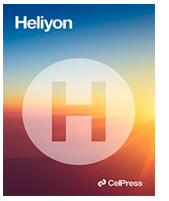
Heliyon 9 (2023) e21576

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Review article

Biological exposure indices of occupational exposure to benzene: A systematic review

Razzagh Rahimpoor [a,*], Hamed Jalilian [b], Heidar Mohammadi [a], Abdulrasoul Rahmani [a]

[a] Department of Occupational Health and Safety, Research Center for Health Sciences, School of Health, Larestan University of Medical Sciences, Larestan, Iran
[b] School of Architecture, Planning and Environmental Policy, University College Dublin, Dublin, Ireland

ARTICLE INFO

Keywords:
Biologic monitoring
Biomarkers
Benzene
Occupational exposure

ABSTRACT

The current study aimed to systematically review the studies concerning the biological monitoring of benzene exposure in occupational settings. A systematic literature review was conducted in Scopus, EMBASE, Web of Science, and Medline from 1985 through July 2021. We included peer-reviewed original articles that investigated the association between occupational exposure to benzene and biological monitoring. We identified 4786 unique citations, of which 64 cross-sectional, one case-control, and one cohort study met our inclusion criteria. The most studied biomarkers were urinary *trans*-trans muconic acid, *S*- phenyl mercapturic acid, and urinary benzene, respectively. We found the airborne concentration of benzene as a key indicator for choosing a suitable biomarker. We suggest considering urinary benzene at low (0.5–5.0 TLV), urinary SPMA and TTMA at medium (5.0–25 and 25–50 TLV, respectively), and urinary phenol and hydroquinone and catechol at very high concentrations (500 and 1000 TLV $\leq$, respectively). Genetic polymorphism of glutathione *S*-transferase and oral intake of sorbic acid have confounding effects on the level of U-SPMA and U-TTMA, respectively. The airborne concentration, smoking habit, oral consumption of sorbic acid, and genetic polymorphism of workers should be considered in order to choose the appropriate indicator for biological monitoring of benzene exposure.

1. Introduction

Benzene is the most common aromatic hydrocarbon used in a variety of industries and is naturally occurring in some environments.

Abbreviations: **ACGIH**, American Conference of Governmental Industrial Hygienists; **TLV**, Threshold limit value; **U**, Urine; **Bl**, Blood; **Cr**, Creatinine; **U–B**, Un-metabolized benzene in urine (μg. L^{-1}); Bl-B: U–**B**, Un-metabolized benzene in blood (μg. L^{-1}); **U-TTMA**, Trans, Trans-muconic acid in urine (μg. g Cr−1, *: μg. L^{-1}); **U-SPMA**, *S*- phenyl mercapturic acid in urine (μg. g Cr−1, *: μg. L^{-1}); **U-Hq**, Hydroquinone in urine (mg. g Cr−1, *: mg. L^{-1}); **U-Ph**, Phenol in urine (mg. g Cr−1, *: mg. L^{-1}); **U–Ca**, Catechol in urine (mg. g Cr^{-}1, *: mg. L^{-1}); **Exh-B**, Un-metabolized benzene in exhaled air (mg. L^{-1}); **CS**, Cross-sectional; **CC**, Case-control; **Ex**, Exposed; **nEx**, Non-exposed; **NR**, Non report; **ND**, Not detected; **SD**, Standard variation; **GM**, Geometric mean; **GSD**, Geometric standard deviation, mean; **P**, Percentile.

* Corresponding author. Department of Occupational Health Engineering, Research Center for Health Sciences, School of Health, Larestan University of Medical Sciences, P.O. Box: 125, Postcode: 74331-93514, Larestan, Iran.

E-mail addresses: razzaghrahimpoor@yahoo.com (R. Rahimpoor), Hamed.jalilian@ucd.ie (H. Jalilian), Heidar.m1388@gmail.com (H. Mohammadi), Rahmaniabdolrasoul218@gmail.com (A. Rahmani).

https://doi.org/10.1016/j.heliyon.2023.e21576
Received 16 January 2023; Received in revised form 19 October 2023; Accepted 24 October 2023
Available online 31 October 2023

Consequently, it is possible for workers and the general public to be exposed to some occupational and accidental hazards. Generally, workers in a wide range of workplaces may expose to benzene and this exposure might be significant in oil processing industries, polymer or resin factories, rubber production facilities, and gasoline stations, oil processing industries, polymer or resin factories, rubber production facilities, and gasoline stations [1–4].

Human biomonitoring is identified as complementary to environmental monitoring and a useful tool for accurately assessing occupational exposure to chemicals, which is conducted periodically monitoring the amounts of unchanged chemical or its metabolites in the body's biological fluids, physiological changes, or enzymatic alteration [5]. A chemical may undergo several biotransformation processes (from entry into the body to excrete), resulting in a range of biomarkers [6]. So far, various biomarkers have been used to estimate occupational exposure to benzene as well as related health risk [2]. These biomarkers include unchanged benzene in blood [7], urine [8], and exhaled breath [9], ring hydrolyzed metabolites including phenol [10], catechol [11], and hydroquinone [12] in urine, ring open metabolites including Trans, *Trans*-muconic acid (TTMA) [13,14] and *S*- phenyl mercapturic acid (SPMA) in urine [15, 16], and blood protein adducts [17,18].

Until now, researchers have studied several biomarkers for biological monitoring of exposure to benzene, and sometimes conflicting results are seen because different biomarkers have been introduced and recommended at different levels of external exposure [19]. When conducting such studies, careful attention should be paid to confounding factors such as smoking, eating habits, timing of sampling during work shifts, selection of control groups. If these criteria are taken into monitoring, the results of the study can be expected to give a more accurate correlation between the exposure concentration and the level of metabolites in the body [20,21]. To the best of our knowledge, there are no published studies or comprehensive guidelines to provide conclusive evidence for determining the optimal benzene metabolites for varieties of concentrations and there is a tenuous compromise between various researchers in this area. Therefore, in this systematic review, we sought to these questions: Which benzene biomarkers should be selected for which level of benzene exposure? What are the confounding factors in the biological monitoring of benzene? What are the confounding factors in the biological monitoring of benzene?

2. Materials and methods

We registered this systematic review in the PROSPERO database (number: CRD42021268528) and the PRISMA statement was used which is an evidence-based minimum set of 27 items for reporting systematic reviews and meta-analyses [22].

2.1. Search strategy

A Systematic search was conducted in the online database SCOPUS, EMBASE, Web of Science, and PubMed (Medline) for time windows of 1985 to July 1, 2021, without geographic or language restriction. We used combinations of exposure and biomonitoring keywords with the Boolean operator "OR" and "AND" (Title, Abstract, and Keywords). The exposure keywords were "Benzene", "occupational exposure", "Workplace", "occupations", and biomonitoring keywords were "Biological monitoring", "Biomonitoring", "Biomarker", "urine", "blood", "breath air", "trans, trans, Muconic acid", "S- Phenylmercapturic acid", "Hydroquinone", "Phenol", and "Catechol". Furthermore, we used the Medical Subject Heading (MeSH) terms, including the "Benzene", "Biological Monitoring", "Biomonitoring", "Occupational Exposure", "Occupational Groups", "Occupations", "Muconic acid", "S-Phynel- N- actylcesteine", "Phenol", as well as "Hydroquinone". Details about the Search Strategy are available in the electronic supplementary.

2.2. Eligibility criteria

The original peer-reviews articles with the following criteria were included in the current review: (1) observational article (cross-sectional, cohort, case-control), and longitude, (2), full-text articles, (3) present original data, (4) preferred biological monitoring of occupational exposure to benzene, and (5) simultaneously reported benzene exposure and biomarker (s) concentration.

We excluded (1) published letters to the editor, (2) review articles, (3) single case studies, (4) modeling studies without original data, (5) laboratory, mechanism, or clinical articles, (6) non-occupational studies, (7) animal studies, and (8) non-English articles.

2.3. Study selection

The researchers (R.R and H.M) assessed the title, abstract, and keywords of records were screened. Moreover, the full text of some papers was evaluated if the title, abstract, and keywords did not supply enough data to prove its eligibility for the current study. A third party (AR. R) was included in the decision-making process, if R.R and H.M were not able to reach an agreement.

2.4. Data extraction

We (R.R and H.M) used a standardized sheet for extraction following data from included studies: study details (Author, publication year, study design, country of origin, and workplace industry), personal confounding factors, methods (number of an air sample, media, time, and number of the biological samples), and outcome data (descriptive statistics of inhalation concentration exposure and any biomarkers). Data were extracted separately in different occupational groups, exposed and non-exposed, male and female, pre, during, and post-shift work, and smokers and non-smokers. The average level of inhalation occupational exposure was categorized according to the TLV: $\leq$0.02, 0.02–0.2, 0.2–1.0, 1.0–2.0, 2.0–10, 10–20, and $\geq$20 times the TLV. Thus, it was classified into 7

categories (1: ≤0.032, 2: 0.032–0.32, 3: 0.32–1.6, 4: 1.6–3.2, 5: 3.2–16, 6: 16–32, and 7: >32 mg m^{-3}).

2.5. Risk of bias in individual studies

A score for quality, the Newcastle-Ottawa scale was used to assess the appropriateness of research design, representativeness of the sample, sample size, objectivity/reliability of outcome measurement, Comparability, and appropriate statistical analyses of cohort and case-control studies [23]. A modified from the Newcastle-Ottawa scale was used for cross-sectional studies [24]. Score disagreements were resolved by consensus after reference back to the original article. Finally, studies with a mean score greater than or equal to five were included. In brief, we considered seven sources of bias and classified the studies into low risk of bias (two stars), medium risk of bias (one star), high risk of bias (no star) (Table 2). The sum of stars indicates for each study the total risk of bias with a maximum of 10 stars referring to the lowest risk of bias [25].

2.6. Statistical analysis

In descriptive mode, the quantitative data were reported as mean, median, standard deviation (SD), minimum (min), and maximum (max). Qualitative data were reported as number (n) and percentage (%). The appropriate data were extracted from included studies using format prepared in Microsoft Excel Version 2019 and exported to the Statistical Package for Social Sciences (SPSS), version 22 (IBM, Armonk, NY, USA) for all analyses. All graphs were obtained from the Excel version 2019 (Microsoft, New Mexico, USA).

3. Results

3.1. Study selection

Initial systematic searches identified a total of 4786 records and after removing duplicates retrieved 4072 articles for screening titles and abstracts. We excluded 3828 records by screening titles and abstracts and another 178 when full-text locked. Finally, 66 studies were included in the systematic review (Fig. 1).

3.1.1. Study characteristics

A total of 64 cross-sectional studies (96.97 %) one case-control and one cohort study were eligible to be included in the current review. Of the 66 studies included, 40 were published between 1986 and 2009, and 26 were published more recently from 2010 to 2019 (Table 1). Most of studies conducted in the Italy (36.4 %), following by China (18.2 %), Iran (7.6 %), Thailand (6.1 %), Bulgaria (3.0 %), Brazil (3.0 %), Norway (3.0 %), South Korea (3.0 %), Singapore (3.0 %), and another (16.7 %); Belgium, Croatia, England, Estonia, France, Germany, India, Netherland, Tunisia, Sweden, and the USA. Two studies were done on the same workers, but they reported different metabolites [11,26].

