lemon juice, respectively; they confirmed the same results and recommended the use of glass or steel containers for food packaging.[31,32] Ebrahimi *et al*. conducted a study on the migration of phthalates in bottled water and reported the presence of phthalates in water bottles and their adverse effect on human health.[33] In a study by Kouhpayeh *et al*., the phthalate esters in doogh also showed that in all doogh samples, the highest concentration was related to DEHP.[13]

Due to the high use of phthalate esters in the plastics industry, the possibility of their migration from plastic packaging to food and the general concern about the contamination of dairy products, especially milk, with phthalate esters, the aim of this study was to investigate the release of four phthalate esters, including DEP, DBP, BBP, and DEHP during the allowable consumption time for evaluating the presence of the desired compounds in pasteurized milk with plastic packaging during production to consumption in one of the cities of Iran.

Materials and Methods

Material

Standards of four types of phthalates, including BBP, DEP, dibutyl phthalate (DBP), and diethylhexyl phthalate (DEHP) were purchased from Sigma Aldrich. Acetonitrile, carbon tetrachloride, methanol, and trichloroacetic acid with analytical purity were prepared from Merck.

Preparation of samples

Using a checklist prepared in person by 20 vendors in reputable stores in Isfahan, the best-selling brand of milk was determined by the type of milk packaging (plastic bottle and nylon bag) and the types available, in terms of fat content (low-fat and high-fat); based on this, 7 high consumed brands that were available continuously in all seasons were finally selected and on the last day of the expiration date, they were collected from the stores available in the city and the two factories located in the city. According to the ethical issues, brands were coded with codes A, B, C, D, E, F, and G, as observed in Table 1. Furthermore, the factory samples that were collected after final processing and before packaging were labeled with K code. Two codes 1 and 2 were used to determine the type of plastic bottle and nylon bag packaging. Moreover, two codes, X and Y, were utilized to determine low-fat and high-fat milk. The selected brands were 63 samples with a total of three repetitions.

Table 1: Coding and the number of samples

Sampling location	Brand	Sample number	Number of repetitions	Total
Store	A	4	3	12
	B	3	3	9
	C	3	3	9
	D	2	3	6
	E	2	3	6
	F	1	3	3
	G	1	3	3
Factory	A.K	4	3	12
	G.K	1	3	3
Sum total				63

Test method

To synthesize the samples, stock solutions of four phthalates, i.e., DEP, DBP, BBP, and DEHP with a concentration of 1000 mg/L were prepared using their standard sample, and the necessary concentrations were prepared using this solution to draw the calibration curve.

In this study, the dispersive liquid-liquid microextraction method was used for milk samples.[34] First, 20 ml of milk sample was added to a 50 ml glass vial. Then, 0.2 g of trichloroacetic acid was added to each of the tested milk samples, and Vortex was performed for 60 s and then placed in an incubator for 1 h. The sample was centrifuged for 5 min, and 5 cc of its upper phase was passed through a 0.24 µm syringe filter and poured into a secondary glass falcon.

Then, in a vial, 500 µl of acetonitrile (as a disperser solvent) and 50 µl of carbon tetrachloride (as an extractor solvent) were first mixed. After that, the total volume of the solution obtained was injected into the sample by a Hamilton syringe 1000 µl. The solution was centrifuged at 4000 rpm for 5 min until a cloudy phase formed at the end of the glass falcon. Finally, 2 µl of the final phase formed for the analysis were injected into the chromatographic gas device (model GC Agilent 7890 and Mass 5975, made in the United States) under the device conditions, according to Table 2. Figure 1 shows the chromatograms of phthalate esters in the standard and milk samples.

Statistical analysis

In the present study, the data were reported as mean (standard deviation). Data analysis was performed using independent *t*-tests and analysis of variance. SPSS software (version 22, SPSS Inc., Chicago, IL, USA), was used to analyze the data.

