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Review

Risk assessment of Benzene, Toluene, Ethyl benzene, and Xylene (BTEX) in the atmospheric air around the world: A review

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ABSTRACT

Volatile organic compounds, such as BTEX, have been the subject of numerous debates due to their detrimental effects on the environment and human health. Human beings have had a significant role in the emergence of this situation. Even though US EPA, WHO, and other health-related organizations have set standard limits as unhazardous levels, it has been observed that within or even below these limits, constant exposure to these toxic chemicals results in negative consequences as well. According to these facts, various studies have been carried out all over the world – 160 of which are collected within this review article, so that experts and governors may come up with effective solutions to manage and control these toxic chemicals. The outcome of this study will serve the society to evaluate and handle the risks of being exposed to BTEX. In this review article, the attempt was to collect the most accessible studies relevant to risk assessment of BTEX in the atmosphere, and for the article to contain least bias, it was reviewed and re-evaluated by all authors, who are from different institutions and backgrounds, so that the insights of the article remain unbiased. There may be some limitations to consistency or precision in some points due to the original sources, however the attempt was to minimize them as much as possible.

1. Introduction

Since the dawn of industrialization, the presence of air pollutants – due to natural and anthropogenic activities – in the biosphere has been regarded as a crucial concern (Besharatlou et al., 2021; Tajer et al., 2021; Aghaei et al., 2022; Zahed et al., 2022; Salehi et al., 2023). These pollutants are distributed and transported into the atmosphere and surface of the Earth via wind, rain, snow, to name but three, leading to irreversible, adverse effects on both environment and human beings. Air pollutants include particulate matter, gases, ultra-fine particles, and heavy metals, with some of the most common compounds being CO_2, SO_2, CO, NO, NO_2, O_3, and volatile organic compounds (Lerner et al., 2014; Waked et al., 2016; Kumar et al., 2017; Salehi and Anbia, 2017; Salehi et al., 2020; Salehi and Hosseinifard, 2021). One of the notorious groups of toxic VOCs – known as "BTEX" – is made up of four members: Benzene, Toluene, Ethyl-Benzene, and different isomers of Xylene as shown in Fig. 1 (Du et al., 2014; Masih et al., 2016; Garg and Gupta, 2019; Sjöström et al., 2019; Kuppusamy et al., 2020b; Yu et al., 2022). These hydrocarbons have high vapor pressure and are enormously found in the air as well as the soil and the water. BTEX impose carcinogenic and non-carcinogenic damages on human being along with their harmful effects on global warming and tropospheric ozone formation (Kashyap et al., 2019; Cruz et al., 2020; Turner et al., 2020; Wickliffe et al., 2020; Barul and Parent, 2021; Hanif et al., 2021). The most abundant sources of BTEX are as follows: gasoline, vehicular exhaust, anthropogenic activities, and biogenic resources endangering inhabitants of urban areas as well as workers in these industries (Alenezi and Aldaihan, 2019; Fontes et al., 2019; Dimitriou and Kassomenos, 2020; Hsieh et al., 2020; Ojimelukwe et al., 2021; Wang et al., 2021). Different petrochemical procedures and accidents happening in gas and oil extraction - such as pipeline explosions, oil spills, and crude oil deposits contribute to the BTEX release into the air, soil, and water (Tang et al., 2013; Wollin et al., 2020; Jang et al., 2021; Chen et al., 2022; Stewart et al., 2022). In addition, the solvents and chemicals – for

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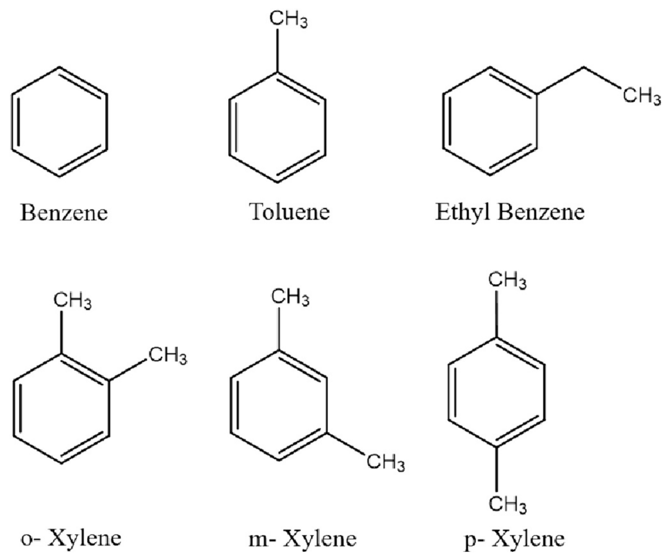

Fig. 1. BTEX group members (Kuppusamy et al., 2020b).

example, Naphta – being used in petrochemical industries contain a range of different VOCs such as BTEX which evaporate easily into the air and cause pollution (Yuan et al., 2020). When the present BTEX concentration in the atmosphere raises above the limit announced by US EPA and EU, they are considered toxic and hazardous. This critical threshold for BTEX is 5 μg / m^3 (Charbotel et al., 2014; Kuranchie et al., 2019). US EPA has classified these contaminants into 3 groups according to the extent of damage they impose on human life; Benzene, as a group 1 member, is a human carcinogen chemical; Ethylbenzene, as a member of group 2B, is an animal carcinogenic chemical, and Toluene as well as Xylene, as group 3 members, show non-carcinogenic negative effects. As BTEX members are small molecules showing lipophilic features which contribute to their penetration into the human body, exposure to these air pollutants happens via three principal pathways: 1. Inhalation, 2. Ingestion, and 3. Dermal penetration. Among the aforementioned pathways, inhalation is regarded as the main route. Accordingly, during the recent decade, several studies have been conducted to maintain beneficial information about BTEX level and their potential damage to the environment as well as human health. Additionally, by doing so, risk assessments in HSE systems will be more precise and efficient leading to safer and more protected workplaces.

