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Review Article

Changes in Oxidative Stress Parameters in Terms of Simultaneous Exposure to Physical and Chemical Factors: A Systematic Review

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Abstract

Background: Physical and chemical factors of workplace, either alone or in combination, contribute to oxidative stress that is harmful to the body. The combined impact of physical and chemical components of the work environment on oxidative stress was examined in this research.

Methods: Research articles published from 2000 to 2021 on this topic in reliable national and international databases were collected and analyzed. Based on the preliminary screening, 120 articles were selected for the first stage. The relevance and quality of 85 suitable papers were found appropriate and evaluated by examining the purpose of the study in the next phase.

Results: The data collected and presented from the articles cover simultaneous exposure to physical risk factors such as noise, radiation, and chemicals such as metal solvents, as well as different types of oxidative stress parameters like MDA, GHS, LOP, 8-OHdG, SOD, CAT, ROS, and other parameters such as research site, co-exposure effects, and target organ. Investigating the combined effect of physical and chemical variables on oxidative stress in the target organs, as well as the interaction of multiple effects on each other, was one of the key goals of the articles (synergistic, reinforcing, additive or antagonistic).

Conclusion: Most of the findings of theses researches generally highlight the synergistic impact of concurrent exposure to chemical and physical risk factors on oxidative stress.

Keywords: Occupational risk factors; Simultaneous occupational exposure; Combined exposure; Oxidative stress

Introduction

Workers in industrial settings are thought of as one of the main foundations of industries; therefore, their absence creates many fundamental issues when putting industrial procedures into practice. Several physical and chemical risk factors, including the presence of workers in industrial settings, have a detrimental impact on their health. Whether intentionally or unintentionally, workers are exposed to these risk factors in a variety of ways (1). A combination of risk factors at work might have more detrimental effects on a person's health (2). The likelihood of the likelihood of workplace injury is influenced by the type, quantity, and number of risk variables, as well as exposure frequency, exposure time, and working conditions (3). Numerous studies have related the oxidative stress caused by them to the damage caused by chemicals (gases and vapors, solvents, and dust) and physical factors (sound, vibration, heat, humidity, radiation, etc.) (4-8). These studies have examined the combined effects of many physical and chemical components in some cases and the impact of a single factor in other cases. Oxidative stress is a condition that may harm proteins, nucleic acids, and cell membranes when it meets reactive oxygen species such as the superoxide anion, H_2O_2, and hydroxyl radicals. Numerous books demonstrate how reactive oxygen species damage accumulates over time and causes a variety of diseases (9).

In general, oxidative stress is characterized as a mismatch between oxidants and antioxidants, and this mismatch increases the contribution of oxidants to antioxidants, which may lead to damage (10). Antioxidants are used by the body to counteract the harmful effects of oxidants (4). Enzymes involved in redox-mediated signaling activities and contributing to the maintenance of redox balance make up the majority of the body's defensive antioxidant structures (11). Superoxide dismutase, catalase, peroxiredoxins, glutathione system, and thioredoxin system are the five primary groups into which cellular antioxidant enzymes are divided (8). In actuality, an antioxidant is a chemical with the capacity to prevent or lessen the oxidation of macromolecules. Protective structures and pathways of anti-oxidants with oxidants include reducing the production of secondary toxic metabolites and inflammatory mediators, suppressing the release of the secondary oxidant chain, restoring damaged molecules, and activating and strengthening the protective structure of endogenous antioxidants (4). Damage to cells, tissues and organ structures due to oxidative stress is associated with a wide range of severe diseases such as cancer, cardiovascular diseases such as high blood pressure and atherosclerosis, neurodegenerative diseases such as Parkinson and Alzheimer's dementia, diabetes, ischemia/perfusion injuries, rheumatoid arthritis, and sometimes even the mechanism of aging (11).

When damaging factors are exposed individually or in combination, antioxidants are suppressed and oxidants are strengthened, causing oxidative stress and organ damage. Recently, studies on the combined effects of harmful factors on oxidative stress biomarkers have become one of the hot topics in the field of toxicology. The simultaneous effect of noise pollution-CH_2O on GCH and MDH parameters is one of these studies, as are others that deal with the simultaneous effect of noise pollution-dust, smoke-PAHs, PAHs-phthalates, metals-pesticides, etc. Research and evaluation have been done on the parameters of MDA and SOD, 8-OHdG, 8-OHdG, 8-OHdG, MDA, and SOD (7, 12-15). Each of these studies—as well as others—has shown some influence on the aforementioned parameters. There is a very strong relationship between the parameters of oxidative stress and concurrent exposure to physical and chemical factors in the workplace, and previous studies paid attention to this; however, there is a need for a thorough study to analyze the type of harmful factors, the type of target tissue, the type of antioxidant parameters, and the effect of Concurrent exposure to physical and chemical factors and oxidative stress.

