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Original article

Risk assessment of exposure to benzoic acid and benzene from consumption of functional drinks

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Summary This study aims to determine content and conduct exposure assessments of benzene and benzoic acid in functional beverages. A total of 47 functional drink products were purchased from convenience stores in Bangkok, Thailand. Benzene and benzoic acid contents were determined by high-performance liquid chromatography (HPLC) and gas chromatography–mass spectrometry (GC–MS), respectively. Risk characterisations of exposures to benzoic acid were assessed by hazard quotient. Margin of exposure and cancer risk approaches were used for exposure assessment of benzene. The results showed that benzoic acid levels ranged from 74–229 mg L^{-1} complying with Thai food standards and the Codex Alimentarius. Benzene concentrations varied between 0.60–551 μg L^{-1}, and 14 samples (30%) had concentrations above the limit of 10 μg L^{-1} recommended by World Health Organization. Regularly high consumption of vitamin C-enriched drinks containing benzoic acid results in high exposure to benzene with attendant cancer risk. To reduce health risks, drinks containing benzoic acid as a preservative should not be fortified with vitamin C.

Keywords benzene, benzoic acid, exposure assessment, process-induced food toxicant, risk characterisation.

Introduction

Benzene is classified as a 'Group I' carcinogen to humans by the International Agency for Research on Cancer. Benzene exposure leads to increase risk of developing lymphatic and haematopoietic cancers, acute myelogenous leukaemia and chronic lymphocytic leukaemia (Goldstein, 2010). Benzene can be introduced into foods in various ways, including environmental contamination, migration from plastic packaging and formation during food processing. In non-alcoholic beverages, benzene can be formed from decarboxylation of the preservative benzoic acid in the presence of vitamin C (Salviano dos Santos *et al.*, 2015). Benzoic acid is a commonly used antimicrobial preservative in food and beverages, especially in soft drinks. Vitamin C is naturally present in some foods (*e.g.* fruits) and may be added as an antioxidant or as a supplementary source of vitamin C (Salviano dos Santos *et al.*, 2015).

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Previous studies have reported some factors that influence benzene formation in foods and beverages. Both intrinsic factors (*e.g.* benzoic acid, vitamin C, pH, metals and types of added sugar) and extrinsic factors (temperature, UV radiation, storage time, *etc.*) affect benzene formation (Haws *et al.*, 2008; Nyman *et al.*, 2010; Ibolya *et al.*, 2012; Salviano dos Santos *et al.*, 2015). Gardner and Lawrence (1993) found a correlation between benzene formation and levels of benzoic acid and vitamin C. Benzene formation increased with higher vitamin C concentrations. The highest level of benzene formation was found at pH 2, and the benzene level decreased considerably from pH 3 to pH 5, with no detectable benzene level at pH 7 (Gardner & Lawrence, 1993). Metal ions such as copper (Cu) and iron (Fe) are catalysts of decarboxylation of benzoic acid to benzene by vitamin C (Gardner & Lawrence, 1993; Medeiros Vinci *et al.*, 2011 2011). Aprea *et al.* (2008) reported that higher levels of sucrose proportionally reduced benzene formation. It was also found that glucose and fructose were more potent inhibitors of benzene formation compared to sucrose. A previous study showed the effects of

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temperature and UV on benzene formation in beverages (McNeal *et al*., 1993). The study was conducted using aqueous models containing similar sodium benzoate and vitamin C contents to commercial drinks. It was found that drinks stored at 45 °C or under UV light for 20 h had a higher benzene content of around 300 μg L^{-1}. In contrast, drinks kept in a dark container at room temperature for 20 h had only 4 μg L^{-1} benzene content. However, the benzene levels were increased to 266 μg L^{-1} after 8-day storage (McNeal *et al*., 1993). Lertborwornwong (2021) studied benzene formation under different conditions using pasteurised orange juice. The researchers concluded that low pH, high pasteurising temperature and high storage temperature increase benzene formation. Chelating agents including disodium EDTA and sodium hexametaphosphate reduced the benzene production in beverages.