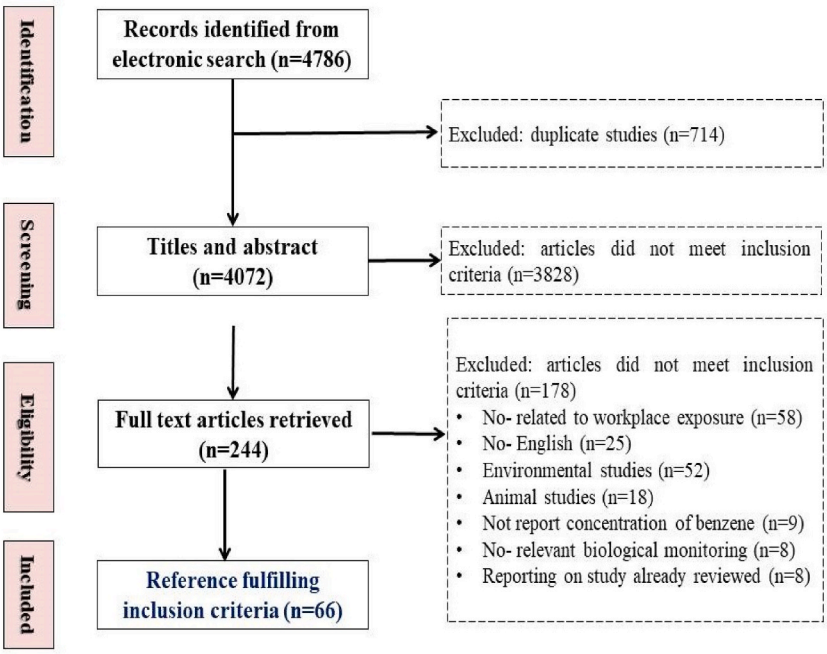


Fig. 1. PRISMA diagram for screening and selection papers.

Table 1
Details of the included studies in analysis.

Reference	Design	Location	Industry/Profession	Population	Biological matrix (Sampling time)
[10]	CS	China	Shoe factories	Ex:152, nEx:131	Urine (Post shift), Breath air (Post shift)
[27]	CS	UK	Coke oven	Ex:53, nEx:12	Urine (Pre and post shift), Blood (Pre and post shift), Breath air (Pre, mid and post shift)
[11]	CS	China	Shoe factories	Ex:152, nEx:131	Urine (Post shift)
[26]	CS	China	Shoe factories	Ex:152, nEx:213	Urine (Post shift)
[14]	CS	China	Petrochemical	Ex:14, nEx:8	Urine (Post shift)
[13]	CS	France	Perfume industry	Ex:23, nEx:79	Urine (Post shift)
[28]	CS	Germany	Car mechanics	Ex:20, nEx:6	Urine (Pre, mid and post shift), Blood (Post shift)
[29]	CS	Europe	Oil and gas industries	Ex:188, nEx:52	Urine (Pre and post shift)
[30]	CS	Singapore	Petrol refineries	Ex: 285	Urine (Post shift)
[17]	CS	Croatia	Shoe making	Ex:49, nEx:27	Urine (Pre and post shift), Blood (Post shift)
[12]	CS	Belgium	Coke plants,	Ex:200, nEx:200	Urine (Pre and post shift), Breath air (Post shift)
[31]	CS	Estonia	Petrochemical	Ex:90, nEx:39	Urine (Post shift), Blood (Post shift), Breath air (Post shift)
[32]	CS	Singapore	Gasoline terminals and refinery workers	Ex:280	Urine (Post shift), Blood (Post shift)
[33]	CS	China	Not defined	Ex:38, nEx:17	Urine (Post shift)
[34]	CS	Italy	Office worker	Ex: 100	Urine (Post shift), Blood (Post shift)
[35]	CS	South Korea	Resident near Petrochemical	Ex: 115	Urine (Post shift), Blood (Post shift)
[36]	CS	China	Glue- and shoe-making	Ex:25, nEx:25	Urine (Pre and post shift)
[37]	CS	Italy	Gasoline station	Ex:190	Urine (Pre and post shift), Blood (Post shift)
[8]	CS	China	Natural rubber	Ex:44, nEx:44)	Urine (Post shift)
[38]	CS	Italy	Pharmacies	Low Ex:12, High Ex: 19	Urine (Post shift)
[39]	CS	Italy	Traffic Wardens	Ex: 66, nEx:33	Urine (Post shift), Blood (Post shift)
[40]	CS	Tunisia	Gasoline station	Ex: 30, nEx:20	Urine (Pre and post shift)
[9]	CS	USA	Automobile mechanics	Ex: 82	Breath air (Pre and post shift)
[41]	CS	China	Glue-making	Ex: 130, nEx:51	Urine (Pre and post shift)
[42]	CS	Bulgaria	Petrochemical	Ex: 148	Urine (Pre and post shift)
[43]	CS	Brazil	Oil refinery	Ex: 36, nEx:116	Urine (Post shift)
[44]	CS	Italy	Traffic wardens and chemical laboratory	Ex:62	Urine (Post shift)
[45]	CS	Italy, Bulgaria	Petrochemical	Ex: 623	Urine (Post shift)
[46]	CS	Italy	Gas station attendants	Ex:366, nEx:49	Urine (Pre and post shift)
[47]	CC	Bulgaria	Petrochemical workers	Ex:158, nEx:50	Urine (Pre and post shift)
[48]	CS	Thailand	Petrochemical and station attendants	Ex:135	Urine (Pre and post shift), Blood (Post shift)
[49]	CS	China	Not defined	Ex:130, nEx:51	Urine (Pre and post shift)
[50]	CS	India	Gasoline station workers	Ex:29, nEx:30	Urine (Post shift)
[51]	CS	Italy	Gasoline filling-station	Ex: 33	Urine (Pre and Post shift)
[52]	CS	China	Shoe and cloth making	Ex:250, nEx:139	Urine (Post shift)
[53]	CS	Norway	Oil tank workers	Ex:10, nEx:9	Urine (Pre shift, Post shift, Next Pre shift), Blood (Pre shift, post shift, Next pre shift)
Reference	**Design**	**Location**	**Industry/Profession**	**Population**	**Biological matrix (Sampling time)**
[54]	CS	Iran	Taxi driver, Petrol station workers	Ex: 85, nEx:60	Urine (Post shift)
[55]	CS	Iran	Street sweepers	Ex:40, nEx:40	Urine (Post shift)
[56]	CS	Italy	Urban Policemen	Ex:114	Urine (Post shift)
[57]	CS	Italy	Traffic policemen	Ex:100	Urine (Post shift)
[58]	CS	Thailand	Traffic policemen	Ex:24, nEx:24	Urine (Pre and post shift), Blood (Post shift)
[59]	CS	Italy	Petrochemical	Ex:145	Urine (Post shift)
[60]	CS	Italy	Petrochemical and station attendants	Ex:82, nEx:51	Urine (Post shift)
[61]	CS	Italy	Petrol Refinery	Ex:168, nEx:108	Urine (Post shift)
[7]	CS	Italy	Fuel terminals	Ex: 41, nEx:31	Urine (Post shift)
[62]	CS	Italy	Traffic policemen	Ex: 70, nEx:40	Urine (Post shift)
[63]	CS	Italy	Traffic policemen	Ex: 130	Urine (Pre and post shift)
[64]	CS	Italy	Not defined	Ex: 137	Urine (Post shift)
[65]	CS	China	Shoe-making	Ex: 44	Urine (Pre and post shift)
[66]	CS	Italy	Oil refinery	Ex: 32, nEx:65	Urine (Pre and post shift)
[67]	Cohort	Italy	Petrochemical	Ex:28	Urine (Post shift)
[68]	CS	Norway	Offshore petroleum	Ex: 25, nEx:18	Urine (Pre and post shift), Blood (Pre and post shift)
[69]	CS	Italy	Traffic policewomen,	Ex: 69, nEx:22	Urine (Post shift), Blood (Post shift at last day of week)
[70]	CS	Italy	Traffic policemen.	Ex:139, nEx:110	Urine (Post shift), Blood (Post shift)
[71]	CS	China	Shoe-making	Ex: 55	Urine (Post shift)
[72]	CS	Iran	Petrochemical workers	Ex: 104	Urine (Post shift)
[73]	CS	Italy	Petrol station workers	Ex: 89, nEx:90	Urine (Baseline [Frist day of the week], pre and post shift)

(*continued on next page*)

Table 1 (*continued*)

Reference	Design	Location	Industry/Profession	Population	Biological matrix (Sampling time)
[74]	CS	Iran	Petrochemical workers	Ex: 84	Urine (Pre and post shift)
[75]	CS	Iran	Chemical workers	Ex:108, nEx:140	Urine (Pre and post shift)
[76]	CS	Thailand	Car parking workers	Ex: 50	Urine (Pre and Post shift)
[16]	CS	Italy	Coke production	Ex: 93	Urine (Post shift)
[21]	CS	Italy	Refinery workers	Ex:146, nEx:25	Urine (Post shift)
[77]	CS	South Korea	Maintenance workers	Ex: 474	Urine (Post shift)
[78]	CS	Thailand	Gasoline station	Ex: 170	Urine (Post shift)
[79]	CS	Brazil	Filling station workers	Ex: 86	Urine (Post shift)
[80]	C–C	Sweden	Transporting Gasoline	Ex: 22, nEx:21	Urine (Pre and post shift) Breath air (Pre and post shift)

3.2. Risk of bias in individual studies assessment

The quality of included studies was to be good (mean: 7.73, range: 6–10). Of the 66 studies, 2 (3.03 %) scored 10, 13 (19.7 %) scored 9, 21 (31.81 %) scored 8, 27 (40.91 %) scored 7, and 3 (4.55 %) scored 6 (Table 2).

3.3. Level of inhalation exposure to benzene and its biological indicators

Occupational exposure to benzene often occurs through inhalation way, although skin exposure may also occur [5]. The American Conference of Governmental Industrial Hygienists (ACGIH) has recommended a threshold limit value (TLV) of 0.064 mg m^3 (0.02 ppm) for airborne exposure, which is accepted by many countries worldwide [82,83]. Benzene can cause leukemia and pancytopenia by targeting the hematopoietic system, and therefore is classified as carcinogenic to humans (1A) [84]. Additionally, the evidence indicated that airborne exposure to benzene associated with acute and chronic adverse effects on numerous systems of the body, including the nervous system, inhalation system, immune system, and reproductive and developmental systems [54,84,85].