This review article collects and summarizes relevant, existing knowledge from a wide range of interdisciplinary sources and different fields. One of the main goals of this article is to synthesize and summarize the accessible knowledge on BTEX risk assessment to obtain an overview of this topic. Moreover, by bringing together diverse sources of information, this review paper can provide valuable insights and enhance the general understanding of this topic.

The innovative aspect of this review is providing a comprehensive evaluation of BTEX levels in the biosphere, their detrimental effects on human health, and proposed strategies for managing and mitigating their impact.

2. Methods of data collection

The method of collecting all the relevant materials and information is searching by the keywords "air pollution", "BTEX and toxicity", "cancer risk assessment", and "risk management". Then, after sorting the results, different search criteria such as subject area and other relevant keywords were fine-tuned while irrelevant information being excluded from the results; in this process, the attempt was to choose the knowledge from reliable databases and to pick the studies with complete results to avoid misguidance. The authentic databases being utilized were "Science Direct", "Web of Science", "Scopus", "Google Scholar", to name but a few. The mentioned procedure was a simultaneous work done by each individual author of the article, and after merging all into one manuscript, it underwent careful evaluation by each one of the authors who are from different fields and different affiliations. By so doing and by comparing similar scientific works with one another, bias introduction to the review article was avoided, the quality of the work was gradually enhanced, and at the same time, it was cross-checked not to have any missing results or ambiguities. In some cases, to have the results in a nutshell for the audience to easily understand, data from several sources was extracted and reorganized into a table (e.g., Table 1).

3. Results and discussion

3.1. BTEX exposure routes

3.1.1. Inhalation

BTEX members impose danger on human health through direct and indirect pathways. Their penetration via inhalation is the direct route resulting in serious carcinogenic and non-carcinogenic problems, and their contribution to ozone and NO_2 formation is regarded as the indirect one. In other words, different photochemical reactions in the air assist the transformation of BTEX to their proxy form (RO_2) using

Table 1
Comparison of BTEX concentration in different regions.

Benzene	Ethyl Benzene	Toluene	Xylenes	References
142.2	10.48	122.3	10.53	Delhi, outdoor, (Wollin et al., 2020)
2.63	15.28	15.78	3.46 (p-Xylene)	Leon, outdoor, (Cerón Bretón et al., 2020)
5.42	3.97	11.23	8.32 (p-Xylene)	Carmen, outdoor (Cerón et al., 2013)
4.52	1.44	12.36	2.04	Paris, outdoor, (Monod et al., 2001)
16.7	6.8	40.5	17	Algeria, outdoor, (Kerchich and Kerbachi, 2012)
2.73	3.86	16.56	13.85	Sakaka, outdoor, (El-Hashemy and Ali, 2018)
3.54	2.34	161.37	12.21	South Korea, outdoor, (Kashyap et al., 2019)
8.98	2.69	24.79	14.63	Delhi, outdoor, (Kashyap et al., 2019)
27.2	12.0	29.3	32.7	Hebei, outdoor, (Liu et al., 2015)
9.2	4.4	14.5	11.1	Beijing, outdoor in table (Liu et al., 2015)
7.7	17	43	23	Jordan, indoor, (Alsbou and Omari, 2020)
34.4	28.0	58.9	88.3	Hebei, indoor, (Liu et al., 2015)
723	373	545	710	Kuwait, gas station, (Al-Harbi et al., 2020)
30.30	7.04	12.09	20.20	Shiraz, bus terminal, (Dehghani et al., 2018)
1.78	0.51	5.19	1.13	Ahvaz, outdoor, (Rad et al., 2014)
32.40	62.38	16.10	13.82	Ardabil, indoor, (Baghani et al., 2018)
2.29	0.8	5.52	4.47	Maragheh, outdoor, (Behnami et al., 2023)
75.1	54.8	34.1	19.5	Tehran, indoor, (Dehghani et al., 2019)
224.88	489.27	475.64	865.96	Tehran, bus terminal, (Golkhorshidi et al., 2019)
466.09	493.05	873.13	910.57	Tehran, CNG station, (Baghani et al., 2019)
3.19	1.54	6.08	2.34	Asaloyeh, outdoor, (Tarassoli et al., 2019)
238	69	130	118	Tehran, outdoor, (Asadi and Mirmohammadi, 2017)

hydroxyl radicals ($OH^{\bullet}$) which form NO_2 via a photochemical reaction with NO. In the next step, the NO_2 molecule reacts with BTEX in the air leading to tropospheric ozone (O_3) formation. Inhalation of high concentrations of Ozone leads to respiratory problems, eye irritation, body infections, and adverse effects on crops as well as the ecosystem (Hickman et al., 2010; Burney and Ramanathan, 2014; Kim et al., 2014; Ly et al., 2020; Rajasekhar et al., 2020). Therefore, outdoor air quality depends upon the amount of these toxic chemicals, and it is necessary to control their level to be in the safe range, especially for the ones who work in more polluted areas outside.