The maximum limits of benzene in foods and beverages have not been established by the Codex Alimentarius Commission, which is the international food standard organisation. However, the maximum permissible levels of benzene in drinking water have been established as maximum of 10 μg L^{-1} by the World Health Organization (WHO, 2017), 5 μg L^{-1} by the US Environmental Protection Agency (USEPA, 2018) and 1 μg L^{-1} by the European Commission (European Commission, 1998). These limits have also been applied as the maxima for benzene content in non-alcoholic beverages.

Benzene formation could occur in beverages because benzoic acid, a precursor to benzene, is commonly added to beverages as a preservative. Benzene contamination of beverages was initially reported by the United States Food and Drug Administration in 2006 (USFDA, 2006). It was reported that 63% of carbonated drinks samples were contaminated and the highest benzene level was 88 μg L^{-1} in soft drinks containing both benzoate and vitamin C. A study conducted by collecting samples from local markets in Iran found that the average concentrations of benzene in carbonated beverages and fruit juices were 3.57 and 5.17 μg L^{-1}, respectively. The highest concentration of benzene was detected in orange juice at 11.20 μg L^{-1} (Heshmati *et al*., 2018). Techakriengkrai and Lertborwornwong (2013) determined benzene levels in commercial fruit-flavoured drinks in Thailand and found that 27% of samples contained benzene levels ranging from 5.47 to 16.91 μg L^{-1}. In 2006, the International Council of Beverages Associations stated that to reduce the benzene formation in beverages, vitamin C should be removed, reduced or replaced if benzoic acid is present. However, high levels of vitamin C are currently added to some beverages, especially functional beverages, with benzoate.

Functional drinks can be defined as drinks with beneficial effects related to improving health and well-being and/or reduction in risk of diseases (Ashwell, 2022). Functional drinks have become popular worldwide among health-conscious consumers (Orrù *et al*., 2018; Nazir *et al*., 2019). Functional beverages can be classified into four main groups, namely energy drinks, sports drinks, enriched drinks and nutraceutical drinks (Smith, 2013; Garg & Ahuja, 2015).

A risk assessment is a science-based evaluation of the potential adverse effects on human health from exposure to a chemical. Risk assessments consist of hazard identification, dose–response assessment, exposure assessment and risk characterisation. Hazard identification depends on the availability of toxicological data to assess whether chemicals can cause adverse health effects in humans. Dose–response assessment characterises the relationship between the dose of exposure and the adverse effects. Exposure assessment is conducted to determine the extent of the exposure. Risk characterisation is the final process to assess the adverse health effects. Hazard quotient (HQ) calculation is a common approach applied for estimating the health risk from exposure to food additives. Margin of exposure (MOE) and cancer slope factor (CSF) are widely used approaches for the quantitative risk assessment of carcinogens.

Published information on benzene content in beverages in Thailand is limited. No information on benzene exposure *via* functional beverage consumption of the Thai population has been published. This study aims to determine benzene and benzoic acid content in functional beverages, to estimate exposure and to assess health risks of benzoic acid and benzene from the consumption of functional beverages in the Thai population.

Materials and methods

Sample collections

This study focuses on commercially available functional beverages in convenience stores located in Bangkok's Central Business District because of the wide variety of such products available in this area. In Thailand, functional drinks can be divided into four groups, namely energy drinks, enriched drinks, nutraceutical drinks and sports drinks. A total of 47 functional beverage products with added benzoate were identified and collected from September to December 2020. At least six bottles of each beverage, with a minimum total volume of 500 mL, were collected and stored in a temperature-controlled icebox at less than 4 °C during transportation to the laboratory. Information of individual beverage products, including ingredients, food additives,

nutrition facts, manufacturing date, expiration date, manufacturer, and packaging material, was recorded. Each type of functional beverage was pooled into a one-litre bottle, gently homogenised by manual shaking, covered with foil and stored in a refrigerator at 4 °C until further analysis.