Results

Sixteen samples of packaged pasteurized milk were collected from stores and PAEs were measured using the gas chromatography-mass spectroscopy device. The results are shown in Table 3.

In addition to the stores, a part of the milk samples was collected from two factories after final processing and before packaging. The results of the mean concentrations of phthalate esters in pasteurized milk taken from the factories are shown in Table 4. In addition, 7 high-consumed brands of milk were examined in this study [Figure 2], which the highest concentration of phthalate esters was related to brand D at 0.42 µg/l.

Discussion

According to Table 3, the highest mean concentrations of phthalate esters, i.e., DEP, DBP, DEHP, and BBP in 16 samples collected from stores were 0.05 µg/l, 0.06 µg/l, 0.25 µg/l, and 0.25 µg/l, respectively. Among the mean concentrations obtained, the maximum value was related to DEHP and BBP. Among the analyzed samples, the D1y brand, which is a full-fat milk sample, had the highest total phthalate esters (0.59 µg/l). The predominance of DEHP among other phthalate ester isomers has also been demonstrated in other studies due to its widespread use in a variety of products, and the allocation of 35% of the total global production of phthalates has been proven in previous studies.[18] Based on the results of evaluating the exposure of toxic effects of

Table 2: Gas chromatography/mass spectrometry device condition for the analysis of the samples

Parameter	Value
Injector temperature	280°C
Mode split	5:1
Dimension columns DB5	30 m × 250 µm × 0.25 µm
Columns flow (He)	0.5 ml/min
Oven temperature	100°C hold for 5 min, 15°C/min to 280°C
Maximum oven temperature	280°C hold for 7 min
Run time	24 min
Thermal aux	300°C
Solvent delay	13 min

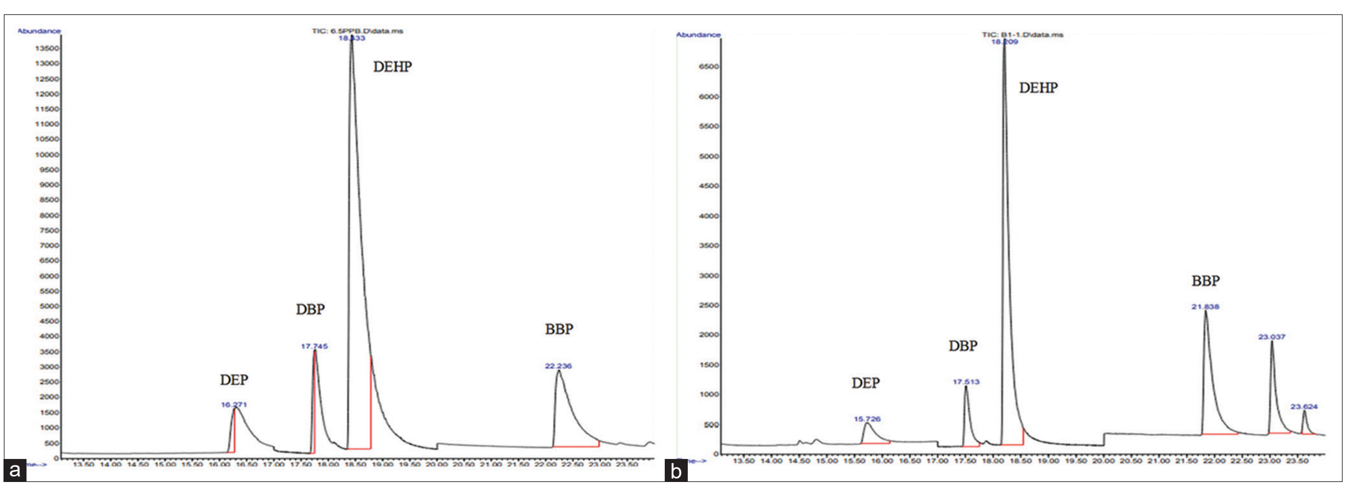

Figure 1: Chromatograms of phthalate esters in standard (a) and milk samples (b)