Table S1 describes the main findings of all identified studies evaluating occupational exposure to benzene and its biological monitoring. The results reflects that the inhalation and biological monitoring of occupational exposure to benzene has been carried out in various type occupations, most of which were involved in the production, extraction, consumption, and storage of benzene. Data analysis shown that the average level of inhalation exposure to benzene in different industries is almost twelve times higher as the TLV-TWA level. Additionally, the mean concentration of inhalation occupational exposure to benzene in different industries is almost three hundred times higher as the TLV-TWA level (Mean: 19.34, Median: 0.54, SD: 56.98, Range: 0.005–357.8, and TLV-TWA: 0.064 mg m^{-3}). The results showed that the concentration of inhalation exposure in 18 studies was less than 0.032 mg m^{-3}, in 23 studies in the range of 0.032–3.2 mg m^{-3} (13 studies in the range of 0.032–0.32, 6 studies in the range of 0.32–1.6, and 4 studies in the range of 1.6–3.2 mg m^{-3}), in 16 studies was in the range of 3.2–32 mg m^{-3} (12 studies in the range of 3.2–16.0 and 4 studies in the range of 16.0–32.0 mg m^{-3}), and in 8 studies was higher than 32.0 mg m^{-3}. Figs. 2–5 represent the mean concentration of examining biomarkers based on the various levels of inhalation occupational exposure.

3.3.1. Inhalation exposure to benzene in different occupations

In this review study, based on the type of job and industry, the level of inhalation exposure to benzene and the level of its biological indicators were analyzed. Preliminary results showed that workers in the workplaces often deal with the manufacturing, using and storing of benzene, and based on that, the identified studies were classified into 5 categories as follows: A) industries user benzene as a solvent (shoe making, glue making, chemical industries, paint and printing plants, coke plants, perfume industries, car and automobile mechanic, pharmaceutical industries, and maintenance workers), B) industries manufacturer benzene and its derivatives (petrochemical, oil refining, fuel terminal workers, oil depots workers, and offshore petroleum workers), C) Fuel distribution stations (gasoline and gas stations), D) traffic police and drivers (bus and taxi drivers, oil tank drivers, street sweeper, traffic warden and traffic police), and E) office workers. The results showed that the highest and lowest concentration of occupational exposure to benzene were reported in industries user benzene as a solvent and Fuel distribution stations (42.72 ± 71.73 and 0.26 ± 0.38 mg m^{-3}, respectively), respectively. Figs. S1–S4 depict the average concentration of benzene biomarkers based on the type of industries.

3.4. Biological indicators of benzene

A valid biomarker exposure must be correlated with the external dose of the interest chemical, and also be useful to assess dose-response and dose-effect relationships [21]. Therefore, the main role of biomarkers is to assess occupational exposure to chemical toxins through all absorption routs of and also complement workplace environmental monitoring data [5,86,87].

The well-recognized metabolic pathways of benzene in the biotransformation process are enzyme-dependent and accessible to these enzymes (GST, CYP, CYP2E1, NQO1, and MPO) might change at different concentrations [16,88]. This can cause changes in the benzene biomarker levels at different concentrations of exposure to benzene [52].

Although different types of biomarkers were identified in various industries (Fig. 6), TTMA in urine (47 studies), SPMA in urine (32 studies), and urinary benzene (21 studies) were the most commonly used metabolites. It should be noted that urinary hydroquinone and urinary catechol biomarkers had been investigated prior to 2007 (See Table S1).

Table 2
Quality assessment of included studies using Newcastle-Ottawa scale.

Reference	Methodology quality (5)	Comparability (2)	Outcome or exposure (3)	Total score (10)
Cross- Sectional studies (n = 64)rowhead				
[10]	★★★	★	★★	6
[27]	★★★	★★	★	6
[11]	★★★	★★	★★	6
[26]	★★★★	★★	★	6
[14]	★★★★★	★	★	5
[13]	★★★★	★★	★★★	8
[28]	★★★★	★★	★★	8
[29]	★★★★	★★	★★	8
[30]	★★★	★★	★★★	8
[17]	★★★	★★	★★	7
[12]	★★★★	★★	★★	8
[31]	★★★★	★★	★★	8
[32]	★★★	★	★★	6
[33]	★★	★	★★	5
[34]	★★★	★	★★	6
[35]	★★★	★★	★★	7
[36]	★★★★	★★	★★	8
[37]	★★★★	★	★★	7
[8]	★★★	★★	★★	7
[38]	★★★	★	★★	6
[39]	★★★	★★	★★	7
[40]	★★★	★	★★	6
[9]	★★★	★★	★★	7
[41]	★★★★	★	★★	7
[42]	★★	★	★★	5
[43]	★★★	★★	★★	7
[44]	★★	★★	★★	6
[45]	★★★	★★	★★★	8
[46]	★★★★	★★	★★★	9
[47]	★★★	★★	★★	7
[48]	★★★	★	★★	6
[49]	★★	★	★★	5
[50]	★★	★	★★	5
[51]	★★★	★★	★★	7
[52]	★★★★★	★★	★★★	10
[53]	★★	★	★★	5
[81]	★★★	★	★★	6
[55]	★★★	★	★★	6
[56]	★★★★	★	★★	7
[57]	★★★	★★	★★★	8
[58]	★★★★★	★★	★★	9
[59]	★★★	★★	★★★	8
[60]	★★★★	★★	★★★	9
[61]	★★★★★	★★	★★	9
[7]	★★★★★	★	★★★	9
[62]	★★★	★★	★★★	8
[63]	★★★	★★	★★	7
[64]	★★★	★	★★	6
[65]	★★★	★★	★★	7
[66]	★★★★	★★	★★★	9
[68]	★★★★	★★	★★	8
[69]	★★★★★	★★	★★	9
[70]	★★★★★	★★	★★★	10
[71]	★★★★	★	★★	7
[72]	★★★	★	★★	6
[73]	★★★★	★★	★★★	9
[74]	★★★	★	★★	6
Reference	Methodology quality (5)	Comparability (2)	Outcome or exposure (3)	Total score (10)
[75]	★★★★	★★	★★	8
[76]	★★★	★	★★	6
[16]	★★★	★★	★★	7
[21]	★★★★	★★	★★★	9
[77]	★★★★	★★	★★	8
[78]	★★★	★★	★★	7
[79]	★★★	★★	★★★	8
Case- Control study (n = 1)rowhead				

(*continued on next page*)

Table 2 (*continued*)

Reference	Methodology quality (5)	Comparability (2)	Outcome or exposure (3)	Total score (10)
[80]	★★★★	★★	★★	8
Retrospective cohort Study (n = 1)rowhead				
[67]	★★★★	★★	★★★	9

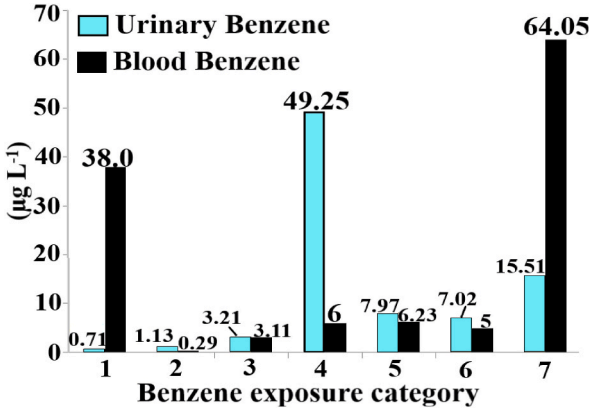


Fig. 2. Concentration of urinary benzene and blood benzene by the levels of inhalation exposure to benzene (1: <0.032, 2: 0.032–0.32, 3: 0.32–1.6, 4: 1.6–3.2, 5: 3.2–16, 6: 16–32, and 7: >32 mg m^{-3}).

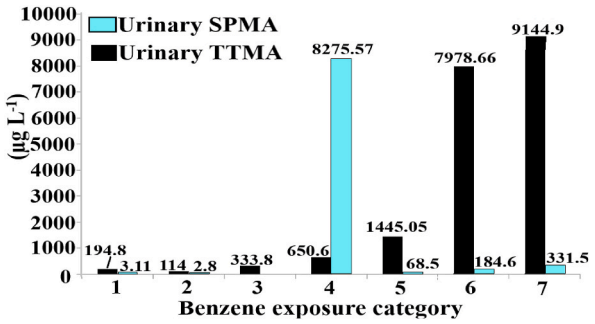


Fig. 3. Concentration of urinary *S*-PMA and urinary TTMA by the levels of inhalation exposure to benzene (1: <0.032, 2: 0.032–0.32, 3: 0.32–1.6, 4: 1.6–3.2, 5: 3.2–16, 6: 16–32, and 7: >32 mg m^{-3}).

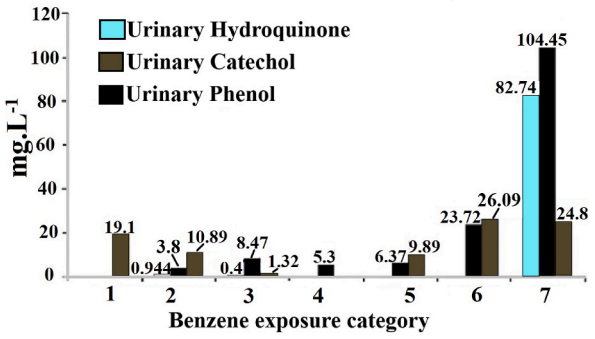


Fig. 4. Concentration of urinary hydroquinone, urinary phenol, and urinary catechol by the levels of inhalation exposure to benzene (1: <0.032, 2: 0.032–0.32, 3: 0.32–1.6, 4: 1.6–3.2, 5: 3.2–16, 6: 16–32, and 7: >32 mg m^{-3}).

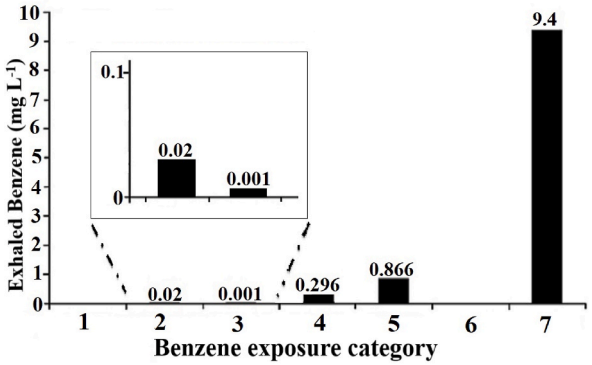


Fig. 5. Concentration of exhaled benzene by the levels of inhalation exposure to benzene (1: <0.032, 2: 0.032–0.32, 3: 0.32–1.6, 4: 1.6–3.2, 5: 3.2–16, 6: 16–32, and 7: >32 mg m^{-3}).