Reagent and standard solutions

Benzoic acid (99.98% purity) was purchased from Sigma-Aldrich (Laramie, WY, USA). Acetic acid, ammonium acetate, potassium hexacyanoferrate trihydrate, sodium acetate (anhydrous), sodium hydroxide and zinc acetate dehydrate were purchased from Merck (Darmstadt, Germany). Acetonitrile and methanol for high-performance liquid chromatography (HPLC) were purchased from JT Baker (Illkirch, France). Carrez I solution was prepared by dissolving 10.6 g potassium hexacyanoferrate trihydrate in deionised water and adjusting the volume to 100 mL . Carrez II solution was prepared by dissolving 22 g zinc acetate dehydrate in deionised water, adding 3.2 mL acetic acid and adjusting the volume to 100 mL.

Determination of benzoic acid

The determination of benzoic acid was conducted following the method used by Can *et al.* (2011), with some modifications, in an ISO/IEC 17025:2017 accredited laboratory. Briefly, a 4 mL sample of functional beverage was pipetted, weighed, and 40 mL of extract solution, a mixture of methanol and acetate buffer solution (37:63 v/v) with a pH of 4.5, was added. Benzoic acid in the sample was extracted in an ultrasonic bath (GT Sonic-D3, China) at room temperature for 15 min. Carrez I and Carrez II solutions (1 mL each) were added to precipitate proteins in the samples. The extracted solutions were filtered through a Whatman No. 1 filter paper. The filtered solution (20 μL) was injected into a reverse-phase HPLC system equipped with a HPLC pump (model 515, Waters, Milford, MA), C18 analytical column (250 mm × 4.6 mm, 5 μm; LiChrospher® 100, Merck, Darmstadt, Germany) and coupled with a UV-detector (UV-2075 Plus, Jasco, Tokyo, Japan). The mobile phase consisted of 80% acetate buffer at a pH of 4.5 and 20% acetonitrile. A flow rate of 1.4 mL min^{-1} and a wavelength of 230 nm were used. A calibration curve of benzoic acid standard solutions with concentrations of 0.5, 5, 10, 20, 30 and 50 mg L^{-1} was used to quantify benzoic acid in samples. The limit of detection (LOD) of the determination of benzoic acid was 1.5 mg L^{-1}, and the limit of quantitation (LOQ) was 5 mg L^{-1}. Quality control of benzoic acid analysis was performed to check the accuracy and precision of the method *via* spiked samples and duplicate samples, respectively.

Determination of benzene

The functional beverage samples were sent to the Thailand Institute of Scientific and Technological Research laboratory for benzene analyses using headspace gas chromatography–mass spectrometry (HS-GC–MS) technique. The determination of benzene content in the beverages was carried out following the methods of Ibolya *et al.* (2012) and Nyman *et al.* (2008) with some modifications. Briefly, a four-gram sample of beverage was weighed into a 10-mL headspace vial and one millilitre of internal standard (1 mL L^{-1} isopropyl alcohol) was added. A calibration curve of benzene standard solutions with concentrations of 0.5, 2.5, 5, 50 and 100 μg L^{-1} was used to quantify benzene levels in the samples. Samples were injected into a single quadrupole GC/MS System (GC–MS-QP2010, Shimadzu, Japan) with ultra-pure helium as the carrier gas at a flow rate of 1.0 mL min^{-1}. The GC column used for benzene separation was a VF-624 ms column (30 m × 0.25 mm I.D., 1.40 μm). The LOD and LOQ of benzene analyses in samples were 0.15 and 0.5 μg L^{-1}, respectively.