Table 3: Mean concentration of phthalate esters in pasteurized milk with plastic packaging (store) (µg/l)

Sample milk	DEP	DBP	DEHP	BBP	ΣPAEs
A_1x	0.02±0.006	0.03±0.014	0.09±0.085	0.09±0.033	0.23
A_1y	0.02±0.003	0.02±0.011	0.06±0.043	0.05±0.031	0.15
A_2x	0.02±0.004	0.02±0.007	0.07±0.046	0.05±0.032	0.16
A_2y	0.05±0.03	0.03±0.017	0.1±0.099	0.09±0.086	0.27
B_1x	0.02±0.007	0.03±0.001	0.12±0.105	0.09±0.024	0.26
B_1y	0.02±0.002	0.03±0.013	0.09±0.034	0.1±0.068	0.24
B_2x	0.02±0.002	0.02±0.005	0.07±0.027	0.05±0.02	0.16
C_1x	0.02±0.005	0.03±0.006	0.09±0.053	0.09±0.036	0.23
C_1y	0.02±0.005	0.03±0.019	0.06±0.044	0.11±0.097	0.22
C_2x	0.03±0.003	0.02±0.01	0.14±0.101	0.15±0.168	0.34
D_1x	0.02±0.019	0.03±0.005	0.08±0.045	0.08±0.037	0.21
D_1y	0.03±0.002	0.06±0.023	0.25±0.222	0.25±0.183	0.59
E_1x	0.02±0.001	0.03±0.01	0.08±0.016	0.07±0.035	0.20
E_1y	0.03±0.009	0.04±0.015	0.16±0.114	0.13±0.086	0.36
F_2x	0.02±0.002	0.03±0.011	0.07±0.036	0.07±0.043	0.19
G_2y	0.03±0.003	0.03±0.012	0.07±0.026	0.07±0.039	0.20

DEP: Diethyl phthalate, DBP: Dibutyl phthalate, BBP: Benzyl butyl phthalate, DEHP: Diethylhexyl phthalate, PAEs: Phthalic acid esters

Table 4: Average concentration of phthalate esters in pasteurized milk (factory) (µg/l)

Sample milk	DEP	DBP	DEHP	BBP	ΣPAEs
A_1x.K	ND	0.02±0.006	0.03±0.003	0.05±0.029	0.1
A_1y.K	ND	0.04±0.0003	0.02±0.007	0.1±0.002	0.16
A_2x.K	ND	0.04±0.01	0.02±0.006	0.08±0.013	0.14
A_2y.K	ND	0.03±0.012	0.05±0.019	0.07±0.053	0.15
G_2y.K	0.02±0.003	0.02±0.0005	0.03±0.00005	0.03±0.00002	0.1

ND: Not detected, DEP: Diethyl phthalate, DBP: Dibutyl phthalate, BBP: Benzyl butyl phthalate, DEHP: Diethylhexyl phthalate, PAEs: Phthalic acid esters

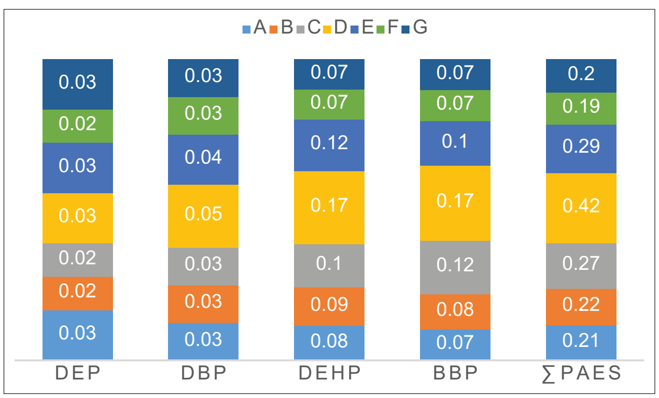

Figure 2: Comparison of the mean concentration of phthalate esters between different brands (µg/l)

