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Research Article

Quality Control of the Migration of Bisphenol a from Plastic Packaging into Iranian Brands of Food Grade Oils

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ABSTRACT

Background: Bis-phenol A (BPA) can migrate into food stuff from packaging materials and accounts for food contamination. This research was designed to measure BPA contamination in the Iranian brands of food grade oils and to find out the possible effect of production date on the amount of BPA migration.

Methods: Ten well-known and top selling oils packed in various containers, were selected and sampled according to their batch number and production date stated on the label. Subsequently, BPA was extracted by reverse phase dispersive liquid-liquid extraction (RP-DLLME) method and quantified by HPLC.

Results: The measured quantity of BPA in the food grade oil was ranged between 0.5 to 4.37 µg/g of oil samples regardless of the date of production, the Batch Number, and the producing company.

Statistical analysis revealed that the difference of BPA content in oil samples did not depend on their production date.

Conclusion: According to the amount of allowable migration introduced by European committee, the amount of BPA migration and consequently contamination of almost all tested samples exceeds SML. Considering the toxic effects reported especially in fetus and young children, prompt regulatory interference is needed in this area.

Introduction

Bisphenol A (BPA) is a synthetic compound which is produced by conjugation of two phenols with an acetone in an acidic environment. This compound is used as a monomer for synthesis of polycarbonate plastics and is classified as a "high production volume chemical". Theoretically, Polycarbonate plastics are formed by the reaction of BPA and carbonic acid (Figure 1). These plastics have various applications in the modern world. They have been widely used in food and drinking packages as well as some medical devices. In addition, most of the other plastics that are tough and transparent are made up of BPA. These plastics are used as packaging materials in baby milk bottles, mineral water bottles, pasteurized milk and food grade oil bottles, as well as the inner cover of the metal cans; hence some BPA may migrate into the packed food.[1-3]

Nowadays BPA may constitute a considerable part of daily food intake in modern life style. Researchers have found BPA in human urine samples of more than 90 percent of Americans.[4] These findings show that, the higher the amount of the food being intake, the higher the amount of BPA in their urine samples.[5]

Phenolic groups in BPA are similar to phenolic groups in estradiol so this compound is able to mimic estrogenic effects in human body.[6] The effects are too weak to consider BPA as a pharmacologic agent, and it has never been used so;[7,8] however it is potent enough to interfere with normal metabolic pathways and it is hard to detect impurities in oil samples.[9,10] It has been reported that exposure to BPA results in sexual impotency in the male workers, several times more than the average population.[11,12] Additionally prolonged exposure to this compound is related to repeated abortions,[13] together with secondary developmental defects of genital system in fetus, infants and young children.[14-17]

The interfering effects of BPA may also get involved in carcinogenic pathways. A review article published by the Nature publishing group concludes that this compound may increase the risk of some cancers.[18] It has been theorized that the significant increment in breast cancer in the past 50 years may be due to exposure to BPA in the world's population.[19,20] Some other complications attributed to BPA are prostate hyperplasia or cancer, weight gain and neoplastic changes.[4,21,22] Due to toxic effects of BPA, governments and organizations have

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assessed health issues in this regard and some stated limitations. The World Health Organization WHO formed an expert panel and concluded that it is premature to consider public limitations for BPA.[23,24] The US Food and Drug Administration, FDA, published a report indicating possible hazards of BPA, and thereafter cancelled the approval of BPA-based plastics as packaging material for baby formula or baby bottles. The European Union and Canada performed the same limitations.[25,26] The U.S. Environmental Protection Agency (EPA) has determined the toxic level as much as 50 µg/kg/day; nevertheless amounts less than this level are not considered quite safe.[27] European Commission (EC) have also presented a specific migration limit (SML) of BPA to food stuff as 0.6 µg/g of the food substance.[28]

Currently the quantity of BPA in food with BPA-based packages is regarded as a safety indicator. In this study a defined approach was used in the sampling of the oils based on their batch number and production dates. Finally the results of different samples were compared and the effect of these parameters on the BPA content was fully discussed.