A study in Kuala Lampur, Malaysia showed that the average concentration of BTEX was about 49.56 ± 23.71 μg / m^3, and Toluene was the major pollutant with a mean level ranging from 2.76 ± 2.05 μg / m^3 to 22.31 ± 11.54 μg / m^3. Results revealed that the most polluted hours were during rush hours in the morning and the most contaminated areas were in this order: roadsides, gasoline stations, petrochemical industries, and airports (Latif et al., 2019).

In another study in Gorakhpur, India, the ambient air of four different sites in different seasons was examined during a year, and it revealed that industrial and residential regions were the most and the least contaminated areas, respectively. The average level of Benzene, Toluene, Ethyl benzene, and Xylene were 15.9, 3.9, 28.2, and 2.8 μg/m^3, respectively. These results indicated that concentration of Benzene and Ethyl benzene was above the standard threshold (Masih et al., 2016).

Moreover, the indoor air and its quality depends on the outdoor pollution, furnishing materials, features of the building, and indoor activities – such as chemicals used in beauty salons (Lamplugh et al., 2019; Moradi et al., 2019), mosquito-repellent materials (Lu et al., 2020) cleaning agents (Sofuoglu et al., 2011), as well as coal and wood combustion for cooking and heating (Liu et al., 2015; Vinnikov et al., 2021). In addition, one should keep in mind that BTEX are used as solvents or adhesives in different enterprises apart from the petrochemical industry, thus they influence the breathing air inside a building as well (Carlsen et al., 2018; Guo et al., 2020; Martellini et al., 2020).

During a survey in several photocopy and printing centers in Sakaka, Saudi Arabia, the indoor/outdoor ratio for BTEX was measured, and most of the results exceeded 1 suggesting the BTEX emission was higher inside these areas. According to the results, among BTEX, Toluene played the main role in indoor pollution within these buildings, and its concentration was higher than its safe limit (El-Hashemy and Ali, 2018).

In a research study in Harbin, China, during 5 years, the indoor air quality of many small places - from houses to hospitals - were examined; eventually, it was indicated that Toluene and Xylene levels were highest in public bath places, yet their concentrations were within the standard range (Zhang et al., 2020). Despite this result, BTEX concentration in newly painted, decorated rooms were higher than the standard limit. In addition, their mean concentration inside the rooms was higher during summer due to humidity and high temperature (Zhang et al., 2021).

Table 1 summarizes several results indicating BTEX concentration in various regions which have been studied worldwide during last two decades.

3.1.2. Ingestion

The ingestion of BTEX pollutants through water and air poses a significant health risk to humans. Since the onset of 21st Century, as the technology and drilling procedures have advanced, "shale gas boom" - one of the unconventional natural gas (UNG) discoveries – have increased by means of Hydraulic Fracturing (HF). Due to UNG development, concentration of hydrocarbon pollutants, whether in air or water, has increased (Gross et al., 2013; Drollette et al., 2015). The UNG method involves using over 10,000 m^3 of water, which includes adhesives such as BTEX; up to 80% of which returns to surface and ground water, which may be consumed as drinking water (Adgate et al., 2014; Meszaros et al., 2017; Asejeje et al., 2021; Wu et al., 2021). A study, in Sullivan County, examined the BTEX amount released during HF process in surface water. Regarding the statistics, 69% of the study cases contained at least one member, and 23% of the cases contained all the BTEX members (Meszaros et al., 2017).

In a another study, the concentration of BTEX in groundwater was examined; their concentration in first day of sampling after operation was higher than the limit given by US EPA for drinking water: Benzene, Ethyl Benzene, Toluene, and Xylene was 5, 700, 1000, 10,000 (ppb), respectively (Gross et al., 2013; Asejeje et al., 2021).

In addition to groundwater, surface water (i.e. seas and oceans) and its ecosystem are also endangered by these pollutants threatening human health as well (Bartilotti et al., 2021).

3.1.3. Dermal

Dermal absorption of BTEX is a kinetic process and depends on hydrophobicity, molecular size, and hydrogen-bond-forming ability of these chemicals (Kupczewska-Dobecka et al., 2010). Accordingly, dermal pathway, especially for policemen and firefighters who are in chronic exposure to hazardous chemicals and pollutants, is of great concern. In a research, it was revealed that Benzene absorption flux (J_{ss}) during dermal exposure is in the range of 99–1855 μg/ cm^2/h within in-vitro examinations. As the exposure increases from splash-type to immersion-type, the uptake level of Benzene through skin appreciates as well (Frasch and Barbero, 2018).

Regarding firefighters, although they wear protective masks and clothes, they are not 100% protected, that is to say, during a study, it was demonstrated that VOCs penetrate firefighters' bodies through their skin (Fent et al., 2014).

3.2. Toxicity of BTEX

Regarding the information in (3.1.1), inhalation is the major path through which BTEX members enter human body. In addition, traffic smokes and petroleum are main sources of these toxic and hazardous chemicals. Thus, employees in petrochemical plants and pollutant workplaces are more subjected to these toxic VOCs, and it is necessary to conduct research over risk assessment of BTEX in such contaminated workplaces (Fizal et al., 2018; Shinohara et al., 2019; Vargas et al., 2020). In Table 2, different occupations and the amount of occupational BTEX exposure are listed (Kuppusamy et al., 2020a).

Regarding reports, short time exposure to these chemicals results in quite a few adversities such as irritation, damage to nervous and respiratory system, headache, and vertigo. In the meantime, chronic exposure develops kidney, blood, and liver afflictions in adults (Chen et al., 2018; Goodkind et al., 2019; Davidson et al., 2021), and mid-pregnancy inflammation in pregnant mothers (Cassidy-Bushrow et al., 2021). Additionally, neurodevelopmental and educational problems in children results from prenatal and childhood chronic exposure to this group of VOCs (Volk et al., 2021; Araya et al., 2021). Table 3 indicates examples of these adverse effects on humans body (Kuppusamy et al., 2020b).