Exposure assessment of benzoic acid and benzene from functional beverage consumption

The present study used secondary data on functional beverage consumption from a national consumption survey and a previous study for the estimation of exposures to benzoic acid and benzene. Data on energy drink and sports drink consumption were gained from the national consumption survey of Thailand (ACFS, 2016). Data on intake of enriched drinks and nutraceutical drinks were obtained from a study conducted by Sultana *et al.* (2017). The exposure assessment was conducted based on the WHO approach to risk assessment of chemicals in foods (WHO, 2009). Three exposure scenarios were estimated: estimated daily intake (EDI), high consumer model, and worst-case scenario of exposure. EDI scenarios were calculated from the mean consumption (*per capita*) and mean/median concentration of the chemicals. High consumer models were estimated from 97.5^{th} percentile consumers only instead of the average *per capita* consumption. For worst-case scenarios, 97.5^{th} percentile consumption of consumers only and 97.5^{th} percentile concentrations of the chemicals were used for calculating benzoic acid or benzene exposure.

Risk characterisation of benzoic acid (non-carcinogenic effects)

HQ was calculated from the ratio of potential exposure to benzoic acid and its health-based guidance value. The acceptable daily intake (ADI) value of

5 mg kg BW^{-1} day^{-1} was used for benzoic acid (JECFA, 2015). For interpretation, if HQ is not greater than 1 (HQ ≤1), exposure to benzoic acid indicates minimal or no health risk. An HQ value of more than 1 was considered an adverse health concern (WHO, 2009).

Risk characterisation of benzene (carcinogenic effects)

MOE is commonly used for human health risk assessment of carcinogenic and genotoxic hazards. The risk characterisation of benzene was estimated using MOE and cancer risk approaches. MOE values were calculated by dividing the benchmark dose lower bound of benzene of 1.2 mg kg BW^{-1} day^{-1} by the estimated daily benzene exposure (USEPA, 2000). MOE values greater than 10 000 are acceptable, and values lower than 10 000 may raise public health concerns (Benford, 2016; WHO, 2009). Lifetime cancer risk is an index calculated using the chronic dietary intake of a chemical hazard and its potency factor (PF). The PF, also referred to as the slope factor, is the risk produced by ingesting an average dose of 1 mg kg BW^{-1} day^{-1} of the hazard over a lifetime. CSF of 1.5×10^{-2} (mg kg BW^{-1} day^{-1})$^{-1}$ was adopted from USEPA (2000). The estimated values were compared with the recommended de minimis (10^{-5}) for estimating lifetime cancer risk. A value greater than 10^{-5} is deemed to imply excess risk of developing cancer.

Statistical analysis

The levels of benzoic acid and benzene were presented as mean ± standard deviation, median, 97.5 percentile, minimum and maximum. For the normal distribution, one-way analysis of variance and Tukey's *post hoc* tests were used. For the non-normal distribution, the Kruskal Wallis test and Bonferroni-corrected Mann–Whitney *U* test were used to examine the statistically significant differences between beverage groups. All statistical analyses were performed using the SPSS statistical software (SPSS version 18; IBM, Chicago, USA) with α level of significance of 0.05.

Results and discussion

The concentration of benzoic acid in commercial functional beverages

Benzoic acid levels in each type of functional beverage are shown in Table 1. Average levels of benzoic acid between beverage types were not significantly different. The maximum benzoic acid level of 229 mg L^{-1} was found in the group of nutraceutical drinks. Although the manufacturer used benzoic acid according to the food standard, a higher level of benzoic acid could result from that naturally found in various plant ingredients in some nutraceutical drinks (Del Olmo *et al.*, 2017). The benzoic acid content in all functional drink samples complied with the food standard of Thailand (Ministry of Public Health, 2020) and the Codex Alimentarius Commission (Codex Alimentarius, 2019), established at 250 mg kg^{-1}. A previous study analysed benzoic acid levels in processed foods collected in South Korea and reported that the highest average level of benzoic acid, 168 mg kg^{-1}, was found in beverages (Jung *et al.*, 2022). A previous study in Canada and the United States reported that the average benzoic acid level of energy drinks was 109 mg kg^{-1}, while benzoic acid was not detected in any of the sports drink samples (Darch *et al.*, 2021).