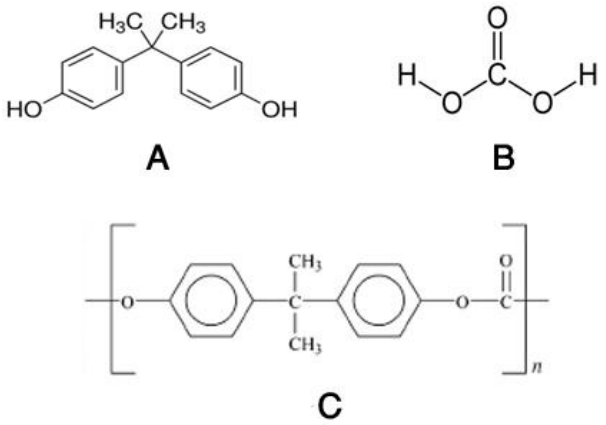

Figure 1. Chemical structure of A) BPA, b) Carbonic acid and c) Polycarbonate.

Materials and Methods

BPA (2,2-Bis(4-hydroxyphenyl)propane) (Purity>99%) was purchased from Sigma Aldrich (Sigma Aldrich, Germany). All solvents such as methanol, tetrahydrofuran and n-hexan were provided from Labscan analytical science (Lab scan, Ireland). All other chemicals were from (Merck, Germany).

Sampling

A field survey was performed to determine the available food grade oils in Tabriz city retail markets. Finally 10 well-known Top selling domestic brands which were packed in plastic containers, were selected. Three different Batch numbers of each brand within the first, second and third, "3 months" of their production date, were sampled and stored in home condition. Moreover, 20 extra samples were also sampled from non-Top selling oils packed in glass or metal containers only within their first three months of production for blank determinations. Sample O which was a homemade oil derived from animal source butter and named yellow oil, was also tested to be used as blank in HPLC analysis (Table 1).

Subsequently, BPA was extracted by reverse phase dispersive liquid-liquid microextraction (RP-DLLME) method introduced by Liu et al., and quantified by HPLC (knauver, Germany).[29] Table 1 summarizes the oil type and container-cap characteristics for all samples.

Table 1. Different samples characteristics.

Brand Number	Oil Type	Container - Cap
Brand 1	Frying oil	Plastic-Plastic
Brand 2	Sunflower oil	Plastic-Plastic
Brand 3	Frying oil	Plastic-Plastic
Brand 4	Frying oil	Plastic-Plastic
Brand 5	corn oil	Plastic-Plastic
Brand 6	Sunflower oil	Plastic-Plastic
Brand 7	Frying oil	Plastic-Plastic
Brand 8	Sunflower oil	Plastic-Plastic
Brand 9	Frying oil	Plastic-Plastic
Brand 10	corn oil	Plastic-Plastic
A	Grape seed Oil	Glass-Metal
B	Sesame Oil	Metal-Plastic
C	Solid Vegetable Oil	Metal-Plastic
D	Olive Oil	Metal-Plastic
E	Solid Vegetable Oil	Metal-Metal
F	Olive Oil	Glass-Metal
G	Animal Source Oil	Metal-Metal
H	Olive Oil	Glass-Metal
I	Coconut Oil	Glass-Metal
J	Omega 3 Oil	Metal-Plastic
K	Castor Oil	Glass-Metal
L	Olive Oil	Glass-Plastic
M	Olive Oil	Glass-Metal
N	Almond Oil	Glass-Metal
O	Animal Based Oil (homemade)	Glass-Metal
P	Grape seed Oil	Glass-Metal
Q	Olive Oil	Glass-Metal
R	Olive Oil	Glass-Metal
S	Omega 3&6 Oil	Metal-Metal
T	Canned Butter	Metal-metal

Measurements

Standard Preparations

Standard stock solution was prepared by dissolving BPA standard powder in methanol, resulting in the concentration of 1 mg/ml. Using this stock, diluted standard concentrations of 0.5, 2.5, 5, and 10 µg/g of oil sample were also prepared using methanol as a diluent.

HPLC system

HPLC system was consisted of a C_{18} column (MZ analytical) (4.6* 25cm, 5 µm) and a UV detector set at 277 nm. The mobile phase was composed of water: methanol (36: 64) containing 0.5% THF with a flow rate of 1 ml/min.

Each diluted standard concentration was injected to HPLC system and peak area and height were computed and recorded. Every sample was injected at least 3 times. Relative validation factors including linearity, Repeatability, accuracy, Limits of detection (LOD) and limit of quantification (LOQ) as well as system suitability parameters such as resolution, capacity factor and theoretical plate number were calculated and reported in Table 2.

Table 2. Relative validation factors and system suitability parameters.

Linear range	LOD	LOQ	Precision RANGE (Repeatability) (%RSD)	Accuracy range	Capacity factor	Resolution The peak before and after	Theoretical plate number
0.5-10 µg/g	0.15 µg/ g of oil.	0.45 µg/ g of oil.	0.7-2.65	98.53±1.7 and 96.13±2.3	5	1.45&1.5	3893.8

Blank oil determination

Different brands (n=20) with non-plastic containers were tested in order to find a blank oil free from BPA (Table 1).