Methods

We developed a review manual and reported the process of our review and results according to the PRISMA guideline. PRISMA primarily focuses on reporting reviews evaluating the effects of interventions (16).

Based on data searches in reliable databases (Google Scholar, Web of Science, ProQuest, Taylor and Francis, WILEY, and PubMed) on physical and chemical occupational risk factors affecting oxidative stress parameters from 2000 to 2021, this systematic review analysis was carried out. Using the key terms of physical and chemical factors, risk factors, environmental hazards and oxidative stress, simultaneous exposure, combined exposure, simultaneous occupational exposure, combined occupational exposure, simultaneous occupational exposure, and combined occupational exposure all occur simultaneously. Either alone or in combination, it was employed. Initial keyword searches in the databases produced 10,400 items, 10,410 of excluded because they were duplicates. Then, based on their titles and abstracts, 400 articles were extracted. The next step the next step involved removing 180 articles due to lack of relevance to the subject and another 35 due to lack of creativity, lack of content, or use of language that was out of context.

Overall, 85 articles were ultimately left for final evaluation. The final selected articles were examined for quality assessment by using of strengthening the reporting of observational studies in epidemiology (STROBE) checklist with a score of 0 to 34 (17). In this review, studies were classified into three groups according to their obtained score: poor quality, from 0 to 12; moderate quality, ranging from 13 to 23; and high quality, ranging from 24 to 34.