Benzene concentrations in commercial functional beverages

The benzene concentrations of these 47 functional beverage samples ranged from 0.60–551 μg kg^{-1}. The median level of benzene in enriched drinks was significantly higher than the other types of beverages. Fourteen functional drink samples (29.79%) had benzene concentrations above the WHO limit of 10 μg L^{-1} (WHO, 2017). Among the samples, enriched drinks contained significantly higher benzene levels than those of other types of beverages (Table 1). This could be due to the fact that all enriched beverage samples used in the study contained benzoic acid and a high level of vitamin C. The containers of these drinks were

Table 1 Benzoic acid and benzene levels in four groups of functional beverages collected in Bangkok, Thailand

		Benzoic acid level (mg L^{-1}; ppm)				Benzene level (μg L^{-1}; ppb)			
Functional drink group	***N* (47)**	**Mean ± SD**	**Median**	**97.5 PCTL**	**Min-Max**	**Mean ± SD**	**Median**	**97.5 PCTL**	**Min-Max**
Energy drinks	22	161.33 ± 22.48^{a}	164.12	184.23	73.67–185.00	33.69 ± 95.25	3.11^{b}	325.80	0.95–348.24
Sports drinks	6	157.83 ± 10.40^{a}	158.73	158.79	138.94–167.94	15.62 ± 34.01	1.80^{b}	74.60	0.60–85.01
Enriched drinks	5	155.06 ± 15.51^{a}	159.49	163.78	125.38–170.42	280.15 ± 243.11	293.58^{a}	516.37	19.89–551.03
Nutraceutical drinks	13	180.95 ± 27.54^{a}	182.31	211.62	134.96–228.62	21.93 ± 34.32	2.27^{b}	89.30	0.60–118.00

Different superscript letters denote significant differences in benzoic acid and benzene levels between groups of functional drinks ($P < 0.05$).

transparent glass bottles, which may have increased exposure to UV light and heat during transportation and storage resulting in benzene formation. The benzene levels detected in the beverage samples in this study were higher than the values reported in some previous studies. Some functional drinks included in this study were fortified with high levels of vitamin C, up to approximately 0.1% (1000 mg kg^{-1}). Previous studies have investigated benzene formation in beverages with naturally present vitamin C levels. Techakriengkrai and Lertborwornwong (2013) found 5.47 to 16.91 μg kg^{-1} benzene contents in 13 out of 48 fruit-flavoured beverage samples collected in Thailand, and 8% of the samples had benzene higher than 10 μg kg^{-1}. Lertborwornwong (2021) reported that the highest benzene level of 47 μg kg^{-1} was found in the model solution of pasteurised orange juice containing 200 mg kg^{-1} sodium benzoate and 120 mg kg^{-1} vitamin C stored at 45 °C for 3 months. Gregrova *et al.* (2014) reported less than 10 μg kg^{-1} benzene concentration from the investigation of 49 soft drink samples on the Czech market.

Exposure assessment and risk characterisation of benzoic acid from functional beverages

Exposure levels of benzoic acid from consumption of all four groups of functional drinks are shown in Table 2. For the high consumer model and worst-case scenario, sports drinks were the major contributor to the benzoic acid intake. All exposure scenarios showed that the average and 97.5th percentile intakes of benzoic acid from functional beverages were well below the acceptable daily intake (ADI) level (Fig. 1). The risk characteristic of benzoic acid from functional beverage consumption was calculated as a HQ by dividing benzoic acid exposure by ADI. The HQ value in all scenarios was less than one, indicating that no adverse health effects can be expected as a result of exposure to benzoic acid from the studied functional drink samples. Although the results showed that consumers might be safe from benzoic acid through functional drink consumption, they could have additional exposure to benzoic acid from other food categories (Darch *et al.*, 2021; Jung *et al.*, 2022). Exposure to benzoic acid *via* non-alcoholic drink intake varied considerably between different countries. Martyn *et al.* (2017) conducted benzoate exposure from non-alcoholic beverages in Brazil, Canada, Mexico and the United States. The average intake of benzoic acid of subjects in these four countries was notably lower than 5 mg kg BW^{-1} day^{-1}. Darch *et al.* (2021) reported that benzoic acid exposure from water-based flavoured beverages in the Canadian and US populations did not exceed the ADI.