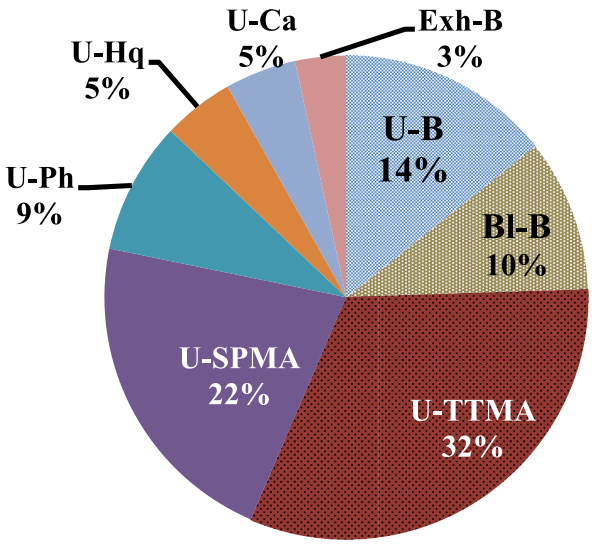


Fig. 6. The benzene biomarker addressed by the included studies.

3.5. Confounding factors

Several inter or intra-covariates such as age, gender, smoking, diet, body mass index, and single-nucleotide polymorphism can affect the metabolism rate of benzene [21]. For example, cigarette smoking with directly expose a person to benzene, equal to low-level occupational exposure, increase urinary *S*-PMA and TTMA or a diet containing sorbic acid and its salts can significantly alter the level of the urinary TTMA [7,18,89,90].

The results of the confounding effect of smoking habit on the level of biomarkers of benzene exposure, the covariates considered in the studies, as well as a summary of the study outcomes are found in Table S2. Overall, U-TTMA (n = 18), U-SPMA (n = 16) and urinary benzene (n = 11) were identified as suitable and valid biomarker monitoring of workers exposed to benzene (Table S2).

Of the 66 included studies, 36 studies (54.54 %) examined the effect of smoking habit on the concentration of benzene biomarkers has been investigated and the concentration of biomarkers has been reported for the smoker and non-smoker workers separately. The results of most studies indicate that smoking before and during the work shift had a significant confounding effect on the concentration of benzene biomarkers such as of U-TTMA (22 studies), U-SPMA (13 studies) and urinary benzene (10 studies) (Table S2). The significant effects of smoking habit on the U-TTMA and U-SPMA level (with 20 % concentration variance) have been reported in workers exposed to benzene by inhalation (<0.48 mg m^{-3}: <0.3 time the TLV) [33,41,44,49,55,59,67,68,75,77,91].

Additionally, three studies confirmed that sorbic acid consumption has a significant effect on the U-TTMA levels (M. Carrieri et al., 2006; Jalai et al., 2017; Panev et al., 2002). It was observed in three studies, that alcohol consumption 48 h before sampling had no a significant influence on the level of benzene biomarkers [12,43,56]. Several studies revealed that co-exposure to toluene can be confounding factors effect in changing the concentration of both U-TTMA and U-SPMA biomarkers [21,26,56].

4. Discussion

The results of the current systematic review show that none of the introduced biomarkers to date are able to function optimally for the biological monitoring of all workers employed in different industries. Because the biotransformation process benzene is an enzymatic pathway that benzene undergoes after entering the body depend on the concentration exposure. Therefore, before choosing the optimal biological index, the concentration and the route of exposure, as well as the personal habits of workers, should be assessed.

4.1. Biotransformation process of benzene

The level of exposure determines which enzymatic pathway is activated for detoxification and excretion of benzene from the body. In the phase II, benzene is metabolized to benzene oxide or benzene oxepin through an oxidation reaction (by cytochrome P450: CYP2E1). Then, depending on the concentration of xenobiotic exposure to benzene, benzene oxide follows different pathway: Non-enzymatic rearrangement (metabolized to phenol), hydrolysis to a ring-opening dihydro dial (metabolized to TTMA), and glutathione conjugation (metabolized to SPMA). These metabolites may undergo further metabolism by oxidation (phenol to hydroquinone or catechol), dehydrogenation (TTMA to catechol and SPMA to hydroquinone), or conjugation with sulfate or glucuronic acid (phenol to phenol sulfate) [92,93].

4.2. Optimal biological index according to the level of inhalation exposure

The best biomarker is the one that has the highest sensitivity and specificity in relation to exposure, outcome, or susceptibility. Most studies indicate that the best exposure biomarker may depend on the level of inhaled benzene exposure as follows: un-metabolized benzene in urine at low concentration (0.032–0.32 mg m^{-3}:0.05–5 times the TLV) [8,16,37,45,46,56,57,61,64,66,68,73,92], U-SPMA at medium concentration (0.32–1.6 mg m^{-3}) [7,12,15,16,21,28,35,36,41,45,49,57–59,62,67,70,71], and U-TTMA at high concentration (1.6–3.2 mg m^{-3}) of inhalation benzene exposure [8,10,12,14,16,28,29,31,33,41,45,49,50,59,65,67,70,72,78,80,81]. In contrast, ten studies reported that U-TTMA is not an accurate biomarker at concentrations less than 0.32 mg m^{-3} [46,50,52,53,58,63,67,74,76,80].

With increasing benzene concentration above 3.2 mg m^{-3} (>50 times the TLV), the biomarkers metabolized during phase II of the benzene biotransformation are better suited to assess inhalation exposure as follows: U-Ph [10,11,36] and U-Hq (at $\geq$ 32 mg m^{-3}) [10,36], and U–Ca (at $\geq$ 64 mg m^{-3}) [26,33]. Therefore, the concentration of inhaled benzene exposure plays a key role in choosing the optimal biomarker of biological benzene exposure.

Studies have shown that blood benzene is suitable for biological monitoring of exposure to benzene at very low concentrations less than 0.032 mg m^{-3}. Blood benzene is an indication of recent external exposure to benzene, i.e. background or environmental exposure, and when occupational benzene exposure is short-term (i.e. a few minutes), blood benzene along with air sample can be used as a suitable biomarker in the biological monitoring of benzene [58,61,92,94].

In occupational exposures near or below the TLV level, the lack of strong consistency between the results of most occupational studies makes it difficult to select appropriate exposure metabolites [19]. For instance, some studies have suggested that TTMA is the best metabolite exposure below the TLV [40,42], while several studies recommend SPMA [29,49] or unmetabolized benzene in urine [46,56]. In these cases, if the exposure metabolites are not properly selected, the results of biological monitoring may not be helpful in detecting the early adverse changes in the body [87]. This is in spite of the fact that the TLV changes annually and has a downward trend: from 1977 to 2022 it has decreased by about 500 times (32–0.064 mg m^{-3}) [95–98]. It should be noted that this downward trend can be seen in other organizations that publish the occupational exposure limit for benzene [95,99,100]. Generally, with the reduction of the TLV of benzene, as a rule, the level of occupational exposure of workers will decrease, and it affects the choice of optimal biological exposure index. So that the recommended biological exposure index of benzene by the ACGIH in 1994, and 2000 to 2021 were proposed the urinary phenol, and both urinary TTMA and urinary SPMA, respectively [96–99]. This evidence indicates that the change in BEI of benzene will corresponds to the trend of TLV and therefore the level of inhalation exposure to benzene should be determined prior to select the best biomarker.

On the other hand, the results showed that the concentration of inhalation exposure to benzene is differs among the workers in various industries. The highest concentration of occupational benzene exposure was reported among workers in solvent-related industries (42.72 $\pm$ 71.73 mg m^{-3}) and also oil and gas-related industries (13.19 $\pm$ 61.33 mg m^{-3}). The highest concentration of U–B, U-TTMA, U-SPMA, U-Ph, and U-Hq observed in highly-exposed workers (i.e., industries related to solvents). Occupational exposure to benzene among workers in these industries is very higher than among office workers (6.57 $\pm$ 13.11 mg m^{-3}), traffic policies or drivers (0.75 $\pm$ 2.86 mg m^{-3}), or fuel distribution station workers (0.26 $\pm$ 0.38 mg m^{-3}). It should be noted that U-Ph and U-Hq biomarkers were not determined in traffic policies or drivers, fuel distribution station workers, and office workers. In addition, the number of studies on office workers is limited (5 studies) and even some of them have not defined office workers in industrial and non-industrial settings, and the range and standard deviation in the concentration of benzene and its biomarkers is very wide [16,33–35,49].

Biomarkers for nucleic acid methylation have been the focus of recent research on biological monitoring of exposure to low levels of benzene in public and industrial environments [101,102]. The most common of these biomarkers are malondialdehyde, 8-hydroxylamine, 8-hydroxy 2′deoxyguanosine, 8-hydroxy-7,8-dihydroguanosine, 5-methyl-cytosine, 1-methyl-guanine, and 7-methyl-guanine [103,104]. It has been reported in previous studies that the biomarkers of 8-hydroxy-7,8-dihydroguanosine and 5-methyl cysteine could be utilized to assess changes in the nucleic acid methylation status due to exposure to low levels of benzene [101–103]. Non-occupational confounding factors have been proven to have a significant impact on these biomarkers and may reduce their

validity [103,105,106]. To assess the accuracy and validity of these biomarkers, it is necessary to conduct more studies.

4.3. Confounding factors

4.3.1. Tobacco smoke

The results of most studies confirm that the effect of smoking before and during the work shift has a significant confounding effect on the concentration of biomarkers Exh-B, U–B, U-TTMA and U-SPMA after exposure to benzene at low concentrations ($\leq$0.48 mg m^{-3}). Carbonaro et al. confirmed that the SPMA and TTMA concentrations are lower, and TTMA/SPMA ratio is higher in non-smokers than in smokers [107]. The reviewed studies showed that the concentrations of TTMA and SPMA in post-shift urine samples obtained from smoker workers were 1.5–2 times higher than non-smokers [7,16,21,37,40,46,55,57,59–61,66,67,72,73,75,78,79,91]. Previous studies confirmed the benzene in cigarette tobacco and reported that smoking leads to chronic exposure to low levels of benzene and increases the risk of leukemia [108–111]. After smoking a cigarette, about 0.46 mg m^{-3} of benzene enters the respiratory tracts, which is more in heavy smokers, and this may confound the biological outcome of occupational exposure to benzene at low concentrations [56,73,79,93,109,112,113]. Over the past two decades, applying legal restrictions and reducing the level of threshold limit values have played a significant impact on reducing human exposure to benzene in public and occupational settings [100,114–116]. However, ignoring lifestyle parameters (i.e. cigarette smoking habit) when determining biological exposure limits leads to unrealistic and inaccurate results [20,21,117]. In some studies, it has been acknowledged that in addition to personal questionnaires, it is important to measure the level of urinary metabolites of nicotine (such as cotinine) to control the confounding effect of tobacco smoking on the level of urinary metabolites of benzene. Because some people are environmental exposed to tobacco smoke and consider themselves non-smoker [102,118,119]. It may be better to recommend the BEI of benzene for smoking and non-smoking workers separately. Of course, avoiding smoking during the work shift and also comparing the concentration of biomarkers in biological samples pre and post-shift can be helpful in controlling for this confounding factor.