Table 2
Most prevalent occupations with exposure to BTEX (Kuppusamy et al., 2020a).

Occupation	Benzene (N_{jobs} = 496) %	Toluene (N_{jobs} = 659) %	Xylene (N_{jobs} = 371) %
Motor vehicle mechanic and repair	13.9	9.7	17.3
Food and beverage service workers	0	10.5	0
Logging and timber-related occupations	9.3	0.5	0
Carpentry, cabinet and wood furniture making	7.9	9.3	9.7
Shoemaking and repair	4.6	3.6	6.2
Printing Press	2.8	2.7	3.2
Painting, paperhangers and decorating	4.0	5.6	8.1
Firefighters	2.4	1.8	1.6
Service station attendants	1.0	0.75	1.3

Table 3
Adverse effects of long-term exposure to toxic VOCs (Kuppusamy et al., 2020b).

Respiratory symptoms	Mental health effects	Latent Health conditions	Positive Biomarkers
Wheezing and breathlessness	Psychological stress	Skin cancer	Structural chromosomal alteration
Nocturnal breath shortness	Depression	Lung Cancer	Elevated levels of vascular endothelial growth factors
Chronic cough	Post-traumatic stress disorder	Reproductive toxic effects	Elevated levels of basic fibroblast growth factor
Lower respiratory tract symptoms	Elevated anxiety disorder	Developmental toxic effects	Elevated 8-isoprostane levels in exhaled breath

3.2.1. *Risk assessment*

Regarding the significance of reported cases damaged by chronic exposure to these toxic, hazardous adulterates, experts were urged to evaluate BTEX risks. To this end, several formulas and parameters were defined to help measuring the standard limits, which are elaborated upon hereunder.

CR and HQ are the abbreviated forms of cancer risk and hazard quotient, respectively; CR indicates that a chemical has carcinogenic effects, and HQ refers to non-carcinogenic adverse effects. According to US EPA, in the case of BTEX, the standard HQ and life time cancer risk (LTCR) level must be below one and less than 10^{-6}, respectively (Alsbou and Omari, 2020).

Mathematical equations used for these terms are as follow:

$$EC = (CA \times ET \times EF \times ED)/AT \quad (1)$$

Where EC is emission exposure, CA is the targeted chemical concentration (μg/m^3), ET is exposure time (h/d), EF is exposure frequency (d/y), ED is exposure duration (y), and AT is the average life time of the chemical (h).

$$HQ = EC/RFC \quad (2)$$

Where RFC is the chronic reference concentration (μg/m^3) for the targeted chemical.

$$CR = IUR \times EC \quad (3)$$

Where IUR is inhalation unit risk for the chemical (μg/m^3) (Alsbou and Omari, 2020).

In order to appreciate the applicability of the aforementioned formulas, here are several examples illustrating the risk evaluation of BTEX exposure and their levels in various, distinct regions.

In Japan, during four seasons, three different gas stations were studied. Exposure concentration of benzene and toluene as well as benzene/toluene ratio in spring were much higher than winter; these results were due to temperature and gasoline content differences. The measured lifetime cancer risk for refueling workers was 2.2×10^{-5}, which indicated cancer risk probability (Shinohara et al., 2019).

A study in Thailand focused on petroleum station workers in three different regions, i.e. urban, suburban, and rural areas, in order to estimate cancer risk probabilities. As Table 4 shows, the average LTCR of BTEX across all these three regions was in the range of 1.4×10^{-5}–8.0×10^{-5} which is significantly dangerous, and the most hazardous area was suburban where plants and industries are located (Chaiklieng et al., 2019).

Table 4
The average lifetime cancer risk classified by zones (Chaiklieng et al., 2019).

Concentration value used	Urban ($n = 48$)	Suburban ($n = 60$)	Rural ($n = 42$)
Individual	1.8×10^{-5}–5.1×10^{-5}	1.9×10^{-5}–8.0×10^{-5}	1.4×10^{-5}–4.7×10^{-5}
50th Percentile	1.4×10^{-5}–4.9×10^{-5}	2.2×10^{-5}–7.9×10^{-5}	1.3×10^{-5}–4.7×10^{-5}
95th Percentile	2.9×10^{-5}–1.0×10^{-4}	3.1×10^{-5}–1.1×10^{-4}	2.9×10^{-5}–1.0×10^{-4}

The individual, 50th Percentile, and 95th Percentile means used personal benzene concentration, average concentration, and 95th percentile of concentration, respectively for cancer risk assessment.

According to a study in US, adverse effects of BTEX were more detrimental in gas stations located in a very short distance from each other, similar to a cluster. Regarding the outcomes, LTCR assessment of Benzene in a cluster of gas stations is 9.86×10^{-6}, in a single station, however, it is reduced to 2.45×10^{-6} (Hsieh et al., 2021).

In a study in five different sections of a steel plant, Benzene concentration in benzoyl refinement, biochemistry, and energy sections was higher than the standard limit. LTCR for Benzene and Ethyl benzene was 2.9×10^{-5} and 2.5×10^{-6}, respectively. In addition, HQ ratio of Toluene and Benzene was higher than 1 for employees with near thirty-year work experience (Dehghani et al., 2020).