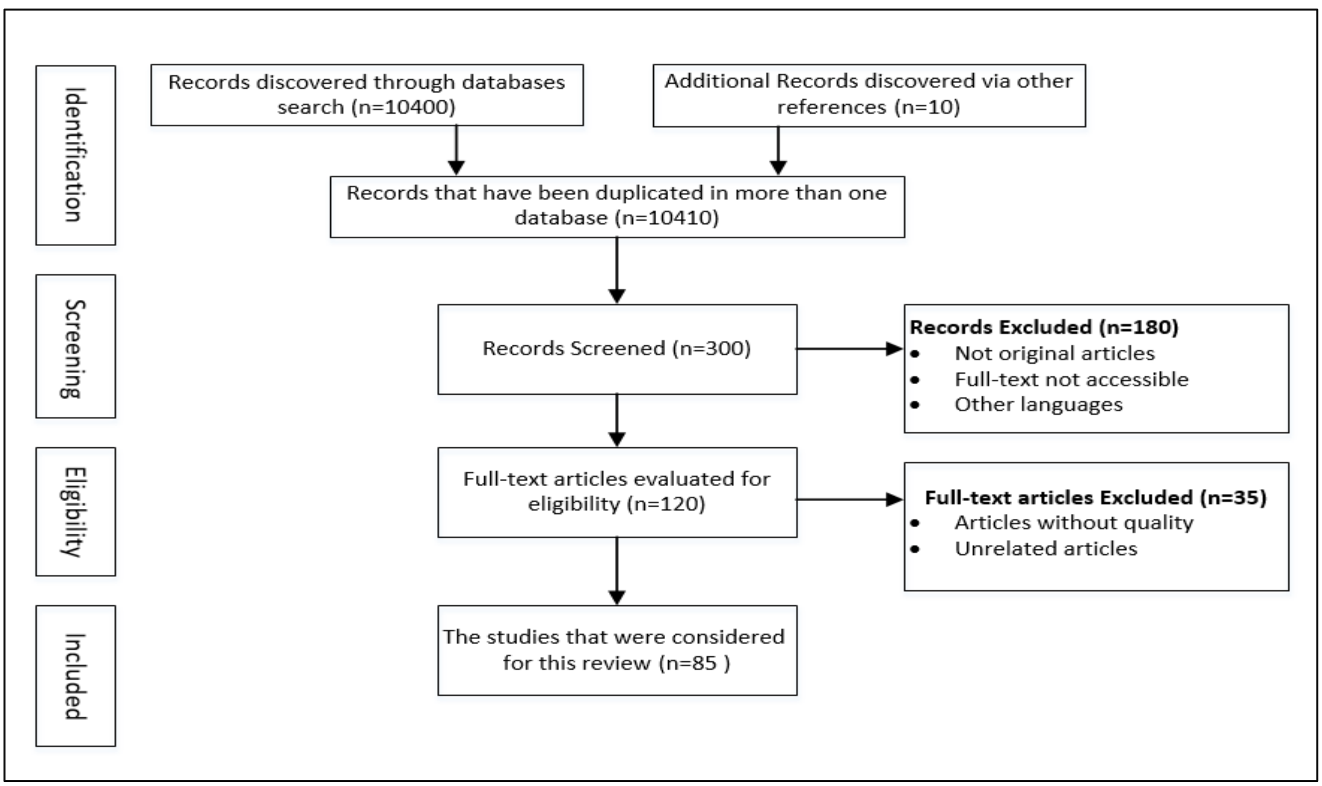

Fig.1: The diagram indicates the process of identifying and selecting scientific articles. (PRISMA)

Results

The search performed for the studies is summarized in Fig. 1. Of 300 potentially relevant studies reviewed, 85 articles were included in this systematic review. Thirty-four other articles were published in other European, American and Asian countries respectively (Table 1). Overall, 85 articles were published in 10 different peer reviewed journals.

Table 1: The country of the first/corresponding authors of articles

Country	*Number of articles(n)*	*Percentage of articles (%)*
China	10	27
USA	3	8.1
India	5	13.5
Iran	7	18.9
Italy	4	10.8
Brazil	3	8.1
Tunisia	2	5.4
Norway	2	5.4
Switzerland	4	10.8
Thailand	1	2.7
Pakistan	3	8.1
France	4	10, 8
Denmark	3	8.1

The earliest article was published in 2000 and the last article were published in 2021. There was an increase in the number of published article on metal and chemical solvent related to stress oxidative from 2008. For example, in 2009, three articles, and in 2010, two articles were published. Eighty-five studies focused on simultaneous exposure to chemical factors and simultaneous exposure to physical-physical factors, including all metal-metal (n=21, 24.70%), metal-solvent (n=18, 21.7%), solvent-solvent (n=14, 16.47%), metal-pesticide (n=10, 11.76%), drugs & metals (n=1, 1.1%), and simultaneous exposure to physical-physical factors (n=18, 21.7%). four studies were review articles (7.70%) and the remaining articles were any type of observational studies (cross-sectional or cohort).

Discussion

This systematic review focused on investigating oxidative stress parameters, the combined effects of physical and chemical occupational factors, and other occupational risk factors. Most of the included studies had a cross-sectional design. These studies provide valid data because field measurements of chemical factors and other risk factors were performed. Most of the studies we identified only examined the combined effects of risk factors on oxidative stress parameters. Another limitation is that in some studies, the magnitude of the combined effects was not clearly stated. Overall, we assessed the compound risk level for each risk factor based on study type, method, data validity, and study population. In addition, there are many confounding factors in the study of compound effects in occupational settings that complicate such studies for years.

According to the review of the literature and the level of evidence, many physical and chemical factors can have adverse oxidative effects on health. These factors include metals (chemical factors), chemical solvents, chemicals, solvents, sound, vibration, heat, electromagnetic waves and metals (chemical factors), and shift work (occupational factor). Some chemical and physical elements that increase oxidative stress are shown in Fig. 2.

