Journal of Environmental and Occupational Science
www.jenvos.com
DOI: 10.5455/jeos.20141223050552

Original Research

Effect of benzene on oxidative stress and the functions of liver and kidney in rats

Alia Abd El-Shakour[1], Ahmad S. El-Ebiarie[2], Yasser H. Ibrahim[1], Ahmed E. Abdel Moneim[2], Asmaa M. El-Mekawy[1]

[1]Air Pollution Department, National Research Center, Giza, Egypt, [2]Zoology and Entomology Department, Faculty of Science, Helwan University, Cairo, Egypt

Address for correspondence: Ahmed Esmat Abdel Moneim, Department of Zoology and Entomology, Faculty of Science, Helwan University, 11795 Helwan, Cairo, Egypt. Tel.: (+20) 1003499114, E-mail: aest1977@hotmail.com

Received: November 24, 2014
Accepted: December 23, 2014
Published: January 14, 2015

ABSTRACT

Aim: Benzene is a volatile organic compound known to be carcinogenic to humans. The present study was conducted to determine the effects of exposure to average indoor concentrations of benzene on liver and kidney of rats. **Methods:** Adult male albino Wistar rats were exposed to 10, 30 and 50 ppm of benzene for 14 days. The effect on lipid peroxidation (LPO), nitric oxide (NO) and glutathione (GSH) as oxidative markers, in addition, liver and kidney function levels were determined in adult male rats. **Results:** Benzene intoxication increased the activities of liver enzymes (alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase) and the bilirubin level, in addition to the levels of uric acid, urea and creatinine were increased in the serum. Moreover, benzene inhalation at 10, 30 and 50 ppm for 14 days in adult male rats enhanced LPO and NO production in both serum and liver with a concomitant reduction in GSH content. **Conclusions:** On the basis of the above results, it can hypothesis that benzene inhalation caused hepatic and renal damages even at low concentration.

KEY WORDS: Benzene, oxidative stress, rats, volatile organic compounds

INTRODUCTION

Volatile organic compounds (VOCs) are pollutants that are often associated with human activities. They are widely encountered in our environment at low levels in the air, water, and even soil [1]. Indoor air pollution is usually first to come to mind when discussing VOCs, because People spent up to 90% of their time indoors [2,3]. Indeed, VOCs concentrations measured in the indoor air often exceed (up to 10 times) concentrations in the outdoor air [1,4].

Benzene is a VOC known to be carcinogenic to humans and is classified as a Group 1 carcinogen [5,6]. Benzene is a ubiquitous pollutant and known human leukemogen. The WHO has estimated that a lifetime exposure of 1 $\mu g/m^3$ of benzene leads to about six cases of leukemia per million inhabitants [7]. Benzene is volatile, well absorbed, extensively metabolized, and does not persist in the body for long periods of time. Benzene can produce neurological impairment and can cause hematological effects including a plastic anemia and acute myelogenous leukemia [1]. Benzene can be enzymatically bioactivated to reactive intermediates that can lead to increased formation of reactive oxygen species (ROS) [8].

Inhalation accounts for more than 95-99% of the benzene exposure of the general population, whereas intake from food and water consumption is minimal [9]. Indoor benzene is associated with human activities such as cleaning, painting, the use of consumer products and mosquito repellents, photocopying and printing, the storage and use of solvents and smoking tobacco [7,10-12]. Therefore, the present study was undertaken to evaluate the oxidative stress induction and tissues injury in liver of adult male rats followed exposure to benzene at different concentrations.

MATERIALS AND METHODS

Animals

Adult male Wistar albino rats weighing 160-200 g (8-10 weeks) were obtained from The Holding Company for Biological Products and Vaccines (VACSERA, Cairo, Egypt). The animals were kept in wire bottomed cages in a room under standard condition of illumination with a 12 h light-dark cycle at 25 ± 2°C for 1 week until the beginning of treatment. They were provided with tap water and balanced diet *ad libitum*. All animals have received human care in compliance with the state authorities following the Egyptian rules of animal protection.