A research in Arad City, Romania, showed that the average LTCR amount of Benzene in this city in winter was about 3×10^{-5}, which indicates the possible risk of cancer in the case of long time exposure. In addition, BTEX concentration was higher during winter than summer (Popitanu et al., 2021).

In a survey in China, indoor air, ambient air, and drinking water were studied. The resulting level of Benzene and Ethyl benzene was higher than 5 μg/m^3, and LTCR of these chemicals was between acceptable and tolerable level, i.e. 1×10^{-6} and 1×10^{-4}, thus the residents were in potential risk of cancer. However, HQ ratio was less than unity, demonstrating low non-carcinogenic toxicity of them (Chen et al., 2021).

Non-electric heaters - especially kerosene, unfluted gas, and wood pot-billed ones - are one of the household sources of BTEX emission making indoor air quality inferior to outdoor in some cases (Liu et al., 2016; Notman, 2020). In a study in Jordan, it was demonstrated that LTCR of Benzene and Ethyl benzene in houses using kerosene heaters were 8.4×10^{-6} and 10^{-5}, respectively (Alsbou and Omari, 2020).

Polluted seafood ingestion can impose a great deal of concerns. In a survey in Niger Delta, over a period of 3 years, it was indicated that LTCR of Benzene for children and adults was 0.65 and 0.30 respectively, which is tremendously higher than the limit proposed by US EPA and WHO. In addition, HQ ratio of BTEX was higher than unity as well (Ojimelukwe et al., 2021).

3.3. *Carcinogenicity, mutagenicity, and teratogenicity of BTEX*

Although physical activity, diet, and alcohol consumption are the main elements in the initiation of cancer, environmental conditions as well as occupational exposure may have 5%–20% contribution to this illness (Blanc-Lapierre et al., 2018; Warden et al., 2018; Barul et al., 2019; Xiong et al., 2021). International Agency for Research on Cancer (IARC) has classified BTEX into three different groups according to their carcinogenicity, among which Benzene is the one contributing to quite a few human cancer cases (Du et al., 2014).

3.3.1. *Benzene*

Benzene is among the 20 most produced chemicals in the United States, and its adverse effects are of great concern (Janitz et al., 2017; Zhao et al., 2021). US OSHA (Occupational Safety and Health Administration) suggests that the maximum exposure concentration of Benzene for employees is 1 ppm for 40 work hours a week; people who are subjected to more levels are vulnerable. However, frequent exposure to low concentration – less than 0.1 ppm of this chemical for a long time develops irreparable devastating consequences as well (Vargas et al., 2020).

According to various records and studies, Benzene participates in blood malignancies, such as Acute Myelogenous Leukemia (AML) (Bai et al., 2014b; Schnatter et al., 2020), hematopoietic malfunctions (Khalade et al., 2010; Qian et al., 2019; He et al., 2020; Chow et al., 2021; Sun et al., 2021), non-Hodgkin lymphoma (Rana et al., 2021) and some types of hematologic cancers. In other words, Benzene contributes to Myelodysplastic Syndromes (MDS) and lymphoid malignancy, especially T-cell lymphoma (Teras et al., 2019). MDS per say results in Cytopenia when the number of blood cells is less than enough – and Anemia, and eventually it develops AML (Dewi et al., 2020; Mundt et al., 2021). In addition, chronic exposure to Benzene is considered as one of the principal factors resulting in lung and prostate cancer as two of the main deteriorating diseases worldwide (Blanc-Lapierre et al., 2018), colorectal cancer (Talibov et al., 2018), and an increase in white blood cell population which is a hallmark of hematopoietic toxicity (Pyatt, 2004; Shallis et al., 2021).

In order to elaborate upon the mechanism through which Benzene imposes carcinogenic effects, it is worth mentioning the following details. Bone marrow is the place where hematopoietic stem cells (HSCs) and progenitors renew themselves and generate new mature blood cells under the regulation of intrinsic and extrinsic factors. If HSCs are damaged or altered, they will regenerate and propagate, turning themselves into Leukemia Stem Cells or Cancer Stem Cells (LSC or CSC) as shown in Fig. 2 (Wang et al., 2012).

In liver and bone marrow, Benzene can be transformed to different metabolites which play a crucial role in its toxicity. This biotransformation procedure happens in several steps as follows: First of all, Cytochrome P450 (CYP 2EI) liver enzyme conducts an epoxidation reaction, then the major portion of benzene oxide molecules are changed first into Phenol and then to Hydroquinone or Catechol. At this stage, the metabolites go through bone marrow, and finally they are transformed to p- and o-benzoquinone, which are more stable and hazardous chemicals, through an oxidation process mediated by Myeloperoxidase enzyme (MPO). However, there is a type of enzyme named Quinoneoxidoreductase (NQO1) which is in charge of catalyzing redox reaction of Benzoquinone to Hydroquinone via the transformation of p- and o- BQs to semiquinone radical, thus detoxification happens. Yet, if the final step is inhibited, semiquinone radical goes back and forms BQ, as well as $O_2^{\bullet}$, an anion radical which in turn changes to H_2O_2 and $HO^{\bullet}$. Thus, BQ-HQ reversible reaction has a crucial importance and its absence causes oxidative stress resulting in adverse phenomenon (Li et al., 2018; Maksoud et al., 2018; Mathialagan et al., 2020). These steps and produced chemicals are shown in Fig. 3 (Moran et al., 1999; Pu et al., 2020).

Accordingly, the presence of Benzene and its metabolites in bone marrow results in human body damages as follows (Wang et al., 2012).