Table 2 Exposure to benzoic acid from functional beverage consumption of Thai population* (mg kg BW^{-1} day^{-1})

	Estimated daily intake		High consumer model		
Functional drink group	**Mean level**	**Median level**	**Mean level**	**Median level**	**Worst-case scenario**
Energy drinks	0.034^{c}	0.034	0.841^{b}	0.855	0.960^{b}
Sports drinks	0.041^{b}	0.041	1.308^{a}	1.325	1.379^{a}
Enriched drinks	0.043^{b}	0.045	0.449^{c}	0.462	0.474^{c}
Nutraceutical drinks	0.051^{a}	0.051	0.524^{c}	0.528	0.613^{c}

Different superscript letters denote significant differences in benzoic acid exposures from different groups of functional drinks ($P < 0.05$).
*Mean of body weight of both genders of Thai population was 57.57 kg.

Exposure assessment and risk characterisation of benzene from functional beverages

The EDI, high consumer model and worst-case scenarios were estimated for the exposure assessment of benzene through functional beverage consumption (Table 3). For the EDI and high consumer scenarios, enriched drinks were the major contributor to benzene exposure of the population. In the worst-case scenario, the highest exposure level was found to be from consumption of energy drinks. The risk characterisation of benzene for its carcinogenic and genotoxic effects was calculated as MOE and cancer risk and is shown in Table 4 and Fig. 2, respectively. In the average consumption scenario, MOE values of benzene exposure were above 10 000 indicating low public health concern. However, benzene exposure calculated from the high consumer model and the worst-case scenario showed that MOE values from consumption of energy drinks, sports drinks and enriched beverages were lower than 10 000, implying potential adverse effect on consumer health. In addition, the worst-case scenario found that the MOE value from consumption of each functional drink group was lower than 10 000. Cancer risk is the theoretical maximum number of cancer cases that are expected to develop due to the exposure to a carcinogen. The acceptable lifetime cancer risk for a carcinogen is 10^{-5} (1 case in 100 000 people). The results showed that cancer risks from benzene exposure estimated from the average consumption scenario of these beverages wer less than 10^{-5}. The findings indicated that there were low cancer risks of benzene exposure from the average consumption of the studied functional drinks. However, in the high consumer scenario, benzene intakes through enriched beverages might increase cancer risk in the Thai population. The