phthalates, especially diethyl hexyl phthalates to humans and animals, the Environmental Protection Agency and the Canadian Health Organization emphasized the need to monitor DEHP levels in foods in contact with products containing plasticizers[11] In 2014, Şenlik *et al*. studied the level of six phthalate esters (DEHP, BBP, DBP, DEP,…) in pasteurized milk samples and packaged pasteurized milk samples. In their study, DBP (3–5 ng/g) and DEHP (0.4–4 ng/g) had the highest concentrations in pasteurized milk. Then, packaged pasteurized milk was examined, and it was observed that the highest concentrations were related to DBP (1–2 ng/g) and DEHP (62–30 ng/g). Because DEHP was higher in packaged milk, DEHP migration from packaging to milk was confirmed.[28] Fierens *et al*. evaluated the transfer rate of phthalate esters through the milk chain. Their results indicated that most phthalate contaminants are related to DiBP, DnBP, DEHP, and BzBP compounds. Phthalate at farms level is likely to be transferred through the cattle feed chain and mechanical milking process, and in industry and retail through the packaging of milk and dairy products. In industry, the rate of DEHP increased from 364 to 426 µg/kg during pasteurization and cooling.[24] The results of the studies are similar to the results of this study.

In addition to the stores, a part of the milk samples from two factories was prepared after final processing and before packaging. The results of the mean concentration of phthalate esters are shown in Table 4. According to this table, the highest mean concentrations of four phthalate esters, including DEP, DBP, DEHP, and BBP, in the 5 samples collected from the factories were 0.02 µg/l, 0.04 µg/l, 0.05 µg/l, and 0.1 µg/l, respectively. According to these results, the highest values obtained for each compound were related to high-fat milk samples. Among the mean concentrations obtained, the maximum value was related to BBP. It is noteworthy that the mean DEP concentration was not found in the four samples and was observed only in the G2y. K brand. Among the samples, the A1y. K brand, a high-fat milk sample, had the highest total phthalate esters (0.16 μg/l). In the general population, high-fat foods are believed to be the main source of exposure to phthalate esters.[35]

In 2016, Sajid *et al*. investigated the levels of phthalate esters in milk samples in Saudi Arabia, they examined three brands of milk and observed that BBP concentration in one of the brands was 15.8 μg/L. Their results also showed that DEP, DIBP, and BEEP were not observed.[26] Selvaraj *et al*. examined the exposure of phthalates in milk and water bottles. According to these results, the highest levels of phthalates in milk and water bottles were 686 ng/l and 7820 ng/l, respectively, and the highest value was related to DEHP. They also obtained mean concentrations in packaged milk (245 ng/l) and raw milk (134 ng/l). In general, among the phthalates, the lowest health risk was related to DEP and the highest was related to DEHP.[36] Yan *et al*. examined milk packaged with plastic bottles in terms of the presence of phthalate esters. In this study, the highest amount of phthalate ester was related to DBP (5.21 ng/g) and no other phthalate esters, including DEP, were found. According to these results, the penetration of phthalate esters from plastic packaging to milk samples was confirmed.[37] The results of the studies are similar to the results of this study.

In this study, 7 high-consumed brands of milk were examined separately [Figure 2], in which the highest concentration of phthalate esters was related to brand D at 0.42 μg/l. Furthermore, the highest mean concentration of DEHP, which has been proven to be a very dangerous and carcinogenic compound, was related to the D brand. In addition to DEHP, another compound with a high mean concentration is BBP, which was also the highest in the D brand. Jia *et al*. measured phthalate esters in dairy products. In their study, DEHP with concentration range (1–936 μg/kg) was found in almost all milk and yogurt samples.[38] In a study conducted in Belgium (2012) on eight major dietary phthalates, it was found that DEHP was the compound with the highest transfer to food products. In this study, food was examined in four different groups in terms of DEHP, and it was observed that high-fat foods (305 g/kg), low-fat foods (19.2 g/kg), and watery foods (0.16 g/kg), and packaging (5.1 ng/cm^2) contained phthalate compounds.[39] The results of the studies are shown in Table 5 which is similar to the results of this study.