1. According to an investigation using ^{14}C and its radioactive properties, experts found out that benzene oxide and p- BQ form covalent bonds with DNA strands in liver and bone marrow in in-vivo study, which, in accompany of other factors, may lead to hematotoxicity (Wang et al., 2012).
2. Benzene metabolites result in chromosomal alteration, i.e., chromosomal translocations and inversions in peripheral blood cells, which, in association with DNA repair functions, causes genomic instability and tumor generation (Chenna et al., 1995; Poon et al., 2014; Yang et al., 2019).
3. Although Benzene and its metabolites are considered as weak mutagen or non-mutagen chemicals in vitro, they can induce mutagenic effects in vivo (Gaskell et al., 2004; Nakayama et al., 2004). In a study, HQ and BQ effect in supF forward mutation assay was examined, that is, experts injected HQ and p-BQ separately and both together into E.coli host cells to observe changes happening to sequences in DNA strands within kidney cell. The results, as they are shown in Table 5, suggested that Benzene metabolites are responsible for gene mutation (Gaskell et al., 2005).

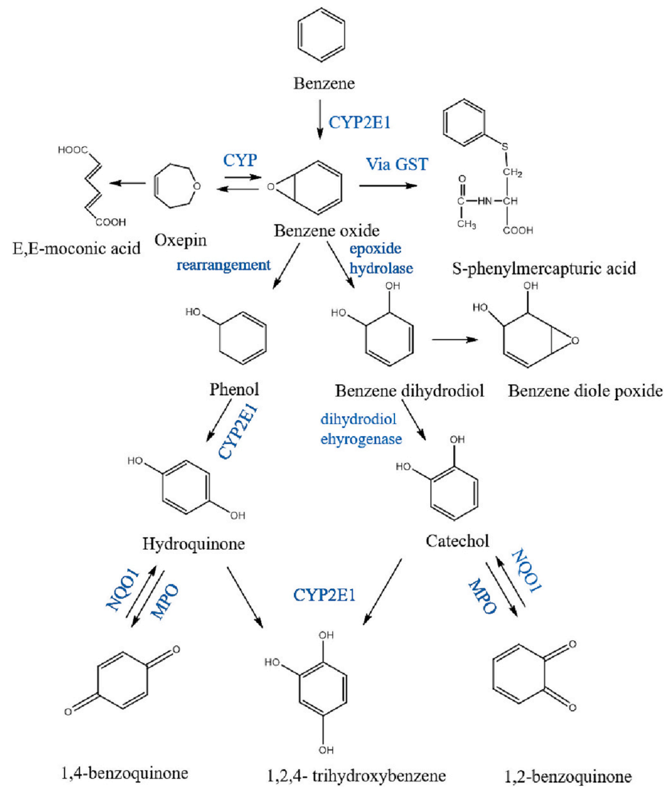

Fig. 3. Benzene mechanism and the formation of its metabolites within liver and bone marrow (Moran et al., 1999).

Table 5
Types of single and tandem mutations observed in *supF* gene after treatment with 20 mM HQ, 20 mM *p*-BQ, and a mixture of 20 mM HQ with 20 mM *p*-BQ into *E. coli* (Gaskell et al., 2005).

Mutations Number of plasmids with mutations (%)	Control	20 mM HQ	20 mM *p*-BQ	20 mM HQ + 20 mM *p*-BQ
Transversions	11(85)	32(57)	33(58)	29(50)
GC → TA	4(31)	9(16)	23(40)	13(23)
GC → CG	7(54)	15(27)	5(9)	7(12)
AT→TA	0(0)	6(11)	5(9)	6(10)
AT→CG	0(0)	2(3)	0(0)	3(5)
Transitions	2(15)	24(43)	24(42)	29(50)
GC → AT	2(15)	19(34)	23(40)	23(40)
AT→GC	0(0)	5(9)	1(2)	6(10)
Total number of single and tandem base substitutions	13 (100)	56 (100)	57(100)	58(100)

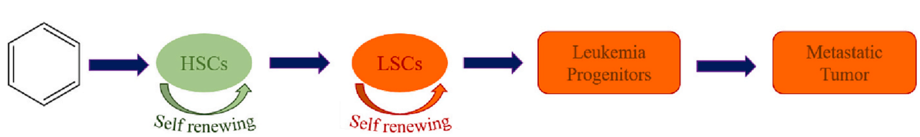

Fig. 2. The mechanism of HSC change into LSC (Wang et al., 2012).

4. BQ, HQ, and phenol react redox reactions in body, so that oxidized as well as reduced products are formed. This phenomenon is regarded as oxidative stress feature of benzene, which may deteriorate macromolecules in human body through different pathways: DNA strand break (DSB), DNA base oxidation, mitochondria damage, and homologous recombination (Wang et al., 2012).
5. Apoptosis as a beneficial function – by means of which human body gets rid of its unwanted cells – may cause hematotoxicity. In other words, Benzene metabolites responsible for the overexpression of pro-apoptotic genes and decrease in expression of anti-apoptotic genes in peripheral blood cells, as well as depreciation in myeloid progenitor cell colonies will contribute to this malicious end (Wang et al., 2012).
6. Benzene metabolites over-activate non-homologous DNA end joining (NHEJ) as a double strand break repair which is error-prone and causes chromosomal mutations – by inducing double-strand break (DSB) and DNA-dependent protein kinease. Thus, this phenomenon causes genomic instability and error-prone DNA repair (Wang et al., 2012).
7. As another damaging mechanism of low-dose exposure to Benzene, it is worth mentioning that Benzene metabolites alter DNA methylation patterns – which is in charge of regulation of gene expression– and mRNA expression profiles (Bai et al., 2014a; Fenga et al., 2016; Spatari et al., 2021). For example, these toxic chemicals increase methylation, i.e., epigenetic changes may happen affecting gene expression through hyper methylation (Jiménez-Garza et al., 2018; Zeng et al., 2021; Van Der Laan et al., 2022).
8. Benzene at low doses contributes to bone marrow depression and blood cell serious damages. It can develop changes in the expression of cytokines and growth factors, which per se results in immunosupperation (Patton et al., 2021).