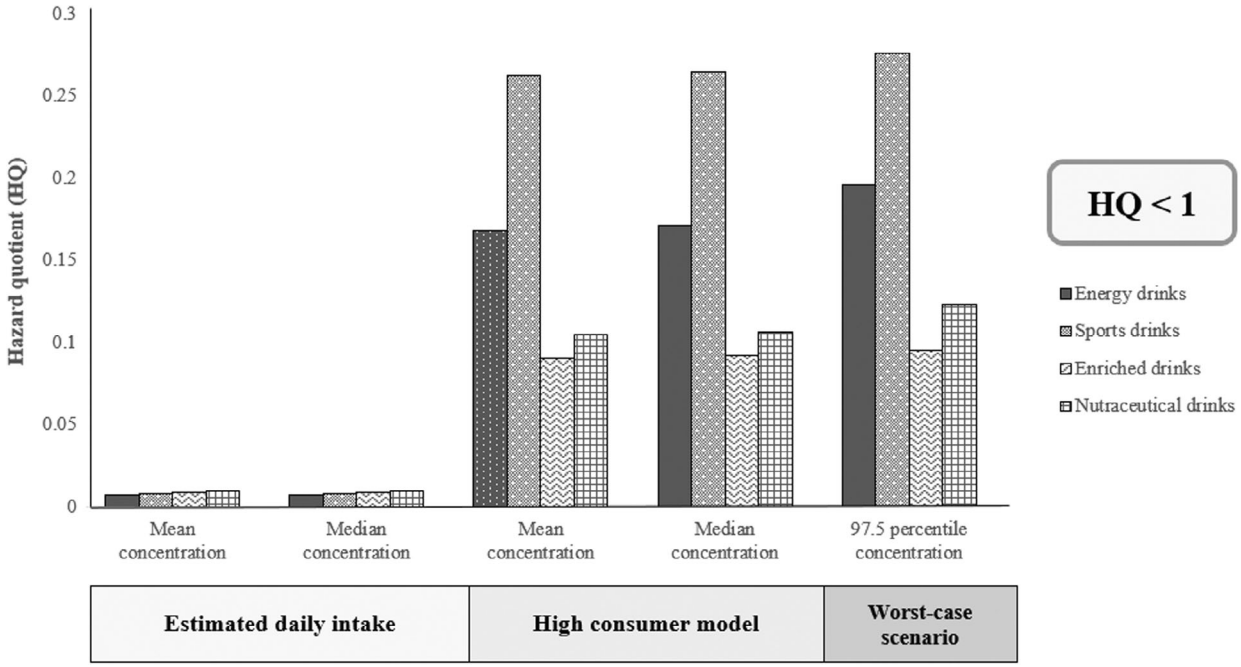

Figure 1 Risk characterisation of benzoic acid exposure from consumption of functional beverages calculated as hazard quotient.

Table 3 Exposure to benzene from functional beverage consumption of Thai population* (μg kg BW^{-1} day^{-1})

	Estimated daily intake		High consumer model		
Functional drink group	**Mean level**	**Median level**	**Mean level**	**Median level**	**Worst-case scenario**
Energy drinks	0.007	0.001[b]	0.176	0.016[b]	1.698[a]
Sports drinks	0.004	0.000[b]	0.136	0.016[b]	0.648[b]
Enriched drinks	0.079	0.082[a]	0.812	0.850[a]	1.496[a]
Nutraceutical drinks	0.006	0.001[b]	0.064	0.007[c]	0.259[c]

Different superscript letters denote significant differences in benzene exposures from different groups of functional drinks ($P < 0.05$).
*Mean of body weight of both genders of Thai population was 57.57 kg.

Table 4 Risk characterisation of benzene exposure from consumption of functional beverages calculated as MOE

	Estimated daily intake		High consumer model		
Functional drink group	**Mean**	**Median**	**Mean**	**Median**	**Worst-case scenario**
Energy drinks	171 429	1 200 000	**6818**	75 000	**707**
Sports drinks	300 000	NA	**8824**	75 000	**1852**
Enriched drinks	15 190	14 634	**1478**	**1412**	**802**
Nutraceutical drinks	200 000	1 200 000	18 750	171 429	**4633**

NA, not applicable.
MOE values of less than 10 000 (in bold) indicate potential adverse health effects.

worst-case scenario showed that high consumption of each functional drink group could increase the risk of cancer.

Studies on benzene exposure from consumption of non-alcoholic drinks and health risks have been conducted in different countries. In 2006, Health Canada investigated potential health risks from benzene exposure from soft drinks and other beverage products. The study concluded that consumption of these beverage products would lead to temporary or non-life-threatening health consequences (Health Canada, 2006). The USFDA assessed the potential human health risks through benzene exposure from beverage consumption in 2008 (Haws *et al.*, 2008). The results showed that cancer risk and HQs estimated from benzene exposure did not exceed the acceptable limits adopted by the US regulatory agencies. In 2018, a study determined benzene levels in 98 food and drink samples in Iran and found that benzene levels in all samples were less than 10 μg kg^{-1}. It was found that there was no serious health concern of exposure to benzene *via* food and beverage consumption, calculated as MOE values, in the Iranian population (Heshmati *et al.*, 2018).