4.3.2. Food preservative

TTMA is metabolized after consumption of the food preservatives containing sorbates (calcium sorbate, potassium sorbate, sodium sorbate, E200, and E201) and sorbic acid (up to 447 mg or three doses of 1 mg kg^{-1}) [120–123]. Likewise, the results of the included studies show that oral intake of sorbic acid has a significant effect on the U-TTMA level, but has no confounding effect on U-SPMA level. Therefore, it is recommended to compare the concentration of TTMA in the pre and post-shift urine samples to control for this confounding factor [42,75,91].

4.3.3. Genetic polymorphism

Some studies have reported the effect of glutathione *S*-transferase (GST) genetic polymorphism on U-SPMA level [32,67,120]. In phase II of the benzene biotransformation process, benzene oxide is metabolized to SPMA by glutathione conjugation, so the U-SPMA is modulated by the genetic polymorphism of GST, since a significant depletion in its urinary excretion was observed in workers with a "null" GSTT1 genotype [120,124,125]. It has been proven that GSTM1 has the same effects, but it only affects smokers [108]. While some studies have suggested that the TTMA/SPMA ratio is a suitable biomarker for controlling the confounding effect of tobacco smoking, researchers have found that GSTTI and GSTM1 polymorphisms have a confounding effect on TTMA/SPMA concentration ratio [49,107,108]. To control this confounding factor, workers with GSTT1 or GSTM1 "null" genotype should be identified as well as the SPMA concentration in urine samples before and after the work shift should be compared [32,49,61,67,108].

Furthermore, previous research has demonstrated that the SPMA precursor (N-acetyl-S(1,2-dihydro-2-hydroxyphenyl)-L-cysteine) in the urine sample may be converted to SPMA during the sample storage or preparation [126–128]. The overestimation of the concentration of SPMA measured can be prevented by hydrolyzing the SPMA precursor by acidifying the urine samples (pH = 2) [29,126]. During the preparation and analysis of urinary SPMA, it is recommended to consider the pH of the sample as a critical factor.

Recent epidemiological studies have shown that environmental exposure to benzene is related to the occurrence of leukemia and other lymphohematopoietic cancers in humans in the general public, which has raised concerns [129–131]. Results from previous studies indicate that the level of environmental exposure to benzene varies greatly (0.001–300 ppm) and is often below 1.0 ppm [56,94,104]. The most common biomarkers used to estimate environmental exposure and risk of benzene in the general population include unmetabolized benzene in blood and urine, urinary TTMA, and SPMA [94,102,132]. This is in spite of the fact that these biomarkers are influenced by confounding factors, as confirmed by previous studies. It has been found that U–B, U-TTMA, and U-SPMA levels differ significantly between smokers and non-smokers, genetic polymorphism on the level of U-SPMA, and the consumption of food preservatives is a major influence on the level of U-TTMA among the general population [102,104,133]. Hence, in order to control confounders, it is suggested to avoid smoking and consuming food preservatives hours before sampling and identify individuals with a "null" GSTT1 genotype.

Limitations observed in some of the included articles were as follows: Indeterminate the occupational history of exposure to benzene, uncertain the number of cigarettes smoked per day, the incompleteness of the descriptive statistics of the results, not comparing the level of biomarkers pre- and post-shift work, failure to measure urine creatinine, and not investigating the relationship between the concentration of inhalation exposure and biomarkers.

We suggest that in the biological monitoring program of occupational exposure to benzene, it is better to consider the following:

- Selection of biological index based on the level of inhalation exposure to benzene
- Measurement of the level of the biological index at pre and post-shift work

- Avoid cigarette smoking on the sampling day
- Avoid eating foods containing sorbic acid and alcohol from 48 h before sampling
- Identification workers with a "null" GSTT1 genotype

Highlights of the current study include a review and summarizing of findings in studies related to biological monitoring of occupational exposure to benzene, summarizing the findings related to the level of each biological index based on the level of inhalation exposure to benzene, summarizing the findings related to the levels of inhalation exposure to benzene and its biological indices based on the type of industry, review of the effect of gender, tobacco smoking, genetic polymorphism, food preservative, and co-exposure to other pollutants on biological indicators of benzene, introduce some of the confounding factors in the biological monitoring of benzene and suggestions on how to control them, and suggest the optimal biological index according to the level of inhalation exposure to benzene.

It is important to note several limitations in this review study. First, only English-language and occupational studies were reviewed and non-English language and environmental exposure studies were excluded from our study. Second, we reviewed the level of exposure to benzene by inhalation way and did not investigate non-inhalation ways. Third, blood protein adducts and the genetic damage indicators of benzene were not investigated. Fourth, our criterion of occupational exposure limit to benzene was ACGIH- TLV and other suggested limits were not taken into consideration. Fifth, we did not examine the technical-laboratory capabilities necessary to determine each of the biological indexes of benzene, which may affect experts' choice of the optimal index in different countries.

5. Conclusions

This current systematic review showed that the concentration of external exposure to benzene has a key role in the choice of the biomarker, therefore, it would be better to choose and measure the index of biological exposure to benzene based on the level of inhalation exposure in the biological monitoring program. In respiratory exposure at levels below and close to the TLV, lifestyle parameters have a significant effect on the concentration of biological indices and have a confounding effect on the results of biological monitoring. In order to choose the appropriate indicator for biological monitoring of benzene exposure, it is recommended to assess the concentration of external exposure, smoking habit, oral intake of sorbic acid, and genetic polymorphism of workers.

Funding

This research work was founded by Larestan University Medical of Sciences (Grant No. 1399-88, IR.LARUMS.REC.1400.004).

Ethics

Not applicable.

Data availability statement

Data included in article/supp. Material/referenced in article.

CRediT authorship contribution statement

Razzagh Rahimpoor: Writing – original draft, Supervision, Project administration, Methodology, Funding acquisition, Data curation, Conceptualization. **Hamed Jalilian:** Writing – review & editing, Visualization, Validation, Software. **Heidar Mohammadi:** Validation, Formal analysis, Data curation. **Abdulrasoul Rahmani:** Validation, Formal analysis, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e21576.

References

[1] H. Bahadar, S. Mostafalou, M. Abdollahi, Current understandings and perspectives on non-cancer health effects of benzene: a global concern, Toxicol. Appl. Pharmacol. 276 (2014) 83–94.