Since there are no national or international standards for phthalate esters in milk, the standards established for mineral water were used in this study. According to EPA rules, the maximum contaminant level (MCL) goals for diethyl hexyl phthalate (DEHP) are zero. The MCL for DEHP was determined to be 6 μg/l in drinking water. The WHO and the EU have also set a permissible level of 8 μg/l for DEHP. Except for DEHP, the amount of MCL in drinking water has not been determined for other phthalates.[12,13,26] According to the study, the mean concentrations of DEP, DBP, DEHP, and BBP in all samples were lower than the standard. The highest mean concentrations of DEHP and BBP were 0.25 μg/l; but in all cases, it was lower than the standard set by EPA, WHO, and EU in drinking water. There was no statistically significant difference between different brands of milk samples, and the $P < 0.05$ only for DEHP and there was a significant difference between different brands of milk packaging due to the difference in DEHP values [Table 6].

Conclusion

The results of this study showed that among the 7 brands studied, brand D had the highest amount of phthalate esters in pasteurized milk with plastic packaging. In this brand, DEHP and BBP, which are dangerous and carcinogenic compounds, had the highest levels. After this brand, the highest amount of phthalates was related to the brand E. Among the brands surveyed, the brand F had the lowest levels of phthalates; in this brand, the two mentioned compounds (DEHP and BBP) had the lowest levels. Because phthalate esters are lipophilic compounds, they have a high potential for the accumulation in fatty foods. According to the samples taken from stores and factories, the highest phthalate esters were related to high-fat brands.

According to the analysis, the total number of phthalates esters measured in most samples collected from stores was higher than factories. Therefore, by summarizing the research, it can be understood that one of the important factors in the high rate of phthalate esters in the samples taken from stores was the plastic coating of pasteurized milk, which over time, the releases more phthalate esters into food in contact with plastic coating. In general, the results of this study were indicative of a low mean concentration of phthalate esters (DEP, DBP,

Table 5: Overview of phthalic acid esters concentrations in milk samples obtained in several studies

PAEs	Concentrations	Type of milk	References
BBP	15.8 μg/kg	Pasteurized milk	[26]
DBP-DEHP	1-2 to 30-62 ng/g	Pasteurized milk	[28]
DBP	5.21 ng/g	bottles milk	[37]
DEHP	85 μg/kg	Pasteurized milk	[38]

DEP: Diethyl phthalate, DBP: Dibutyl phthalate, BBP: Benzyl butyl phthalate, DEHP: Diethylhexyl phthalate, PAEs: Phthalic acid esters

Table 6: Statistical analysis of ANOVA test for phthalate derivatives determined in different brands of milk samples

Phthalate esters	*P*
DEP	0.989
DBP	0.181
DEHP	0.040
BBP	0.108

DEP: Diethyl phthalate, DBP: Dibutyl phthalate, BBP: Benzyl butyl phthalate, DEHP: Diethylhexyl phthalate

DEHP, and BBP) in pasteurized milk with plastic packaging, and according to Table 5, the results were consistent with the results of other researches. The values obtained were lower than the standard.

According to the results, the use of pasteurized milk with plastic packaging is not considered as a dangerous source of exposure to phthalate esters and the share of pasteurized milk with plastic packaging is insignificant in terms of the presence of phthalate esters. Therefore, the use of pasteurized milk with plastic coatings in the short term does not pose a risk to the consumer, but in the long term, these substances can be problematic due to their accumulation of these substances in the body.

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Conflicts of interest

There are no conflicts of interest.

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