Spiked Oil samples

Blank oil was used to prepare similar concentrations (0.5, 2.5, 5, and 10 µg/g) of BPA. The extraction of BPA from oil samples was performed by RP-DLLME.

Positive controls were made by heating the plastic containers in heat oven up to 40 ºC. For extraction of BPA from oil samples, the method of RP-DLLME was used, reported by Liu et al in 2013.[29] Briefly 1 gr of oil sample in a 15ml falcon was mixed with 4ml of N-Hexane and vortexed. Then 100 micro liters of NaOH (0.2 M) was added and vortexed again. The solution was then centrifuged in 5000 rpm for 5 minutes and the lower precipitate was extracted by Hamilton syringe and transferred to a 1ml micro tube. Then 30 micro liters of H3PO4 (0.4 M) was added and again the solution was centrifuged in 5000 rpm for 5 minutes. The upper supernatant was injected to the HPLC system.

The RP-DLLME absolute recovery power was computed by using BPA calibration equation in methanol.

The absolute recovery percentage was calculated by the following formula:

Absolute Recovery = the calculated quantity/ the theoretical quantity *100

Computer based Analysis

EZChrom Elite HPLC system controlling software was used to calculate peak responses (height and area). Microsoft office excel software was utilized for the further computations.

Finally SPSS statistics21 software was used to compare the calculated quantities. For comparison of means, ANOVA test was used and P values < 0.05 were considered significant.

Results and Discussion

The linear regression of HPLC peak response versus concentration (conc.) resulted the calibration equation for BPA in methanol as (Peak Height = 1032.9×Conc. (µg/ ml) + 134.31) (R^2 > 0.99)).

Within these oil samples packed in non-plastic containers, satisfactory results were achieved using Sample O (Table 1). This oil was used as a blank in HPLC analysis.

The calibration equation of BPA in oil was (Conc. (µg/ g of oil) = 0.002×Peak Height - 0.3395) with an R-squared equal to 0.92.

The absolute recovery was nearly 65% in the current experiments while the relative recovery was near 93% in the spiked samples (87-98%).

The HPLC chromatogram of spiked blank oil with concentration of 10 µg/g is presented in Figure 2.

Limits of detection, LOD, and limit of quantification, LOQ, were calculated to be 0.15 and 0.45 µg/ g of oil and along with other validation factors and system suitability parameters are shown in Table 2.

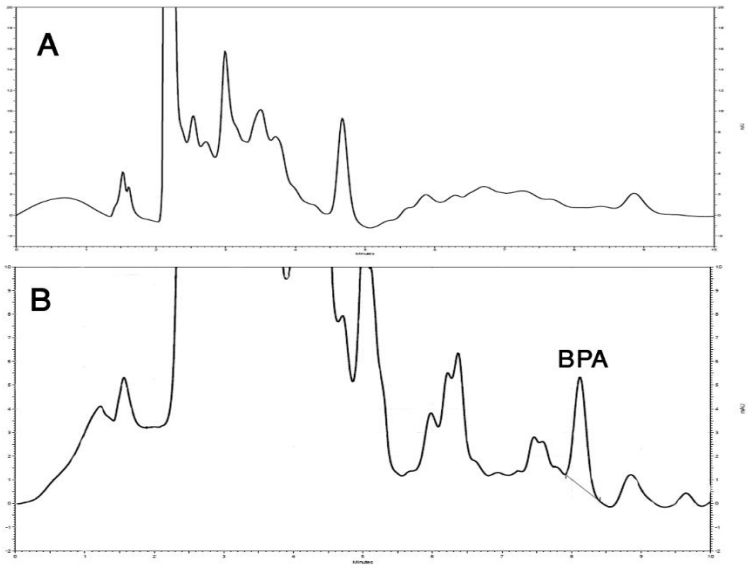

Figure 2. The HPLC chromatogram of A) blank oil, B) spiked blank oil (Conc. = 10 µg/g).