Benzene Exposure System

Rat whole body inhalation exposure was conducted in a chamber (dark plastic box; 50 cm long, 42 cm wide and 40 cm deep; volume = 0.084 m^3) in an experimental room. Chamber airflow entered through two rubbers tubing (5 m length; 1 cm diameter) into two sides of the chamber to allow continuous air revival during the benzene exposure period [13]. Pure benzene was allowed to pass within the airflow with different concentration at each cage (concentration were 10, 30 and 50 ppm).

Rats (in their rearing cages) were placed in the inhalation chamber to benzene (C_6H_6; molecular weight = 78.11; sigma) for 5 h/day (from 9 a.m. to 1 p.m.), 5 days/week (no weekend exposures) for 2 weeks. This experiment was conducted in June 2013.

Benzene Concentration and Gas Chromatographic Analyses

The benzene concentration in the inhalation chamber was measured in a pre-study by gas chromatography. Samples of chamber's air, taken at 30-min intervals during 4 h (exposure period) were injected and analyzed in a gas chromatograph Hewlett-Packard gas chromatography (GC) (Model HP6890), fitted with a flame ionization detector. An HP-5 (30 m ×320 μm ×0.25 μm) capillary column was used with hydrogen as a carrier gas and temperature programming from 30°C (5 min) to 250°C at 10°C min^{-1}. The instrument was checked on a daily basis based on the drift in retention times and responses of selected compounds in the standard calibration injection. The concentrations of benzene were quantified by an external standard calibration.

Experimental Design

Animals were randomly divided into four groups (6 rats/group) as follows:

1) The first group served as control and did not expose to any concentration of benzene.
2) The second group exposed to 10 ppm of benzene vapor.
3) The third group exposed daily to 30 ppm of benzene vapor.
4) The fourth group exposed to 50 ppm of benzene vapor.

The ratio was calculated according to a long-term measurement of the maximum monthly concentration of benzene in the indoor air (10, 30 and 50 ppm are the means of about half year, 2 and 3 years, respectively) [14].

After 24 h of the last exposure, the animals of all groups were sacrificed by cervical dislocation under diethyl ether anesthesia, and blood samples were collected for serum analysis. Parts of liver were excised, weighed and homogenized immediately to give 50% (w/v) homogenate in ice-cold medium containing 50 mM Tris-HCl, pH, 7.4. The homogenate was centrifuged at 3000 rpm for 10 min at 4°C. The supernatant (10%) was used for the various biochemical determinations. Total protein concentration was measured to express the concentration of different homogenate parameters as mg^{-1} protein according to the method of Lowry *et al.* [15] using bovine serum albumin as a standard.

Liver and Kidney Parameters

Serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP), total bilirubin (TB), urea, creatinine and uric acid were determined using Kits purchased from Bio-diagnostic Co., Egypt.

Oxidative Stress

Nitrite/nitrate (NO) and lipid peroxidation (LPO) were assayed colorimetrically in liver homogenates according to the methods of Green *et al.* [16] and Ohkawa *et al.* [17], respectively, where LPO was determined by using 1 ml of trichloroacetic acid 10% and 1 ml of thiobarbituric acid 0.67% which were then heated in a boiling water bath for 30 min. Thiobarbituric acid reactive substances were determined by the absorbance at 535 nm and expressed as malondialdehyde (MDA) formed. NO was determined by optimized acid reduction method at 540 nm. In addition, the hepatic glutathione (GSH) was determined by the methods of Ellman [18]. This method is based on the reduction of Elman's reagent (5,5` dithiobis (2-nitrobenzoic acid) "DTNB") with GSH to produce a yellow compound. The reduced chromogen was directly proportional to GSH concentration, and its absorbance can be measured at 405 nm.

Statistical Analysis

Results were expressed as the mean ± standard error of the mean (SEM). Data for multiple variable comparisons were analyzed by one-way Analysis of Variance. For a comparison of significance between groups, Duncan's test was used as a *post hoc* test according to the Statistical Package Program (SPSS version 17.0) and figures were drawn with Origin (version 8).