[2] L. Falzone, A. Marconi, C. Loreto, S. Franco, D.A. Spandidos, M. Libra, Occupational exposure to carcinogens: benzene, pesticides and fibers (Review), Mol. Med. Rep. 14 (2016) 4467–4474.
[3] E. Partovi, M. Fathi, M.J. Assari, R. Esmaeili, A. Pourmohamadi, R. Rahimpour, Risk assessment of occupational exposure to BTEX in the national oil distribution company in Iran, Chronic Diseases Journal 4 (2018) 48–55.
[4] P. Modesti, G. Reboldi, F. Cappuccio, Newcastle- Ottawa: Quality assessment scale adapted for cross-sectional studies, PLoS One 11 (2016), e0147601.
[5] C. Ladeira, S. Viegas, Human biomonitoring – an overview on biomarkers and their application in occupational and environmental health, Biomonitoring (2016) 3.
[6] R. Bevan, J. Angerer, J. Cocker, K. Jones, H.M. Koch, O. Sepai, G. Schoeters, R. Smolders, L. Levy, Framework for the development and application of environmental biological monitoring guidance values, Regul. Toxicol. Pharmacol. 63 (2012) 453–460.
[7] P. Lovreglio, A. Barbieri, M. Carrieri, L. Sabatini, M.E. Fracasso, D. Doria, I. Drago, A. Basso, M.N. D'Errico, G.B. Bartolucci, F.S. Violante, L. Soleo, Validity of new biomarkers of internal dose for use in the biological monitoring of occupational and environmental exposure to low concentrations of benzene and toluene, Int. Arch. Occup. Environ. Health 83 (2010) 341–356.
[8] S. Waidyanatha, N. Rothman, S. Fustinoni, M.T. Smith, R.B. Hayes, W. Bechtold, M. Dosemeci, L. Guilan, S. Yin, S.M. Rappaport, Urinary benzene as a biomarker of exposure among occupationally exposed and unexposed subjects, Carcinogenesis 22 (2001) 279–286.
[9] P.P. Egeghy, L. Nylander-French, K.K. Gwin, I. Hertz-Picciotto, S.M. Rappaport, Self-collected breath sampling for monitoring low-level benzene exposures among automobile mechanics, Ann. Occup. Hyg. 46 (2002) 489–500.
[10] O. Inoue, K. Seiji, M. Kasahara, H. Nakatsuka, T. Watanabe, S.G. Yin, G.L. Li, C. Jin, S.X. Cai, X.Z. Wang, et al., Quantitative relation of urinary phenol levels to breathzone benzene concentrations: a factory survey, Br. J. Ind. Med. 43 (1986) 692–697.
[11] O. Inoue, K. Seiji, M. Kasahara, H. Nakatsuka, T. Watanabe, S.G. Yin, G.L. Li, S.X. Cai, C. Jin, M. Ikeda, Determination of catechol and quinol in the urine of workers exposed to benzene, Br. J. Ind. Med. 45 (1988) 487–492.
[12] P. Hotz, P. Carbonnelle, V. Haufroid, A. Tschopp, J.-P. Buchet, R. Lauwerys, Biological monitoring of vehicle mechanics and other workers exposed to low concentrations of benzene, Int. Arch. Occup. Environ. Health 70 (1997) 29–40.
[13] P. Ducos, R. Gaudin, J. Bel, C. Maire, J.M. Francin, A. Robert, P. Wild, trans,trans-Muconic acid, a reliable biological indicator for the detection of individual benzene exposure down to the ppm level, Int. Arch. Occup. Environ. Health 64 (1992) 309–313.
[14] W.E. Bechtold, G. Lucier, L.S. Birnbaum, S.N. Yin, G.L. Li, R.F. Henderson, Muconic acid determinations in urine as a biological exposure index for workers occupationally exposed to benzene, Am. Ind. Hyg. Assoc. J. 52 (1991) 473–478.
[15] P.J. Boogaard, N.J. van Sittert, Suitability of S-phenyl mercapturic acid and trans-trans-muconic acid as biomarkers for exposure to low concentrations of benzene, Environ. Health Perspect. 104 (Suppl 6) (1996) 1151–1157.
[16] P. Lovreglio, G. De Palma, A. Barbieri, R. Andreoli, I. Drago, L. Greco, E. Gallo, L. Diomede, P. Scaramuzzo, M.C. Ricossa, J. Fostinelli, P. Apostoli, L. Soleo, Biological monitoring of exposure to low concentrations of benzene in workers at a metallurgical coke production plant: new insights into S-phenylmercapturic acid and urinary benzene, Biomarkers 23 (2018) 70–77.
[17] A. Bogadi-Sare, R. Turk, V. Karacić, M. Zavalić, K. Trutin-Ostović, Red blood cell glycerol lysis and hematologic effects in occupational benzene exposure, Toxicol. Ind. Health 13 (1997) 485–494.
[18] L.-C. Lin, W.-J. Chen, Y.-M. Chiung, T.-S. Shih, P.-C. Liao, Association between GST genetic polymorphism and dose-related production of urinary benzene metabolite markers, trans, trans-muconic acid and S phenylmercapturic acid, Cancer Epidemiol. Biomarkers Prev. 17 (2008) 1460–1469.
[19] G.D. Palma, M. Manno, Metabolic polymorphisms and biomarkers of effect in the biomonitoring of occupational exposure to low-levels of benzene: state of the art, Toxicol. Lett. 231 (2014) 194–204.
[20] S. Dugheri, G. Pizzella, N. Mucci, A. Bonari, G. Cappelli, M. Santillo, I. Rainaldi, I. Pompilio, M. Carrara, V. Rapisarda, S. De Sio, G. Arcangeli, Low-dose benzene exposure monitoring of oil refinery workers: inhalation and biomarkers, Atmosphere 13 (2022) 450.
[21] M. Carrieri, G. Spatari, G. Tranfo, D. Sapienza, M.L. Scapellato, G.B. Bartolucci, M. Manno, Biological monitoring of low level exposure to benzene in an oil refinery: effect of modulating factors, Toxicol. Lett. 298 (2018) 70–75.
[22] A. Liberati, D.G. Altman, J. Tetzlaff, C. Mulrow, P.C. Gøtzsche, J.P.A. Ioannidis, M. Clarke, P.J. Devereaux, J. Kleijnen, D. Moher, The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration, J. Clin. Epidemiol. 62 (2009) e1–e34.
[23] P. Modesti, G. Reboldi, F. Cappuccio, Newcastle-Ottawa Quality Assessment Scale (adapted for cross sectional studies), PLoS One 11 (2016), e0147601.
[24] R. Herzog, M.J. Álvarez-Pasquin, C. Díaz, J.L. Del Barrio, J.M. Estrada, Á. Gil, Are healthcare workers' intentions to vaccinate related to their knowledge, beliefs and attitudes? a systematic review, BMC Publ. Health 13 (2013) 154.
[25] S. Dongus, H. Jalilian, D. Schürmann, M. Röösli, Health effects of WiFi radiation: a review based on systematic quality evaluation, Crit. Rev. Environ. Sci. Technol. 52 (2022) 3547–3566.
[26] O. Inoue, K. Seiji, H. Nakatsuka, T. Watanabe, S.N. Yin, G.L. Li, S.X. Cai, C. Jin, M. Ikeda, Urinary t,t-muconic acid as an indicator of exposure to benzene, Br. J. Ind. Med. 46 (1989) 122–127.
[27] L. Drummond, R. Luck, A.S. Afacan, H.K. Wilson, Biological monitoring of workers exposed to benzene in the coke oven industry, Br. J. Ind. Med. 45 (1988) 256–261.
[28] W. Popp, D. Rauscher, G. Miiller, J. Angerer, K. Norpoth, Concentrations of benzene in blood and S-phenylmercapturic and t, t-muconic acid in urine in car mechanics, Int. Arch. Occup. Environ. Health 66 (1994) 1–6.
[29] P. Boogaard, N. Van Sittert, Biological monitoring of exposure to benzene: a comparison between S-phenylmercapturic acid, trans, trans-muconic acid, and phenol, Occup. Environ. Med. 52 (1995) 611–620.
[30] C.N. Ong, P.W. Kok, H.Y. Ong, C.Y. Shi, B.L. Lee, W.H. Phoon, K.T. Tan, Biomarkers of exposure to low concentrations of benzene: a field assessment, Occup. Environ. Med. 53 (1996) 328–333.
[31] H. Kivistö, K. Pekari, K. Peltonen, J. Svinhufvud, T. Veidebaum, M. Sorsa, A. Aitio, Biological monitoring of exposure to benzene in the production of benzene and in a cokery, Sci. Total Environ. 199 (1997) 49–63.
[32] P. Kok, H. Ong, M. Wong, W. Au, K. Tan, W. Phoon, C. Ong, Environmental and biological assessment of exposure to benzene in petroleum workers, Environ. Monit. Assess. 44 (1997) 425–431.
[33] N. Rothman, W. Bechtold, S. Yin, M. Dosemeci, G. Li, Y. Wang, W. Griffith, M. Smith, R. Hayes, Urinary excretion of phenol, catechol, hydroquinone, and muconic acid by workers occupationally exposed to benzene, Occup. Environ. Med. 55 (1998) 705–711.
[34] P. Carrer, M. Maroni, D. Alcini, D. Cavallo, S. Fustinoni, L. Lovato, F. Visigalli, Assessment through environmental and biological measurements of total daily exposure to volatile organic compounds of office workers in Milan, Italy, Indoor Air 10 (2000) 258–268.
[35] Y. Choi, D. Shin, S. Park, Y. Chung, M. Kim, Biological monitoring of benzene in residents living near petrochemical industrial areas in Korea, J. Occup. Health 42 (2000) 31–37.
[36] Q. Qu, A.A. Melikian, G. Li, R. Shore, L. Chen, B. Cohen, S. Yin, M.R. Kagan, H. Li, M. Meng, Validation of biomarkers in humans exposed to benzene: urine metabolites, Am. J. Ind. Med. 37 (2000) 522–531.
[37] C. Senzolo, S. Frignani, B. Pavoni, Environmental and biological monitoring of occupational exposure to organic micropollutants in gasoline, Chemosphere 44 (2001) 67–82.
[38] G. Sanguinetti, A. Accorsi, A. Barbieri, G.B. Raffi, F.S. Violante, Failure of urinary trans,trans-muconic acid as a biomarker for indoor environmental benzene exposure at PPB levels, J. Toxicol. Environ. Health 63 (2001) 599–604.
[39] F. Tomei, S. Ghittori, M. Imbriani, S. Pavanello, A. Carere, F. Marcon, A. Martini, T. Baccolo, E. Tomao, A. Zijno, Environmental and biological monitoring of traffic wardens from the city of Rome, Occup. Med. 51 (2001) 198–203.
[40] R. Chakroun, N. Kaabachi, A. Hedhili, M. Feki, H. Nouaigui, M. Ben Laiba, A. Mebazaa, Benzene exposure monitoring of Tunisian workers, J. Occup. Environ. Med. 44 (2002) 1173–1178.

[41] A.A. Melikian, Q. Qu, R. Shore, G. Li, H. Li, X. Jin, B. Cohen, L. Chen, Y. Li, S. Yin, R. Mu, X. Zhang, Y. Wang, Personal exposure to different levels of benzene and its relationships to the urinary metabolites S-phenylmercapturic acid and trans,trans-muconic acid, J. Chromatogr., B: Anal. Technol. Biomed. Life Sci. 778 (2002) 211–221.

[42] T. Panev, T. Popov, T. Georgieva, D. Chohadjieva, Assessment of the correlation between exposure to benzene and urinary excretion of t, t-muconic acid in workers from a petrochemical plant, Int. Arch. Occup. Environ. Health 75 (Suppl) (2002) S97–S100.

[43] F.C. de Paula, J.N. Silveira, R.G. Junqueira, E.M. Leite, Assessment of urinary trans, trans-muconic acid as a biomarker of exposure to benzene], Rev. Saude Publica 37 (2003) 780–785.

[44] F.S. Violante, G. Sanguinetti, A. Barbieri, A. Accorsi, S. Mattioli, R. Cesari, C. Fimognari, P. Hrelia, Lack of correlation between environmental or biological indicators of benzene exposure at parts per billion levels and micronuclei induction, Environ. Res. 91 (2003) 135–142.

[45] P.B. Farmer, B. Kaur, J. Roach, L. Levy, D. Consonni, P.A. Bertazzi, A. Pesatori, S. Fustinoni, M. Buratti, M. Bonzini, A. Colombi, T. Popov, D. Cavallo, A. Desideri, F. Valerio, M. Pala, C. Bolognesi, F. Merlo, The use of S-phenylmercapturic acid as a biomarker in molecular epidemiology studies of benzene, Chem. Biol. Interact. 153–154 (2005) 97–102.

[46] S. Fustinoni, M. Buratti, L. Campo, A. Colombi, D. Consonni, A.C. Pesatori, M. Bonzini, P. Farmer, S. Garte, F. Valerio, Urinary t, t-muconic acid, S-phenylmercapturic acid and benzene as biomarkers of low benzene exposure, Chem. Biol. Interact. 153 (2005) 253–256.

[47] S. Garte, T. Popov, T. Georgieva, C. Bolognesi, E. Taioli, P. Bertazzi, P. Farmer, D.F. Merlo, Biomarkers of exposure and effect in Bulgarian petrochemical workers exposed to benzene, Chem. Biol. Interact. 153–154 (2005) 247–251.

[48] P. Navasumrit, S. Chanvaivit, P. Intarasunanont, M. Arayasiri, N. Lauhareungpanya, V. Parnlob, D. Settachan, M. Ruchirawat, Environmental and occupational exposure to benzene in Thailand, Chem. Biol. Interact. 153–154 (2005) 75–83.

[49] Q. Qu, R. Shore, G. Li, L. Su, X. Jin, A.A. Melikian, N. Roy, L.C. Chen, I. Wirgin, B. Cohen, S. Yin, Y. Li, R. Mu, Biomarkers of benzene: urinary metabolites in relation to individual genotype and personal exposure, Chem. Biol. Interact. 153–154 (2005) 85–95.

[50] S. Raghavan, K. Basavaiah, Biological monitoring among benzene-exposed workers in Bangalore city, India, Biomarkers 10 (2005) 336–341.

[51] M. Carrieri, E. Bonfiglio, M.L. Scapellato, I. Maccà, G. Tranfo, P. Faranda, E. Paci, G.B. Bartolucci, Comparison of exposure assessment methods in occupational exposure to benzene in gasoline filling-station attendants, Toxicol. Lett. 162 (2006) 146–152.

[52] S. Kim, R. Vermeulen, S. Waidyanatha, B.A. Johnson, Q. Lan, M.T. Smith, L. Zhang, G. Li, M. Shen, S. Yin, N. Rothman, S.M. Rappaport, Modeling human metabolism of benzene following occupational and environmental exposures, Cancer Epidemiol. Biomarkers Prev. 15 (2006) 2246–2252.

[53] J. Kirkeleit, T. Riise, M. Bråtveit, K. Pekari, J. Mikkola, B.E. Moen, Biological monitoring of benzene exposure during maintenance work in crude oil cargo tanks, Chem. Biol. Interact. 164 (2006) 60–67.

[54] M. Belingheri, S. Fustinoni, G. De Vito, A. Porro, M.A. Riva, Benzene and leukemia: from scientific evidence to regulations. A historical example, Med. Lav. 110 (2019) 234–240.

[55] A. Bahrami, M. Ansari, Exposure of sweepers to volatile organic compounds using urinary biological exposure index, J. Res. Health Sci. 7 (2007) 1–5.

[56] A. Barbieri, F.S. Violante, L. Sabatini, F. Graziosi, S. Mattioli, Urinary biomarkers and low-level environmental benzene concentration: assessing occupational and general exposure, Chemosphere 74 (2008) 64–69.