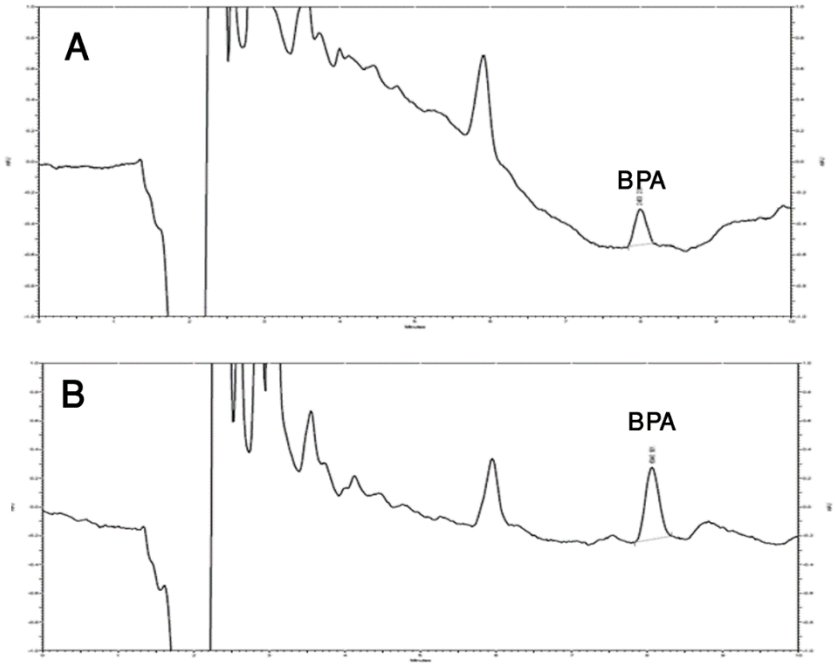

Figure 3. HPLC chromatogram of a brand oil sample, in the first 3 month of production; A) without heating and B) after heating in oven.

Samples tabulated in Table 1, were extracted by RP-DLLME. Three different Batch numbers of each brand within the first, second and third, three months of their production date, were sampled from the retail markets. A total of 9 sample was analyzed form each brand /company. The calculated amount of BPA quantities in the oil samples packed in plastic containers are listed in Table 3.

According to the results, the mean quantity of BPA in oil samples, regardless of their production date and company was between 0.5 to 2.6 µg/g of oil.

Statistical analysis of mean revealed that the difference of BPA quantity in oil samples at the first, second and third 3 months past from their production date is not significant (p value=0.99).

The amount of BPA in some non-plastic containers was large enough to be quantified. Thus the amount of BPA in these brands was calculated and listed in Table 4. As seen the amounts were between 0.5-4.37 µg/g of oil

United States Environmental Protection Agency (EPA) determined the toxic level of BPA allowable intake as 50µg/kg/day for human subjects.[30]

The United States Department of Agriculture (USDA) food availability data, announces average daily salad and cooking oil consumption of an average American (70 kg) to be 39.5 g per person daily.[31]

Based on the calculated range for BPA content in this research (0.5-4.37 µg/g of oil) and the mean absolute recovery of the RP-DLLME HPLC method to be about 65%, one can compute the daily dosage for a 70 kg person when consuming Iranian oil brands. Thus the maximum intake of BPA would be calculated as 4.1µg/kg/day, which is far away from the toxic level (50 µg/kg/day).

Table 3. The quantities of BPA in the oil samples from 10 brands with plastic container and bonnet*.

	First 3 months			Second 3 months			Third 3 months		
Samples	**Batch No1**	**Batch No2**	**Batch No3**	**Batch No1**	**Batch No2**	**Batch No3**	**Batch No1**	**Batch No2**	**Batch No3**
Brand 1	1.19±0.18	1.46±0.09	<0.5	<0.5	0.52±0.11	0.74±0.15	0.86±0.21	<0.5	1.70±0.06
Brand 2	1.73±0.34	0.54±0.28	<0.5	<0.5	1.69±0.31	1.05±0.18	<0.5	2.65±0.04	0.58±0.25
Brand 3	1.37±0.17	<0.5	0.60±0.12	0.60±0.09	0.46±0.12	0.60±0.09	0.63±0.12	<0.5	0.61±0.19
Brand 4	<0.5	0.70±0.21	<0.5	0.53±0.08	<0.5	0.90±0.21	<0.5	<0.5	<0.5
Brand 5	0.52±0.15	<0.5	<0.5	0.72±0.09	0.52±0.12	1.10±0.74	<0.5	<0.5	<0.5
Brand 6	0.93±0.21	1.00±0.18	<0.5	1.12±0.08	<0.5	<0.5	0.52±0.08	1.30±0.19	<0.5
Brand 7	1.38±0.15	0.55±0.06	<0.5	0.61±0.14	1.53±0.10	<0.5	1.37±0.04	<0.5	1.45±0.06
Brand 8	0.71±0.21	<0.5	<0.5	0.51±0.08	1.10±0.18	<0.5	1.30±0.21	<0.5	<0.5
Brand 9	<0.5	0.51±0.08	<0.5	<0.5	<0.5	1.20±0.14	<0.5	<0.5	<0.5
Brand 10	<0.5	0.52±0.15	1.70±0.09	<0.5	1.35±0.07	<0.5	<0.5	<0.5	<0.5

Table 4. The amount of BPA in No-plastic containers.