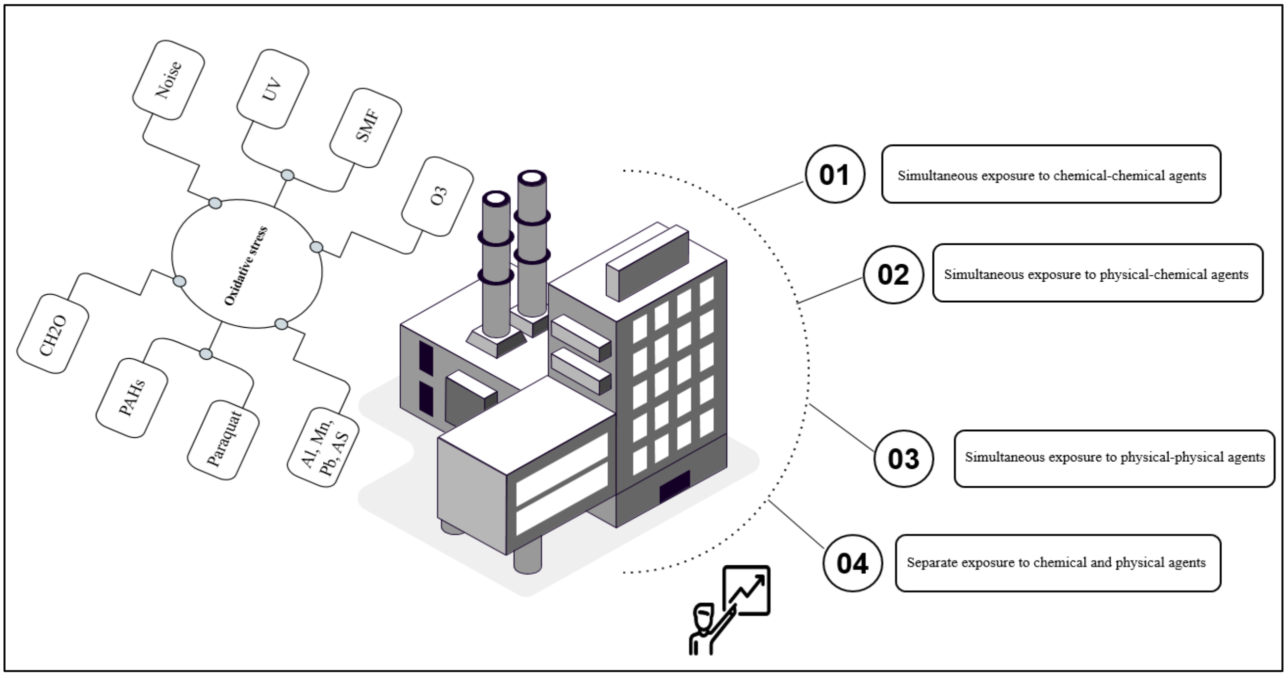

Fig. 2: Some physico-chemical factors that stimulate oxidative stress

According to the results of literature review and general adaptation syndrome (18), simultaneous exposure to stressors leads to a three-phase physiological response. Thus, by perceiving a stressor (such as noise), the sympathetic nervous system is stimulated and the body's resources are mobilized to deal with the danger. Stress is the reaction of the organism's nervous and endocrine systems to environmental demands or pressures. The body tries to limit stress if a stressor persists, the body concentrates resources and resists the stress and remains in a state of alertness (15, 19, 20). Oxidative stress occurs in cells when there is an imbalance in the production of oxidants or reactive oxygen species (ROS) and their ability to be removed by endogenous antioxidants (21). The resulting accumulation of oxidative free radicals can directly damage proteins, DNA, and lipids and lead to cellular dysfunction.
As a result, for a better understanding of this issue, in this study, each of the ways of exposing to these risk factors in the workplace is explained.

Simultaneous exposure to chemical factors

Some of the modes of simultaneous exposure to chemicals seen in the workplace are below:

Metal – metal

Today, the consumption of heavy metals has increased due to industrial and urban development, and one of the prominent side effects of heavy metals is the effects of oxidative stress caused by them (18). These metals significantly increase lipid peroxidation and reduce antioxidant defense in tissues by interfering with antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPX), and catalase (CAT) (19, 20).
Arsenic, lead and mercury are three harmful metals that are abundantly used in industries (22). In the risk assessment, exposure to lead, arsenic and mercury is raised simultaneously by discovering these metals in several high-risk places, either alone or in combination with other metals (23). These metals are known to cause oxidative stress with comparable harmful consequences (24). In this regard, exposure to two harmful metals leads