Observing Teratogenic effects of Benzene revealed transplacental transfer harming a developing embryo and chromosomal abnormalities as a result of chronic exposure to this chemical. Women employees in petrochemical industries had gone through spontaneous abortion, toxemia, and prematurity. Additionally, the adverse effects on men appeared as alternations in sperm count and mobility, viscosity, and liquefaction capacity resulting in congenital abnormalities (Hashemi et al., 2022).

3.3.2. Ethyl benzene, Toluene, and Xylene

As a group 2B member, Ethyl benzene, is one of the chemicals causing cancer in animals; for example, in a study it was observed that this chemical interacts with a spontaneous age-related disease in rodents resulting in malignant kidney tumor. Yet, as such age-related disease is not noticed among human beings, the adverse effects of Ethyl benzene regarding renal tumor are not found yet in human bodies. However, high concentrations of this chemical in ambient air and biosphere as well as its high LTCR level may contribute to detrimental effects on human body, which have not been observed yet (Hard, 2002; Sram et al., 2004).

Toluene as a volatile and lipo-soluble organic solvent is widely used in different industries; occupational chronic exposure to this chemical has broad range of negative effects - from hair loss and respiratory problems to harming nervous system. Lipophilic feature of Toluene contributes to its entrance into cells through their membrane, resulting in cerebellum and hippocampus dysfunction (Soares et al., 2020; Oh et al., 2021). Toluene associates to tumorigenesis in human body. This chemical contributes to hyper phosphorylation in p53 - engaged in tumor emergence - in liver cells resulting in Thyroid cancer which is one of the most ubiquitous lethal diseases occurring worldwide. This illness is specially observed in individuals living in urban areas with high levels of vehicular traffic (Kim et al., 2021).

Xylene, another volatile member of BTEX, is easily absorbed via inhalation, and due to its lipophilic feature, it penetrates body tissues and cells. Yet, this chemical is categorized as a member of Group 3, which is considered non-carcinogenic (Jiménez-Pacheco et al., 2018).

3.4. Risk management

Regarding the increasing rate of industrialization and development of urban life leading to the appreciation in release of pollutants, the Earth residents inevitably cannot help avoiding BTEX exposure. Thus, it is vital to come up with life-saving solutions managing the risks.

In China, experts are always looking for a solution regarding incessant air pollution. Recently, by starting a plan known as “winning the blue-sky defense battle,” governors are trying to manage and reduce the consumption of air polluting agents. In this regard, several measures are being taken: electrification of transport by using renewable energy, utilizing advanced emission inspection devices, redesigning urban regions in order to reduce the need of transportation by automobiles, and appreciation of rail-based transportation system for both people and freights inside the city (Wang et al., 2020). Similarly, a study in the U.S. revealed that although batteries used in plug-in or electric vehicles release contaminants – such as SO_2, the damage caused by these transportation devices are significantly less than what the world is encountering these days. Moreover, the cost needed for provision of these state-of-the-art machines overweighs the high cost of compensating for the damages happening in human body and their ecosystem (Michalek et al., 2011).

During a study, an artificial, closed space named “control ecological life support system” or CELSS, which is utilized in spaceships for space explorations, was studied to observe the amount of pollutants produced in such closed site, as shown in Fig. 4. Within this study, it was observed that the main sources of VOCs in CELSS are biomass burning, construction and ornamental objects, human activities like cooking, and soil. BTEX level in different cabins were monitored; the results, which are available in Table 6, indicated that non-planted cabins, i.e. crew and resource cabins, contained higher amounts of BEX, however the rest 4 cabins including plants had lower amounts. Interestingly, Toluene concentration was similar in all cabins indicating its various sources. Carcinogenic and non-carcinogenic risks were reduced by virtue of green cabins as well. Thus, by growing plants, it is possible to reduce and control the amount of air pollutants and their adverse effects - especially for BEX (Dai et al., 2018).

Since plants are regarded as one of the main effective factors in reducing the amount of air toxicants, decorating plants used in apartments were studied to see whether they are effective. The results of a study considering Z. zamiifolia, one of the ornamental plants growing under low light conditions, showed that this plant can help air filtration by absorbing BTEX, especially Benzene, due to its smaller size resulting in depreciation of BTEX level(Sriprapat and Thiravetyan, 2013).

Beside air, water pollution is of great concern as well. Monitored natural attenuation (MNA), an in situ treatment process, is used for bioremediation of BTEX. This process is conducted under both aerobic and anaerobic conditions; however aerobic biodegradation is more effective in BTEX case. Thanks to microbial communities existing in aquifer sediments, by introducing a low-rate air flow into these aquifer sediments, aerobic biodegradation is carried out (Chen et al., 2010).