RESULTS

Liver Function Levels In Serum of the Different Exposed Groups

Table 1 shows the effect of benzene inhalation at different concentrations (10, 30 and 50 ppm) on liver function levels in serum of rats. From the present data, it can be noticed that ALT and ALP levels in serum is significantly ($P < 0.001$ and $P < 0.05$, respectively) affected with increasing the concentration of benzene. The highest ALT level in serum was recorded at 50 ppm of benzene. Moreover, AST level in serum was significantly ($P < 0.001$) affected with benzene exposure [Table 1]. The maximum AST level in serum was recorded at benzene concentration 10 ppm. Whereas, TB level in serum was decreased significantly at 10 ppm ($P < 0.001$) and 50 ppm ($P < 0.05$) when compared to control rats.

Kidney Function Levels in Serum of the Different Exposed Groups

Exposure to benzene (10 ppm) caused a significant increase in serum urea and creatinine levels when compared to the control values [Table2]. Moreover, inhalation of 30 ppm of benzene

was caused significant ($P < 0.001$) increase in serum urea, uric acid, and creatinine. At the same manner, exposure to 50 ppm of benzene caused a significant increase in urea and uric acid at $P < 0.001$. The maximum effect in the kidney function parameters was seen in 30 ppm exposed rats.

LPO Levels in Serum and Liver of the Different Exposed Groups

Figure 1 shows the effect of inhalation of benzene concentrations 10, 30 and 50 ppm on LPO levels in serum and liver tissue of male rats. From the present data, it can be noticed that benzene inhalation has a significant effect on the levels of serum and hepatic LPO formation on rats. The maximum elevation in LPO levels in both serum and liver were occurred at benzene concentration 30 ppm.

Table 1: The effect of benzene inhalation at different concentrations (10, 30 and 50 ppm) on liver function levels in serum of adult male albino rats

Groups	Liver function			
	ALT (IU/L)	AST (IU/L)	ALP (IU/L)	TB (mg/dL)
Control	72.5±2.23	76.5±1.67	131.5±3.32	0.32±0.017
10 ppm	94.7±1.56^{a**}	96.56±1.58^{a**}	145.89±5.89	0.24±0.006^{a**}
30 ppm	100.9±1.35^{a**}	93.0±2.0^{a*}	155.5±2.46^{a*}	0.31±0.005
50 ppm	102.4±1.09^{a**}	91.04±1.36^{a*}	156.74±5.22^{a*}	0.28±0.011a

Values are means±SEM (n=7), $^{a}P<0.05$, significant change with respect to control group, *,** changes between $P<0.01$ and $P<0.001$, SEM: Standard error of mean, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, ALP: Alkaline phosphatase, TB: Total billirubin

Table 2: The effect of inhalation of benzene concentrations 10, 30 and 50 ppm on kidney functions level (μmol/mg protein) in serum of adult male albino rats

Groups	Kidney functions		
	Urea (mg/dL)	Uric acid (mg/dL)	Creatinine (mg/dL)
Control	31.3±0.71	3.57±0.15	3.54±0.08
10 ppm	36. 99±1.39^{a}	3.71±0.06	4.10±0.06^{a**}
30 ppm	39.80±1.37^{a**}	4.94±0.14^{a**}	4.09±0.08^{a**}
50 ppm	40.11±0.86^{a**}	5.03±0.15^{a**}	3.78±0.06^{a}

Values are means±SEM (n=7), $^{a}P<0.05$, significant change with respect to control group, *,**changes between $P<0.01$ and $P<0.001$, SEM: Standard error of mean

Nitric Levels in Serum and Liver of the Different Exposed Groups

There was a significant decrease in hepatic NO level with increasing the concentration of benzene [Figure 2]. The maximum elevation in NO level was recorded at benzene concentration 50 ppm. On the other hand, exposure to benzene (10 and 30 ppm) was caused a significant increase in NO production in serum of rats. However, there is no significant difference in NO level in serum between control rats and rats exposed to 50 ppm benzene.

Glutathione Levels in Serum and Liver of the Different Exposed Groups

The toxicity of benzene on serum and liver is represented in Figure 3. The exposure of rats to benzene (30 and 50 ppm) caused a significant decrease in GSH levels in serum and liver. GSH contents in the serum and hepatic tissue decreased significantly compared to the controls in a dose-dependent manner. The maximum decrease in GSH levels in both serum and hepatic homogenates were recorded at benzene concentration equal 50 ppm.