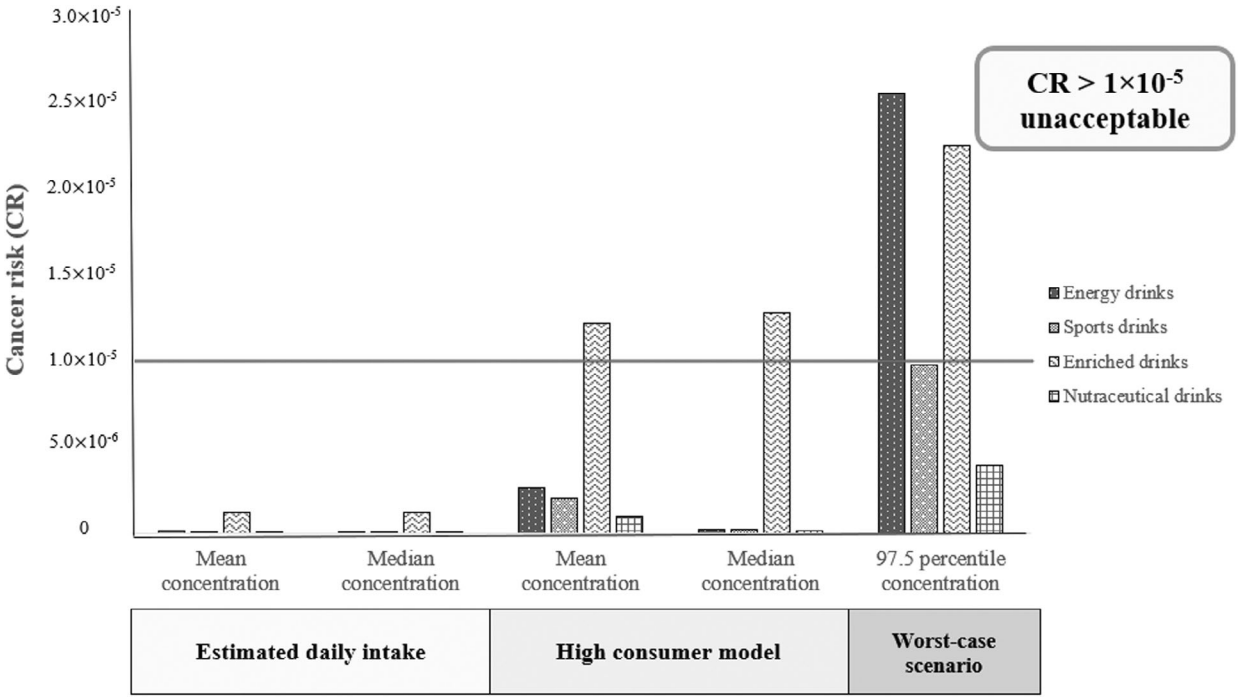

Figure 2 Risk characterisation of benzene exposure from consumption of functional beverages calculated as cancer risk.

Conclusions

All functional beverage samples complied with the regulatory limit of benzoic acid. Around 30% of beverage samples have benzene levels that exceed the WHO recommended level and beverage products fortified with vitamin C have higher levels of benzene. Average exposure to benzoic acid through functional beverage consumption in the Thai population may not pose adverse health effects to consumers. In contrast, regularly high consumption of functional beverages with high benzene levels increases cancer risk. Beverages with added benzoic acid should not be enriched with vitamin C. Information on potential benzene formation in foods and beverages from adding benzoic acid and vitamin C should be provided to the food industry for effective risk management.

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Author contributions

Christina Leesuraplanon: Data curation (lead); formal analysis (equal); investigation (equal); methodology (equal); writing – original draft (lead). **Vijay Jayasena:** Supervision (equal); validation (equal); writing – review and editing (lead). **Weeraya Karnpanit:** Conceptualization (lead); formal analysis (equal); funding acquisition (lead); investigation (equal); methodology (lead); supervision (lead); writing – original draft (equal); writing – review and editing (lead).

Conflict of interest

The authors declare that there are no conflicts of interest.

Ethical approval

The approval for the study was obtained from the Central Institutional Review Board of Mahidol University (MU-CIRB) with protocol number MU-CIRB 2020/308.0110.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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