Accordingly, industry workers, firefighters, and policemen – who are in direct exposure to BTEX – are in danger. They must protect themselves against these toxic chemicals by wearing exclusive face masks, gloves, and full-protective overall clothes, so that they are less subjected to these pollutants via inhalation or dermal exposure (Tompa and Jakab, 2005; Wang et al., 2014).

The other innovative ways to detect and control the BTEX level are as follows: Metal-organic frameworks as adsorbents of BTEX in wastewater or in gaseous state (Lahoz-Martín et al., 2014; Wołowiec et al., 2017; Zhang et al., 2019), 2D surfaces containing SiO_2 adsorbents (Wang et al., 2018a), bioremediation of VOCs in the presence of bacteria with degrading capacity (Bacosa et al., 2021; Eze, 2021; Szentgyörgyi et al., 2022), biosensors and 3D metal oxide nanoparticles as sensors

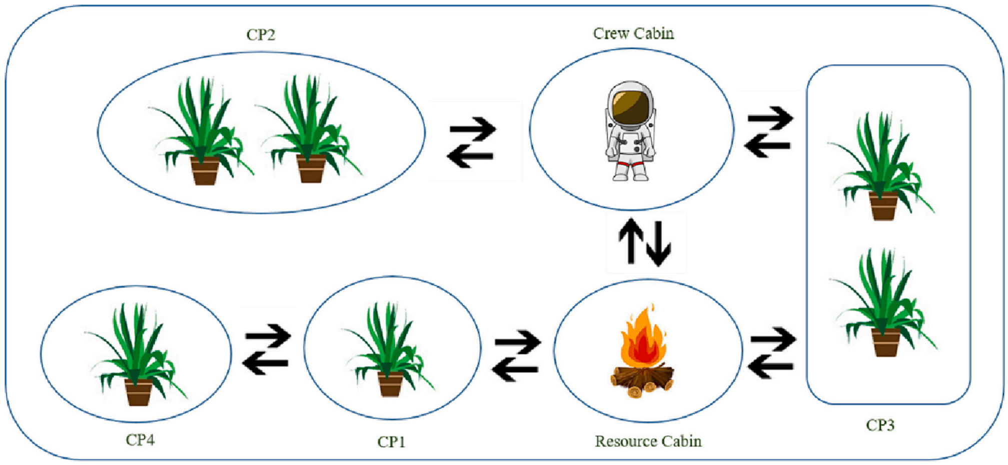

Fig. 4. Schematic view of CELSS (Dai et al., 2018).

Table 6
Concentrations of BTEX (μg/m^3; mean ± standard deviation) (Dai et al., 2018).

Sites	Benzene	Toluene	Ethylbenzene	Xylene
CP1	2.21 ± 2.07	9.2 ± 4.3	3.2 ± 1.7	12.7 ± 8.2
CP2	1.65 ± 1.65	14.9 ± 8.5	5.2 ± 3.9	21.8 ± 16.6
CP3	2.44 ± 3.14	14.7 ± 10.2	11.7 ± 15.4	48.4 ± 56.3
CP4	1.60 ± 1.43	17.4 ± 8.1	2.7 ± 1.8	10.5 ± 8.1
Crew Cabin	4.13 ± 6.62	15.3 ± 7.4	20.5 ± 22.4	87.2 ± 87.3
Resource Cabin	4.38 ± 5.62	11.3 ± 7.6	23.9 ± 45.3	102.5 ± 104.0

(Fayemiwo et al., 2018; Ray et al., 2018; Kou et al., 2019; Seekaew et al., 2019), and Film-based detection in gaseous phase as well as spectroscopy sensing methods (Mccall et al., 2018; Wang et al., 2018b; Thangamani and Pasha, 2021).

4. Conclusion

Eventually, as BTEX are notorious air contaminants endangering human life as well as their environment, these chemicals must be taken much more seriously. In that, considering the inevitable rising rate of population and their need for basic facilities such as vehicles and petroleum, ever-increasing appreciation in BTEX level along with other pollutants is not unexpected. Accordingly, these factors contributing to global warming lead to climate change, sea-level rise, and desertification disturbing the balance of an otherwise stable world. Furthermore, regarding the fact that interaction of two or more factors with one another may lead to a more serious occurrence, which is called "synergistic effect", when BTEX are released, they may come across with other pollutants already existing in the biosphere gases, heavy metals, etc. The exhibiting synergistic effects resulting in more severe, irreversible outcomes. Regarding environmental economics, wealthier countries are able to endure these problems easier than other ones; however, the vulnerable countries suffer more and will be devastated.

The strategies or measures that can be taken to mitigate the risks associated with BTEX exposure which have been cited in this article are as follows: the use of alternative materials or changes in industrial processes, physical modifications to the workplaces (e.g. improving ventilation systems or the use of personal protective equipment), administrative controls involving changes in workplace procedures and regulations, and regular monitoring of BTEX level in the environment.

By providing a thorough overview of the current state of knowledge, this review can help other researchers identify areas that need further investigation and guide the direction of future research in this field. In addition, this article can serve as a valuable resource for the audience who are new to this field and want to quickly gain a concise, general notion about BTEX risk assessment and management.

CRediT authorship contribution statement

Mohammad Ali Zahed: Project administration. **Samira Salehi:** Investigation. **Mahtab Akbarzadeh Khoei:** Writing – original draft. **Pedram Esmaeili:** Writing – review & editing. **Leila Mohajeri:** Conceptualization.

Declaration of competing interest

We confirm that all of the authors of this manuscript have no pecuniary or other personal interest, direct or indirect, in any matter that raises or my raise a conflict in this manuscript.

Data availability

No data was used for the research described in the article.

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