[57] P. Manini, G. De Palma, R. Andreoli, D. Poli, M. Petyx, M. Corradi, A. Mutti, P. Apostoli, Biological monitoring of low benzene exposure in Italian traffic policemen, Toxicol. Lett. 181 (2008) 25–30.

[58] M. Arayasiri, C. Mahidol, P. Navasumrit, H. Autrup, M. Ruchirawat, Biomonitoring of benzene and 1,3-butadiene exposure and early biological effects in traffic policemen, Sci. Total Environ. 408 (2010) 4855–4862.

[59] M. Carrieri, G. Tranfo, D. Pigini, E. Paci, F. Salamon, M.L. Scapellato, M.E. Fracasso, M. Manno, G.B. Bartolucci, Correlation between environmental and biological monitoring of exposure to benzene in petrochemical industry operators, Toxicol. Lett. 192 (2010) 17–21.

[60] M.E. Fracasso, D. Doria, G.B. Bartolucci, M. Carrieri, P. Lovreglio, A. Ballini, L. Soleo, G. Tranfo, M. Manno, Low air levels of benzene: correlation between biomarkers of exposure and genotoxic effects, Toxicol. Lett. 192 (2010) 22–28.

[61] S. Fustinoni, L. Campo, R. Mercadante, D. Consonni, D. Mielzynska, P.A. Bertazzi, A quantitative approach to evaluate urinary benzene and S-phenylmercapturic acid as biomarkers of low benzene exposure, Biomarkers 16 (2011) 334–345.

[62] S. Angelini, R. Kumar, J.L. Bermejo, F. Maffei, A. Barbieri, F. Graziosi, F. Carbone, G. Cantelli-Forti, F.S. Violante, K. Hemminki, Exposure to low environmental levels of benzene: evaluation of micronucleus frequencies and S-phenylmercapturic acid excretion in relation to polymorphisms in genes encoding metabolic enzymes, Mutat. Res. Genet. Toxicol. Environ. Mutagen 719 (2011) 7–13.

[63] L. Campo, A. Cattaneo, D. Consonni, L. Scibetta, P. Costamagna, D.M. Cavallo, P.A. Bertazzi, S. Fustinoni, Urinary methyl tert-butyl ether and benzene as biomarkers of exposure to urban traffic, Environ. Int. 37 (2011) 404–411.

[64] P. Lovreglio, M.N. D'Errico, S. Fustinoni, I. Drago, A. Barbieri, L. Sabatini, M. Carrieri, P. Apostoli, L. Soleo, Biomarkers of internal dose for the assessment of environmental exposure to benzene, J. Environ. Monit. : JEM (J. Emerg. Med.) 13 (2011) 2921–2928.

[65] L. Zhang, F.L. Ye, T. Chen, Y. Mei, S.Z. Song, Trans, trans-muconic acid as a biomarker of occupational exposure to high-level benzene in China, J. Occup. Environ. Med. 53 (2011) 1194–1198.

[66] M. Campagna, G. Satta, L. Campo, V. Flore, A. Ibba, M. Meloni, M.G. Tocco, G. Avataneo, C. Flore, S. Fustinoni, P. Cocco, Biological monitoring of low-level exposure to benzene, Med. Lav. 103 (2012) 338–346.

[67] M. Carrieri, G.B. Bartolucci, M.L. Scapellato, G. Spatari, D. Sapienza, L. Soleo, P. Lovreglio, G. Tranfo, M. Manno, A. Trevisan, Influence of glutathione S-transferases polymorphisms on biological monitoring of exposure to low doses of benzene, Toxicol. Lett. 213 (2012) 63–68.

[68] N.B. Hopf, J. Kirkeleit, M. Bråtveit, P. Succop, G. Talaska, B.E. Moen, Evaluation of exposure biomarkers in offshore workers exposed to low benzene and toluene concentrations, Int. Arch. Occup. Environ. Health 85 (2012) 261–271.

[69] M. Ciarrocca, G. Tomei, M. Fiaschetti, T. Caciari, C. Cetica, G. Andreozzi, A. Capozzella, M.P. Schifano, J.-C. Andre', F. Tomei, A. Sancini, Assessment of occupational exposure to benzene, toluene and xylenes in urban and rural female workers, Chemosphere 87 (2012) 813–819.

[70] C. Manuela, T. Francesco, C. Tiziana, C. Assunta, S. Lara, N. Nadia, A. Giorgia, S. Barbara, F. Maria, C. Carlotta, D.G. Valeria, S.M. Pia, T. Gianfranco, S. Angela, Environmental and biological monitoring of benzene in traffic policemen, police drivers and rural outdoor male workers, J. Environ. Monit. : JEM (J. Emerg. Med.) 14 (2012) 1542–1550.

[71] B.-h. Lv, S.-z. Song, Z. Zhang, Y. Mei, F.-l. Ye, Urinary S-phenylmercapturic acid as a key biomarker for measuring occupational exposure to low concentrations of benzene in Chinese workers: a pilot study, J. Occup. Environ. Med. 56 (2014) 319–325.

[72] R. Rahimpoor, A.R. Bahrami, F. Ghorbani, M.J. Assari, A.R. Negahban, S. Rahimnejad, B. Mehdizadegan, Evaluation of urinary metabolites of volatile organic compounds and some related factors in petrochemical industry workers, Journal of Mazandaran University of Medical Sciences 24 (2014) 119–131.

[73] L. Campo, F. Rossella, R. Mercadante, S. Fustinoni, Exposure to BTEX and ethers in petrol station attendants and proposal of biological exposure equivalents for urinary benzene and MTBE, Ann. Occup. Hyg. 60 (2016) 318–333.

[74] Y. Hajizadeh, H. Teiri, S. Nazmara, I. Parseh, Environmental and biological monitoring of exposures to VOCs in a petrochemical complex in Iran, Environ. Sci. Pollut. Res. Int. 25 (2018) 6656–6667.

[75] A. Jalai, Z. Ramezani, K. Ebrahim, Urinary trans, trans-muconic acid is not a reliable biomarker for low-level environmental and occupational benzene exposures, Saf Health Work 8 (2017) 220–225.

[76] N. Taneepanichsku, W. Loonsamrong, T. Tungsaringkarn, B. Gelaye, M.A. Williams, Occupational exposure to BTEX compounds among enclosed multi-storey car park workers in central Bangkok area, Indoor Built Environ. 27 (2018) 622–629.

[77] D.H. Koh, M.Y. Lee, E.K. Chung, J.K. Jang, D.U. Park, Comparison of personal air benzene and urine t,t-muconic acid as a benzene exposure surrogate during turnaround maintenance in petrochemical plants, Ind. Health 56 (2018) 346–355.

[78] S. Chaiklieng, P. Suggaravetsiri, N. Kaminski, H. Autrup, Factors affecting urinary tt-muconic acid detection among benzene exposed workers at gasoline stations, Int. J. Environ. Res. Publ. Health 16 (2019).