DISCUSSION

Benzene and the Redox Status

Inhalation of benzene results in serious organ system dysfunction. Most solvents are easily absorbed from the blood into lipid-rich tissues and can cause widespread damage. The current results reveal that benzene inhalation at different concentrations (for 10, 30, and 50 ppm) 14 days causes significant increase in serum and liver LPO, this effect increased with increasing the concentration of benzene. Our results are in good agreement with Rana *et al.* [19] who found that administration of benzene to rats induces LPO in liver and bone marrow, increased LPO has been attributed to low GSH. Increased level of LPO was also noticed by Sharma and Sangha [20]. LPO is known to disturb the integrity of cellular membranes, has been implicated in the pathogenesis of various liver and kidney injuries [21]. ROS and LPO have been supposed to serve as common mediators of apoptosis in response to many toxicants and pathological conditions [22].

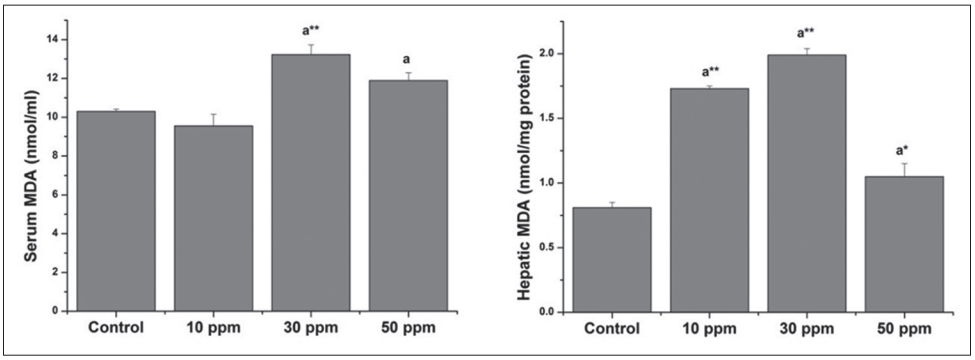

Figure 1: The effect of benzene inhalation at different concentrations (10, 30 and 50 ppm) on lipid peroxidation levels in serum and liver tissue of adult male albino rats

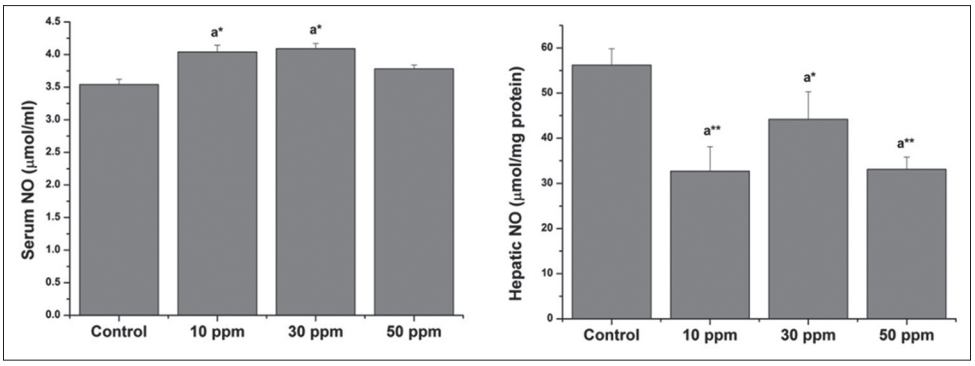

Figure 2: The effect of benzene inhalation at different concentrations (10, 30 and 50 ppm) on nitric oxide levels in serum and liver tissue of adult male albino rats