to reduced accumulation of toxic metals, indicating potential antagonistic interactions. In addition, they showed how simultaneous exposure to lead, arsenic, and mercury caused a rapid increase in oxidative stress in the liver and kidney (24-26).
In the review of studies, copper (Cu) and cadmium (Cd) are two other metals that significantly contribute to environmental degradation. Moreover, in low doses, the unnecessary chemical cadmium is very dangerous to all living organisms (25, 26). Although copper is a critical element in many biochemical processes, it may be toxic when body stores exceed physiological limits (27). In this regard, research that examined the histology and biochemistry of fish showed that exposure to cadmium and copper alone and simultaneously resulted in obvious damage to lipids and tissue structure in the gills, liver, and ovaries. Simultaneous exposure to cadmium and copper significantly increased the mRNA expression of most antioxidant genes and led to more severe lesions in fish tissue than individual exposure to cadmium and copper. Combined exposure to cadmium and copper in water may have a synergistic effect (28, 29).
During the review of studies conducted in industrial areas, in short-term exposure to cadmium (Cd) and lead (Pb) through food, water and air, cadmium in combination with other metals such as lead has seriously disturbed the health of local people (25). In addition, long-term exposure to metals is linked to a number of diseases, including cancer, liver problems, neurological problems, and osteoporosis (30).
Manganese (Mn) is another metal that, in small amounts, is considered as an essential element that plays a role in many important metabolic processes. However, increasing its concentration may be dangerous for the nervous system, blood vessels, heart, lungs and liver. The results of another study regarding the combined exposure to lead, cadmium and manganese metals showed a significant increase in the level of malondialdehyde (MDA) in the heart and liver of animals. In general, AST performance and bilirubin concentration in the group of animals exposed to all three metals increased significantly. There was a positive correlation with blood levels of lead, cadmium and manganese. In this research, cadmium, manganese and lead together have a synergistic effect on increasing cardiac MDA. In combination, lead and manganese increased blood alanine aminotransferase (ALT) activity, an indicator of structural liver damage (28). Moreover, exposure to cadmium and lead causes a significant increase in the level of lipid peroxidation (23).

Metal-chemical solvent

Another factor that workers in various industries face is the exposure of chemical solvents to metals in combination. One of the metals that harms the body and increases oxidative stress is lead (31). Lead induces the release of cytochrome c, which increases intracellular ROS and $Ca2+$ levels while decreasing mitochondrial potential and apoptosis (32, 33). According to various studies, lead and ethanol are among the compounds that exist both in industrial environments and in people's living environments. Exposure to lead and alcohol together may cause neurological problems, oxidative stress, and brain apoptosis. Lead and ethanol act synergistically. Metabolizing enzymes may cause liver cells to undergo apoptosis because of ethanol-induced ROS production. Alcohol use may also lead to excessive production of ROS, which can damage mitochondrial structure and impair the capacity of mitochondria to control internal calcium levels (34).
One of the main pathogenic mechanisms for functional and organ damage caused by heavy metals and chemicals such as toluene is inflammation, mitochondrial dysfunction, and oxidative DNA damage (34,(35)). In this regard, a study on car workers showed that there is a relationship between exposure to toluene and heavy metals and increased activity of liver enzymes, lipid peroxidation, oxidative stress, oxidative DNA damage, and a decrease in antioxidants, which indicates an increased risk of hepatotoxicity and carcinogenesis of liver cells (34).
Another chemical factor that people face in the workplace is exposure to metals and pesticides. In this study, by reviewing the studies that exam-

ined the consequences of metals and pesticides simultaneously, we indicated that having two risk factors have a greater effect on the body than either one alone (7, 46). Metals and pesticides have additive and even opposite effects. Organophosphorus and metal arsenic may have a synergistic effect on ROS, however, they are incompatible with TBARS. Arsenic and dichlorvos have a synergistic effect on liver tissue, but have an opposite effect on the brain (36). Table 1 (supplementary section) summarizes some studies on co-exposure to metals and pesticides.

Solvent – Solvent

Polycyclic aromatic hydrocarbons (PAHs) are a group of solvents that are frequently used in industrial environments. During the review of studies related to exposure to PAHs, we demonstrated that exposure to PAHs, benzene, and toluene (BTs) in combination is unavoidable due to their widespread prevalence in the environment (37). They are associated with aberrant lung processes and asthmatic infections and may easily penetrate human lung tissue by inhalation. In young people, exposure to high concentrations of PAHs and BTs is associated with increased oxidative damage and impaired lung function (15). Similar to this study, children with asthma may have higher levels of oxidative lipid and DNA damage as well as airway inflammation after exposure to PAHs and BTs together (38). During the review of animal studies, the combination of ethanol and m-xylene increased lipid peroxidation in microsomal and lysosomal membranes, and at the same time, it decreased sulfhydryl glutathione levels and GST activity (39). Growing female mice were more susceptible than males to the deleterious effects of exposure to xylene and formaldehyde, as well as their combination, on liver tissue (40).