[79] I.C. Costa-Amaral, L.V.B. Carvalho, M.V.C. Santos, D. Valente, A.C. Pereira, V.O. Figueiredo, J.M. Souza, V.S. Castro, M.F. Trancoso, A.S.A. Fonseca, V. G. Milagres, M.P.R. Mendes, M.J.N. Paiva, L.C. André, R.M. Borges, M.A.C. Menezes, S.R. Alves, E.S. Gonçalves, H.A. Sisenando, J.A. Perini, M.S. Oliveira, M. J. Moura-Correa, L.R. Teixeira, A.R. Collins, R. Mattos, P.N. Sarcinelli, A.L. Larentis, Environmental assessment and evaluation of oxidative stress and genotoxicity biomarkers related to chronic occupational exposure to benzene, Int. J. Environ. Res. Publ. Health 16 (2019).
[80] K. Forsell, I. Liljelind, G. Ljungkvist, R. Nordlinder, E. Andersson, R. Nilsson, Benzene exposure and biomarkers in alveolar air and urine among deck crews on tankers transporting gasoline, Annals of work exposures and health 63 (2019) 890–897.
[81] A.R. Bahrami, A.J. Jafari, H. Ahmadi, H. Mahjub, Comparison of benzene exposure in drivers and petrol stations workers by urinary trans, trans-muconic acid in west of Iran, Ind. Health 45 (2007) 396–401.
[82] ACGIH, Threshold Limit Value for Chemical Substances and Physical Agents and Biological Exposure Indices, ACGIH, Cincnnati, OH, 2021, pp. 112–114.
[83] Environment and Occupational Hygiene Center, Occuoational Exposure of Limit, Centre for Environment and Occupational Hygiene of Ministry of Health, Tehran, Iran, 2021.
[84] IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, Occupational exposures in petroleum refining; crude oil and major petroleum fuels, IARC Monogr. Eval. Carcinog. Risks Hum. (2012) 45.
[85] M.T. Smith, Advances in understanding benzene health effects and susceptibility, Annu. Rev. Publ. Health 31 (2010) 133–148.
[86] S. Amur, L. LaVange, I. Zineh, S. Buckman-Garner, J. Woodcock, Biomarker qualification: toward a multiple stakeholder framework for biomarker development, regulatory acceptance, and utilization, Clin. Pharmacol. Ther. 98 (2015) 34–46.
[87] M. Manno, C. Viau, J. Cocker, C. Colosio, L. Lowry, A. Mutti, M. Nordberg, S. Wang, Biomonitoring for occupational health risk assessment (BOHRA), Toxicol. Lett. 192 (2010) 3–16.
[88] D. Ross, The role of metabolism and specific metabolites in benzene-induced toxicity: evidence and issues, J. Toxicol. Environ. Health 61 (2000) 357–372.
[89] S. Nirmawati, A.R. Tualeka, A.C. Adi, Effect of food containing high Fe (iron) intake to urinary trans, trans-muconic acid (Tt-ma) levels on workers exposed to benzene, Indian J Public Health Res Dev 9 (2018) 53–57.
[90] S.M. Rappaport, S. Kim, Q. Lan, R. Vermeulen, S. Waidyanatha, L. Zhang, G. Li, S. Yin, R.B. Hayes, N. Rothman, M.T. Smith, Evidence that humans metabolize benzene via two pathways, Environ. Health Perspect. 117 (2009) 946–952.
[91] M. Carrieri, E. Bonfiglio, M.L. Scapellato, I. Maccà, G. Tranfo, P. Faranda, E. Paci, G.B. Bartolucci, Comparison of exposure assessment methods in occupational exposure to benzene in gasoline filling-station attendants, Toxicol. Lett. 162 (2006) 146–152.
[92] S. Kim, R. Vermeulen, S. Waidyanatha, B.A. Johnson, Q. Lan, M.T. Smith, L. Zhang, G. Li, M. Shen, S. Yin, N. Rothman, S.M. Rappaport, Modeling human metabolism of benzene following occupational and environmental exposures, Cancer Epidemiol. Biomarkers Prev. 15 (2006) 2246–2252.
[93] S.M. Arnold, J. Angerer, P.J. Boogaard, M.F. Hughes, R.B. O'Lone, S.H. Robison, A. Robert Schnatter, The use of biomonitoring data in exposure and human health risk assessment: benzene case study, Crit. Rev. Toxicol. 43 (2013) 119–153.
[94] C.P. Weisel, Benzene exposure: an overview of monitoring methods and their findings, Chem. Biol. Interact. 184 (2010) 58–66.
[95] A.C. Capleton, L.S. Levy, An overview of occupational benzene exposures and occupational exposure limits in Europe and North America, Chem. Biol. Interact. 153–154 (2005) 43–53.
[96] ACGIH, TLVs® and BEIs® based on the documentation of the threshold limit values for chemical substances and physical agents and biological exposure indices, in: American Conference of Governmental Industrial Hygienists Cincinnati2008, 2010.
[97] ACGIH, TLVs and BEIs, Based on the Documentation of the Threshold Limit Values and Chemical Substances, Cincinnati OH, USA, 2022.
[98] A.C.o.G.I.H. ACGIH, TLVs and BEIs: Based on the Documentation of the Treshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices, Acgih, 2018.
[99] M.T. Diogo, European legal framework related to underground mining and tunnelling concerning commission directive (EU) 2017/164, 31 January establishing a fourth list of indicative occupational exposure limit values, Int. J. Min. Sci. Technol. 30 (2020) 541–545.
[100] R. Rahimpoor, F. Sarvi, S. Rahimnejad, S.M. Ebrahimi, Occupational exposure to BTEX and styrene in West Asian countries: a brief review of current state and limits, Arh. Hig. Rada. Toksikol. 73 (2022) 107–118.
[101] G. Tranfo, E. Paci, M. Carrieri, E. Marchetti, R. Sisto, M. Gherardi, F. Costabile, L. Bauleo, C. Ancona, D. Pigini, Levels of urinary biomarkers of oxidatively generated damage to DNA and RNA in different groups of workers compared to general population, Int. J. Environ. Res. Publ. Health 16 (2019).
[102] G. Tranfo, D. Pigini, E. Paci, F. Marini, R.C. Bonanni, Association of exposure to benzene and smoking with oxidative damage to nucleic acids by means of biological monitoring of general population volunteers, Environ. Sci. Pollut. Res. 24 (2017) 13885–13894.
[103] P. Lovreglio, A. Stufano, R. Andreoli, C. Tomasi, P. Cagnazzi, A. Barbieri, L. Soleo, G. De Palma, Urinary biomarkers of nucleic acid oxidation and methylation in workers exposed to low concentrations of benzene, Toxicol. Lett. 331 (2020) 235–241.
[104] A. Rafiee, J.M. Delgado-Saborit, P.D. Sly, H. Amiri, M. Hoseini, Exploring urinary biomarkers to assess oxidative DNA damage resulting from BTEX exposure in street children, Environ. Res. 203 (2022), 111725.
[105] H.-M. Byun, T. Panni, V. Motta, L. Hou, F. Nordio, P. Apostoli, P.A. Bertazzi, A.A. Baccarelli, Effects of airborne pollutants on mitochondrial DNA Methylation, Part. Fibre Toxicol. 10 (2013) 18.
[106] V. Bollati, A. Baccarelli, L. Hou, M. Bonzini, S. Fustinoni, D. Cavallo, H.-M. Byun, J. Jiang, B. Marinelli, A.C. Pesatori, Changes in DNA methylation patterns in subjects exposed to low-dose benzene, Cancer Res. 67 (2007) 876–880.
[107] D. Carbonari, A. Proietto, M. Fioretti, G. Tranfo, E. Paci, M. Papacchini, A. Mansi, Influence of genetic polymorphism on t,t-MA/S-PMA ratio in 301 benzene exposed subjects, Toxicol. Lett. 231 (2014) 205–212.
[108] A. Mansi, R. Bruni, P. Capone, E. Paci, D. Pigini, C. Simeoni, R. Gnerre, M. Papacchini, G. Tranfo, Low occupational exposure to benzene in a petrochemical plant: modulating effect of genetic polymorphisms and smoking habit on the urinary t,t-MA/SPMA ratio, Toxicol. Lett. 213 (2012) 57–62.
[109] S. Fiebelkorn, C. Meredith, Estimation of the leukemia risk in human populations exposed to benzene from tobacco smoke using epidemiological data, Risk Anal. 38 (2018) 1490–1501.
[110] J.F. Pankow, K. Kim, K.J. McWhirter, W. Luo, J.O. Escobedo, R.M. Strongin, A.K. Duell, D.H. Peyton, Benzene formation in electronic cigarettes, PLoS One 12 (2017), e0173055.
[111] B.R. Appel, G. Guirguis, I.S. Kim, O. Garbin, M. Fracchia, C.P. Flessel, K.W. Kizer, S.A. Book, T.E. Warriner, Benzene, benzo(a)pyrene, and lead in smoke from tobacco products other than cigarettes, Am. J. Publ. Health 80 (1990) 560–564.
[112] R. Rahimpoor, F. Gohari-Ensaf, J. Poorolajal, M.J. Assari, Impact of filter on the estimation of quantitative mixture risk caused by some chemical constituents generated from popular cigarette brands in Iran, Addict Health 12 (2020) 175–185.
[113] M.E. Counts, M.J. Morton, S.W. Laffoon, R.H. Cox, P.J. Lipowicz, Smoke composition and predicting relationships for international commercial cigarettes smoked with three machine-smoking conditions, Regul. Toxicol. Pharmacol. 41 (2005) 185–227.
[114] S.M. Rappaport, Threshold limit values, permissible exposure limits, and feasibility: the bases for exposure limits in the United States, Am. J. Ind. Med. 23 (1993) 683–694.
[115] C.C. Chen, K.Y. Wu, M.J.W. Chang, A statistical assessment on the stochastic relationship between biomarker concentrations and environmental exposures, Stoch. Environ. Res. Risk Assess. 18 (2004) 377–385.
[116] P. Rauscher, American conference of governmental industrial Hygienists (ACGIH) organisational update (march 2022), Occupational Health Southern Africa 28 (2022) 109–110.
[117] S. Fustinoni, L. Campo, G. Satta, M. Campagna, A. Ibba, M.G. Tocco, S. Atzeri, G. Avataneo, C. Flore, M. Meloni, P.A. Bertazzi, P. Cocco, Environmental and lifestyle factors affect benzene uptake biomonitoring of residents near a petrochemical plant, Environ. Int. 39 (2012) 2–7.
[118] S. Fustinoni, L. Campo, E. Polledri, R. Mercadante, L. Erspamer, A. Ranzi, P. Lauriola, C. Alberto Goldoni, P. Bertazzi, A validated method for urinary cotinine quantification used to classify active and environmental tobacco smoke exposure, Curr. Anal. Chem. 9 (2013) 447–456.
[119] A. Florescu, R. Ferrence, T. Einarson, P. Selby, O. Soldin, G. Koren, Methods for quantification of exposure to cigarette smoking and environmental tobacco smoke: focus on developmental toxicology, Ther. Drug Monit. 31 (2009) 14–30.

[120] P. Hoet, E. De Smedt, M. Ferrari, M. Imbriani, L. Maestri, S. Negri, P. De Wilde, D. Lison, V. Haufroid, Evaluation of urinary biomarkers of exposure to benzene: correlation with blood benzene and influence of confounding factors, Int. Arch. Occup. Environ. Health 82 (2009) 985–995.
[121] E. Lück, Food applications of sorbic acid and its salts, Food Addit. Contam. 7 (1990) 711–715.
[122] G. Pezzagno, L. Maestri, M.L. Fiorentino, Trans,Trans-muconic acid, a biological indicator to low levels of environmental benzene: some aspects of its specificity, Am. J. Ind. Med. 35 (1999) 511–518.
[123] L. Maestri, T. Coccini, M. Imbriani, S. Ghittori, L. Manzo, B. Li, G. Pezzagno, Effects of Sorbic Acid Ingestion on Urinary Excretion of Trans, Trans-muconic Acid in Human Volunteers and in Rats Exposed to Low Concentrations of Benzene, Toxicol Lett, 1996, p. 43.
[124] Y. Chen, G. Li, S. Yin, J. Xu, Z. Ji, X. Xiu, L. Liu, D. Ma, Genetic polymorphisms involved in toxicant-metabolizing enzymes and the risk of chronic benzene poisoning in Chinese occupationally exposed populations, Xenobiotica 37 (2007) 103–112.
[125] P. Manini, G. De Palma, R. Andreoli, P. Mozzoni, D. Poli, M. Goldoni, M. Petyx, P. Apostoli, A. Mutti, Occupational exposure to low levels of benzene: biomarkers of exposure and nucleic acid oxidation and their modulation by polymorphic xenobiotic metabolizing enzymes, Toxicol. Lett. 193 (2010) 229–235.
[126] E. Paci, D. Pigini, A.M. Cialdella, P. Faranda, G. Tranfo, Determination of free and total S-phenylmercapturic acid by HPLC/MS/MS in the biological monitoring of benzene exposure, Biomarkers 12 (2007) 111–122.
[127] P.J. Sabourin, W.E. Bechtold, R.F. Henderson, A high pressure liquid chromatographic method for the separation and quantitation of water-soluble radiolabeled benzene metabolites, Anal. Biochem. 170 (1988) 316–327.
[128] O. Inoue, E. Kanno, M. Kakizaki, T. Watanabe, K. Higashikawa, M. Ikeda, Urinary phenylmercapturic acid as a marker of occupational exposure to benzene, Ind. Health 38 (2000) 195–204.
[129] Q. Sun, B. Wang, S. Xu, X. Cong, Y. Pu, J. Zhang, Research development and trends of benzene-induced leukemia from 1990 to 2019-A bibliometric analysis, Environ. Sci. Pollut. Res. 29 (2022) 9626–9639.
[130] D. Loomis, K.Z. Guyton, Y. Grosse, F. El Ghissassi, V. Bouvard, L. Benbrahim-Tallaa, N. Guha, N. Vilahur, H. Mattock, K. Straif, Carcinogenicity of benzene, Lancet Oncol. 18 (2017) 1574–1575.
[131] L.R. Teras, W.R. Diver, E.L. Deubler, D. Krewski, C.R. Flowers, J.M. Switchenko, S.M. Gapstur, Residential ambient benzene exposure in the United States and subsequent risk of hematologic malignancies, Int. J. Cancer 145 (2019) 2647–2660.
[132] R. Duarte-Davidson, C. Courage, L. Rushton, L. Levy, Benzene in the environment: an assessment of the potential risks to the health of the population, Occup. Environ. Med. 58 (2001) 2–13.
[133] D. Carbonari, P. Chiarella, A. Mansi, D. Pigini, S. Iavicoli, G. Tranfo, Biomarkers of susceptibility following benzene exposure: influence of genetic polymorphisms on benzene metabolism and health effects, Biomarkers Med. 10 (2016) 145–163.