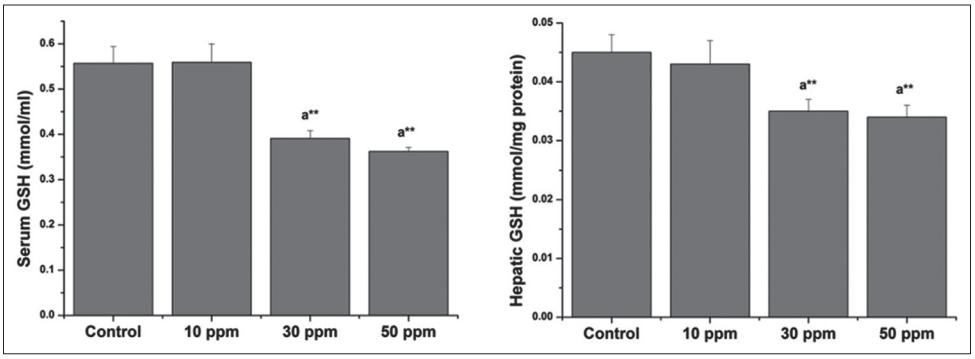

Figure 3: The effect of benzene inhalation at different concentrations (10, 30 and 50 ppm) on glutathione levels in serum and liver tissue of adult male albino rats

The present study reveals that benzene exposure caused a significant increase in serum and hepatic NO level. The elevated NO levels observed may have contributed to the development of protein damage, since NO reacts directly with the tyrosyl radical to form 3-nitrotyrosine [23,24]. Moreover, in high concentrations, NO together with superoxide anion ($O2^{\bullet-}$) give rise to peroxynitrite ($ONOO^{-}$), which is a major nitration agent [23,25]. In addition to protein nitration, peroxynitrite could also induce protein carbonylation, common oxidative protein damage [25]. Both forms of protein damage can lead to changes in protein function and subsequent alteration in biological responses [25].

Liver and serum GSH shows a significant decrease in the animals exposed to benzene. GSH is an important intracellular radical scavenger, which regulates the redox status of many other cellular substances, thus playing an essential role in the detoxication processes [26,27], especially those involved in the biotransformation of benzene [28]. Previous studies indicated that GSH depletion is one of the important consequences of toxic injury and established the critical role of GSH in protecting tissues from toxic effects of accumulating reactive intermediates [22].

These results are supported by the previous study of Raza *et al.* [29] who found a decrease in GSH with a concomitant increase in LPO levels after benzene exposure in rats. GSH is involved in benzene biotransformation in the liver. In the first step, benzene is oxidized to benzene oxide in a reaction catalyzed by cytochrome P450 2E1; rearrangement generates phenol; reaction with GSH catalyzed by GST produces less toxic metabolites, such as S-phenylmercapturic acid, which is excreted in the urine [27,30,31].

The activation of benzene and its metabolites culminates in damage to lipids, proteins, and carbohydrates by various chemical reactions such as oxidation, nitration, and halogenation leading to functional alterations in different tissues [26,28]. Furthermore, chronic benzene exposure compromises antioxidant capacity, which also contributes to the development of oxidative damage in exposed subjects [26]. Measurement of enzyme activity in serum is of importance since it helps to assess the state of the liver and other organs [32].

Benzene and the Cellular Integrity

Liver function levels in serum were significantly affected with exposure to benzene, level of ALT, AST, ALP and TB increased with increasing the concentration of benzene.

The liver has been shown to be one of the target organs of benzene vapors toxicity [33]. The relationship between the hepatic oxidative damage and increase in the activities of such serum enzymes as ALT, AST, ALP and TB has been well documented [33,34]. Exposure to benzene vapors stimulates cellular MDA, a product of LPO [35], which affect the

permeability barrier of the plasma membrane. The result of this study gives an indication that the hydrocarbons and other chemical constituents of the benzene vapors are likely metabolized in the liver, among others, to reactive species which interact with the tissues to cause LPO, thereby exhibiting their toxic or hazardous effects. The observed increase in the activities of plasma ALT, AST, ALP and TB level, is likely to be due to LPO of biomembranes that causes leakage of cellular components [32]. Therefore, it is likely that the increase in the liver enzymes reported in this present study may be due to the accumulation of benzene constituents and their reactive metabolites in hepatic tissues which enhance formation of LPO.

There was a significant effect of inhalation of benzene on kidney functions level in serum of adult male albino rats. The concentrations of urea, uric acid and creatinine in serum were significantly increased with increasing the concentration of benzene. This is in accordance with Jia *et al.* [36]. The kidneys play a special role in concentrating toxic substances within its tubules and excreting them. These functions render it susceptible to damage by certain chemical substances. The kidney is the major organ of excretion of metabolites of benzene components [37].