Simultaneous exposure to physical-physical factors

Physical harmful factors are one of the factors that exist in almost all industries, and the effects of various types of physical factors and their intensity change with the combination of physical harmful factors. One of the most important effects of various physical factors is the harmful effects of oxidative stress in the body, caused by the simultaneous exposure of physical components to each other. This type of combined exposure often occurs in the workplace (41, 42). According to the review of studies conducted from 2000 to 2021, many studies were not conducted regarding the combined effects of physical factors and their effects on oxidative stress parameters, and there are a limited number of animal studies in this regard. According to the review of studies that analyze and examine the simultaneous effects and specific microwaves and sound and their effects on seminal fluid parameters and total antioxidant capacity in adult male rats, compared to the control group, sperm viability and motility in the group exposed to microwaves and the group exposed to microwaves plus noise decreased significantly (43). Another animal study conducted using 25 male Wistar rats showed that after four weeks of exposure, mobile phone electromagnetic field radiation, vibration, and ringtones had a significant effect on anxiety behaviors and oxidative stress in young Wistar rats (44). The results of these studies indicate the cumulative and strengthening effects of exposure to various physical factors. On the other hand, the levels and intensities of physical factors used to conduct these studies are similar to the levels that humans can be exposed to (37). Therefore, in the future, by conducting more studies in this field, these effects can be generalized to humans as well.

Simultaneous exposure to physical-chemical factors

Another prominent example of combined exposure in the workplace is the simultaneous exposure to physical and chemical factors that occurs in many industries where workers are expected to be simultaneously exposed to different types of both (1). According to the studies that investigated the effect of physical and chemical factors on oxidative stress parameters, we showed that long-term occupational exposure to a number of environmental toxins, such as lead and cadmium, might cause oxidative stress and then act as a

mechanism for negative effects on body systems (45). Regarding the physical aspects of the work environment, each of them, including electromagnetic waves and radiation, have the capacity to cause oxidative stress (44, 46, 47). In general, oxidative stress is caused by simultaneous exposure to physical and chemical stimuli. There have been studies in this area, and one that comes to mind is a study in which 42 adult male Wistar rats were simultaneously exposed to formaldehyde and sound. The findings of this study, based on samples of blood and liver tissue of rats, showed a greater effect on the improper functioning of the oxidant/antioxidant system (1). In Sweden, study on 18 healthy subjects showed that noise exposure might lead to oxidative DNA damage (36). Simultaneous exposure to physical and chemical variables has been investigated very little, and noise is one of the physical components that has received more attention.
Table 1 (supplementary section-Not published) shows a summary of the simultaneous exposure to physical factors, chemical factors and physicochemical factors and their effect on oxidative stress.

Conclusion

The current work environment has a variety of physical and chemical components that are harmful to human health. Because these components often coexist in many work environments, simultaneous exposure to them may exacerbate negative effects on human health. A large number of these elements (such as noise and formaldehyde, UV light and oxygen, PAHs and cigarette smoke, and manganese and ethanol) can affect oxidative stress and enhance oxidative and antioxidant parameters. Many of these factors individually or collectively affect the type of antioxidant parameters of oxidative stress, depending on the type of harmful factors and the type of target tissue. The effect of simultaneous exposure to these factors also highlights the significance of these factors. In addition, these elements are related to the complexity of the risk assessment process in workplaces. Most of the researches in Supplementary Table 1 (Not showed. Readers may contact authors if needed) demonstrate the additive effects of simultaneous exposure to physical, chemical, and physical-chemical variables on numerous oxidative stress markers. In this in this regard, a number of laboratory experiments have investigated the interaction between oxidative stress and effective physical and chemical variables.
Future study needs to focus on locating and evaluating the more accurate impact of these dangerous elements in real work environments, which will lead to planning and taking necessary measures to reduce them and provide a safer work environment. Any failure of them leads to irreversible impacts on the workforce and loss of more years for them because of the long-term effects of chemical and physical components in the workplace. Based on the existing understanding, research in this area will be prioritized and constructive measures will be taken to improve the working environment.

Journalism Ethical considerations

Ethical issues (including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) were completely observed by the authors.

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Conflict of Interest

The authors have no conflicts of interest to declare.

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