Sample name	**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**
BPA Quantity (µg/g)	ND	2.77±0.21	4.37±0.14	ND	0.5±0.14	ND	1.96±0.15	ND	1.11±0.03	ND
Sample name	K	L	M	N	O	P	Q	R	S	T
BPA Quantity (µg/g)	1.76±0.27	ND	ND	0.87±0.14	ND	ND	1.46±0.22	1.09±0.04	ND	1.3±0.08

In the other hand an average person is allowed to consume about 88 g oil in a day without reaching the toxic level. But it should be kept in mind that the oils are not the only source of BPA delivery to human body.

Specific migration limit (SML) of BPA into food staff have been determined by European committee as 0.6µg/g of food.[28] This narrow limit results in the safety concern of all tested samples as almost all BPA content of the tested samples exceeds SML. Thus the amount of BPA migration and consequently contamination of tested food grade oils in this survey, is high enough to be considered serious.

A related survey reports the amount of BPA in 11 samples of edible oils from China to be 0.13-2.19 µg/g.[29] Our findings are in good accordance with this report.

Other researchers reported that, oils samples of canned fish contain BPA quantities more than 1 mg/kg,[32] which significantly less than the quantities measured in the current investigation. Another study in Italy reported measurable BPA in 83% of oil samples from canned fish ranging from 6 to 70 ng/ml.[33] This amount is again lower than the quantities measured in the current investigation. Moreover, a review about phenolic compounds in Tunisian olive products and by-products concludes that the amount of phenolic compounds vary from several mg/ml to several hundred mg/ml. Though, most of these compounds were not BPA but other phenols which even showed beneficences like anti-inflammatory effects.[34]

According to results, the amount of BPA could not be predicted based on the trademark, the batch number, or the time period past since the production date. The similar studies measuring BPA in canned food, report even wider ranges.[3,35,36] It is believed that the amount of BPA migration to food is dependent on some factors such as the production process, packaging type and also storing process. According to the present study, heating plastic containers accelerates BPA migration from packaging material into food staff (Figure 3).

On the other hand BPA content of some samples was very low and was not detectable by our method (Table 2). The reason may be related to the application of high quality plastics with low monomer residues.

According to table 1 samples packed in non-plastic containers can be divided to 2 main groups, metal and glass containers. The metal containers always are internally lined with a plastic liner. This plastic is in direct contact with the oil and thus can be a source for BPA migration. In glass containers which is limited to sample A, F, H and I, with metal caps, there is no visible source of plastic part in the finished product. The possible source of BPA contamination in these samples may be related to production process which is ambiguous for the consumer and also the analyst. For example the oils before final packing may be stored or exposed to plastic containers or environment. Thus the presence of trace amounts of BPA in non-plastic glass containers may be originated from previous manufacturing steps as well as raw material sources.

Statistical analysis (ANOVA) revealed that the difference of BPA content in oil samples did not depend on their production date (p-value>0.05).

Most of the toxic effects of BPA, including endocrine and neurologic interference, occur in the toxic level determined by EPA.[11,37]

In addition, it should be kept in mind that children dietary intake based on their low weight may be higher than that of an average adult,[11,38] which may exhibit toxic effects in these consumers. Calculating BPA exposure to fetus is another complex issue, since there are receptors in placenta which specifically accumulate BPA,[2] and it is hard to judge safety of BPA intake in such cases, even in small amounts.

Conclusion

According to the amount of allowable migration introduced by European committee, the amount of BPA migration and consequently contamination of almost all tested samples exceeds SML. Considering the toxic effects reported especially in fetus and young children, prompt regulatory interference is needed in this area. Statistical analysis revealed that the difference of BPA content in oil samples did not depend on their production date.

The evidences indicate that BPA may accumulate in human body leading to toxic effects. Moreover, due to the toxic effects reported especially in fetus and young children, even low quantities of contamination should be considered serious and need regulatory interference.

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Conflict of interests

The authors claim that there is no conflict of interest

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