CONCLUSION

From this study, we conclude the dangerous effects of benzene, especially due to their wide spread: in persons who directly exposed to these substances at work chronically. Exposure to benzene is associated with adverse health effects as toxicity to liver and kidney.

REFERENCES

1. Pohl HR, Scinicariello F. The impact of CYP2E1 genetic variability on risk assessment of VOC mixtures. Regul Toxicol Pharmacol 2011;59:364-74.
2. Petry T, Vitale D, Joachim FJ, Smith B, Cruse L, Mascarenhas R, *et al.* Human health risk evaluation of selected VOC, SVOC and particulate emissions from scented candles. Regul Toxicol Pharmacol 2014;69:55-70.
3. EU. The INDEX Project, Critical Appraisal of the Setting and Implementation of Indoor Exposure Limits in the EU. Final Report. European Commission Joint Research Centre, Institute for Health and Consumer Protection, Physical and Chemical Exposure Unit, Ispra, Italy, 2005. Available from: http://www.ec.europa.eu/health/ph_projects/2002/pollution/fp_pollution_2002_frep_02.pdf. [Last accessed on 2013 Dec].
4. EPA, US Environmental Protection Agency. Indoor air quality, 2010. Available from: http://www.epa.gov/iaq/. [Last accessed on 2007 Mar 12].
5. Medeiros Vinci R, Jacxsens L, Van Loco J, Matsiko E, Lachat C, de Schaetzen T, *et al.* Assessment of human exposure to benzene through foods from the Belgian market. Chemosphere 2012;88:1001-7.
6. IARC. Benzene – IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Vol. 1-42. France, Lyon: International Agency for Research on Cancer; 1987.
7. WHO. WHO Guidelines for Indoor Air Quality: Selected Pollutants. Geneva: WHO Regional Office for Europe; 2010.
8. Winn LM. Homologous recombination initiated by benzene metabolites: a potential role of oxidative stress. Toxicol Sci 2003;72:143-9.
9. MacLeod M, Mackay D. An assessment of the environmental fate and exposure of benzene and the chlorobenzenes in Canada. Chemosphere 1999;38:1777-96.
10. Kim YM, Harrad S, Harrison RM. Concentrations and sources of VOCs in urban domestic and public microenvironments. Environ Sci Technol 2001;35:997-1004.
11. Brown SK. Volatile organic pollutants in new and established buildings in Melbourne, Australia. Indoor Air 2002;12:55-63.
12. Son B, Breysse P, Yang W. Volatile organic compounds concentrations in residential indoor and outdoor and its personal exposure in Korea. Environ Int 2003;29:79-85.
13. Jacquot L, Pourie G, Buron G, Monnin J, Brand G. Effects of toluene inhalation exposure on olfactory functioning: behavioral and histological assessment. Toxicol Lett 2006;165:57-65.
14. Kovalkovičová N, Šutiaková I, Legáth J, Legáth L, Falis M, Pistl J, *et al.* Induction of micronuclei in rat bone marrow after subchronic inhalation exposure to mixture of benzene, cyclohexanone and cyclohexane. Bull Vet Inst Pulawy 2004;48:341-5.
15. Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the folin phenol reagent. J Biol Chem 1951;193:265-75.
16. Green LC, Wagner DA, Glogowski J, Skipper PL, Wishnok JS, Tannenbaum SR. Analysis of nitrate, nitrite, and [15N]nitrate in biological fluids. Anal Biochem 1982;126:131-8.
17. Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal Biochem 1979;95:351-8.
18. Ellman GL. Tissue sulfhydryl groups. Arch Biochem Biophys 1959;82:70-7.
19. Rana SV, Chaudhary N, Verma Y. Circadian variation in lipid peroxidation induced by benzene in rats. Indian J Exp Biol 2007;45:253-7.
20. Sharma D, Sangha GK. Triazophos induced oxidative stress and histomorphological changes in liver and kidney of female albino rats. Pestic Biochem Physiol 2014;110:71-80.
21. Dkhil MA, Al-Quraishy S, Diab MM, Othman MS, Aref AM, Abdel Moneim AE. The potential protective role of Physalis peruviana L. fruit in cadmium-induced hepatotoxicity and nephrotoxicity. Food Chem Toxicol 2014;74:98-106.
22. Abdel Moneim AE. Prevention of carbon tetrachloride (CCl4)-induced toxicity in testes of rats treated with *Physalis peruviana* L. fruit. Toxicol Ind Health 2014.
23. Othman MS, Safwat G, Aboulkhair M, Abdel Moneim AE. The potential effect of berberine in mercury-induced hepatorenal toxicity in albino rats. Food Chem Toxicol 2014;69:175-81.
24. Moro AM, Charão MF, Brucker N, Durgante J, Baierle M, Bubols G, *et al.* Genotoxicity and oxidative stress in gasoline station attendants. Mutat Res 2013;754:63-70.
25. Trujillo M, Alvarez B, Souza JM, Romero N, Castro L, Thomson L, *et al*. Mechanisms and biological consequences of peroxynitrite-dependent protein oxidation and nitration. In: Ignarro LJ, editor. Nitric Oxide. 2nd ed., Ch. 3. San Diego: Academic Press; 2010. p. 61-102.
26. Uzma N, Kumar BS, Hazari MA. Exposure to benzene induces oxidative stress, alters the immune response and expression of p53 in gasoline filling workers. Am J Ind Med 2010;53:1264-70.
27. Fracasso ME, Doria D, Bartolucci GB, Carrieri M, Lovreglio P, Ballini A, *et al.* Low air levels of benzene: correlation between biomarkers of exposure and genotoxic effects. Toxicol Lett 2010;192:22-8.
28. Badham HJ, Winn LM. In utero exposure to benzene disrupts fetal hematopoietic progenitor cell growth via reactive oxygen species. Toxicol Sci 2010;113:207-15.
29. Raza H, Qureshi MM, Montague W. Alteration of glutathione, glutathione S-transferase and lipid peroxidation in mouse skin and extracutaneous tissues after topical application of gasoline. Int J Biochem Cell Biol 1995;27:271-7.
30. Carrieri M, Bartolucci GB, Scapellato ML, Spatari G, Sapienza D, Soleo L, *et al.* Influence of glutathione S-transferases polymorphisms on biological monitoring of exposure to low doses of benzene. Toxicol Lett 2012;213:63-8.
31. Arayasiri M, Mahidol C, Navasumrit P, Autrup H, Ruchirawat M. Biomonitoring of benzene and 1,3-butadiene exposure and early biological effects in traffic policemen. Sci Total Environ 2010;408:4855-62.
32. Al-Olayan EM, El-Khadragy MF, Aref AM, Othman MS, Kassab RB, Abdel Moneim AE. The potential protective effect of *Physalis peruviana* L. against carbon tetrachloride-induced hepatotoxicity in rats is mediated by suppression of oxidative stress and downregulation of MMP-9 expression. Oxid Med Cell Longev 2014;2014:381413.
33. Uboh FE, Akpanabiatu MI, Eteng MU, Ebong PE, Umoh IB.

Toxicological effects of exposure to gasoline vapour in male and female rats. Internet J Toxicol 2008;4.
34. Uboh FE, Akpanabiatu MI, Ebong PE, Eyong EU, Eka OU. Evaluation of toxicological implication of inhalation exposure to kerosene and petrol fumes in rats. Acta Biol Szeged 2005;49:19-22.
35. Uboh FE, Akpanabiatu MI, Ekaidem IS, Ebong PE, Umoh IB. Effect of inhalation exposure to gasoline fumes on sex hormones profile in Wistar albino rats. Acta Endocrinol 2007;4:23-30.
36. Jia C, Batterman S, Godwin C. VOCs in industrial, urban and suburban neighborhoods, Part 1: Indoor and outdoor concentrations, variation, and risk drivers. Atmos Environ 2008;42:2083-100.
37. Rickert DE, Baker TS, Bus JS, Barrow CS, Irons RD. Benzene disposition in the rat after exposure by inhalation. Toxicol Appl Pharmacol 1979;49:417-23.

Source of Support: Nil, Conflict of Interest: None declared.