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ORIGINAL ARTICLE

Health Risk Assessment of Chemicals Using a Semi-Quantitative Risk Method in a Pharmaceutical Factory in Guilan City

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ABSTRACT

Background: Pharmaceutical industries are of great importance as part of organic chemical production in the world; however, due to the repeated exposure to chemicals, workers in these settings may suffer from frequent and various health problems, including allergies, anaphylaxis and asthma. Accordingly, this study aimed at assessing the concentration and health risk of chemicals using a semi-quantitative risk method in a pharmaceutical company.

Methods: In this study, a semi-quantitative, descriptive-analytical field assessment method was used, based on the risk assessment model developed by the Singapore Department of Occupational Health. This method first identifies the health hazards of chemicals, then calculates the risk by measuring the level of exposure, and finally recommends and prioritizes control measures to reduce the risks.

Results: The results showed that 80 percent of the chemicals identified in the factory were at levels two and three (low, medium), whereas the remaining 20 percent were at level four (high). In the laboratory unit, phenol had the lowest risk (2.43) while sulfuric acid had the highest risk (3.5). In the factory production line, methanol had the lowest risk (2.59), whereas hexanol had a medium risk (3.03). In the foil printing unit, benzene had the highest risk (3.6), while xylene had the lowest risk (2.7).

Conclusion: It is recommended that special attention be paid to the foil printing unit of this factory so that, if possible, simultaneous exposure of personnel to benzene, toluene, and xylene is avoided, and engineering-management control methods are also implemented, including increasing the number of workers, and reducing exposure hours.

KEYWORDS: *Risk Assessment; Pharmacies; Laboratory Chemicals; BTX*

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INTRODUCTION

Chemical pollutants in the workplace are dispersed in the air in various forms, such as gases, vapors, and solid or liquid particles, each of which poses specific health threats [1]. The severity and type of damage caused by these substances depend on several factors, including chemical nature of the substance, the routes of exposure (inhalation, skin contact, etc.), duration of exposure, and concentration of the substance in the environment [2, 3]. In recent years, the number of factories producing chemicals has increased, and therefore the number of people exposed to chemicals is increasing [4, 5]. More than 100,000 different chemicals are produced or used in the world annually, but there is comprehensive safety and chemical information for only 10,000 of them (i.e. 10 percent), and according to statistics from the World Health Organization (WHO), one million people die or become disabled annually due to unsafe contact with these substances [6].

In recent years, the pharmaceutical industry has become more important due to increased services and public health benefits. Workers in the pharmaceutical and chemical industries are exposed to different chemicals due to the high speed of development and functional and process characteristics [7, 8]. Based on their biological and chemical nature, the chemicals used pose risks such as carcinogenicity, physical hazards, and environmental hazards [9]. A wide range of occupational diseases have been reported among pharmaceutical workers, including acute poisoning, dysfunction of the reproductive systems, hormonal changes, and the nervous system; the results of assessing the levels of chemical pollution in the workplace air in various pharmaceutical companies indicate that the pollution in these companies can exceed health standards by 1.4 to 5 times [10].

Workers' exposure to various substances can cause allergies and also, exposure to powders used as raw materials in the manufacturing of medicines can cause anaphylaxis and asthma [11]. A study by Sahle Asfaw et al. titled "Determinants of Chronic Respiratory Symptoms Among Pharmaceutical Factory Workers" showed that chronic respiratory symptoms are common among pharmaceutical workers, and that workers with a history of respiratory diseases are three times more likely to develop them than those without a history [12]. Extracting and applying occupational exposure limits for individual chemicals is one of the basic methods in controlling occupational health risks, but in combined exposures to several chemicals, this method alone is not sufficient and requires up-to-date resources [13]. Chemical risk assessment identifies real and potential hazards by analyzing the pathways, levels, and duration of exposure, and plays a key role in the update process by organizing and utilizing existing data [14]. Sufficient evidence and studies have been provided by domestic and foreign authors regarding the epidemiological characteristics and causes of occupational diseases caused by chemical; however, insufficient attention has been paid to the chemical safety of pharmaceutical workers [15-17]. Considering the health effects and risks of chemicals on pharmaceutical workers and the importance of effective management of these substances, this study was conducted with the aim of risk assessment of exposure to chemicals using a semi-quantitative risk method in a pharmaceutical factory in Guilan. So far, various methods have been proposed for assessing risks of chemicals by organizations related to safety and health issues [18]. Considering that the semi-quantitative risk assessment method has not been carried out in pharmaceutical companies so far and it is possible to use the results of this study in similar companies, it was deemed necessary to conduct a study with the goal of assessing the concentration and health risk of chemicals using the semi-quantitative risk method in a pharmaceutical company.

MATERIALS AND METHODS

In this study, in a pharmaceutical factory in Guilan city, the risk of chemicals was assessed using a semi-quantitative, descriptive-analytical field assessment method based on the risk assessment model developed by the Singapore Department of Occupational Health.

This method first identifies the health hazards of chemicals, then calculates the level of risk by measuring the level of exposure and finally recommends and prioritizes control measures to reduce the risks. This method is limited to the pathogenicity of the substances [19].

According to the guidelines of the Singapore Department of Occupational Health, the semi-quantitative risk assessment method is carried out in 11 steps, as follows:

1. Formation of a working group
2. Decomposing the process into smaller tasks
3. Identification of chemicals
4. Determining the hazard rating (HR)
5. Inspection and interview with officials and personnel
6. Collecting information about the duration and frequency of exposure

7. Determination of exposure rating (ER)
8. Determining the risk rating (RR)
9. Implementation of corrective actions
10. Documentation of evaluation results
11. Review of assessment results

Based on the above steps, a work team was first formed, which included the factory's safety and health unit, the factory's occupational health expert, supervisors of various units, and researchers. In the second stage, the various factory units were divided into smaller processes, the processes were divided into smaller tasks, and finally the workers were grouped according to location and work tasks. In the third stage, all chemicals (raw materials, intermediates, main and by-products) were identified by reviewing warehouse documents, records, labels, and visiting storage and consumption locations. In the fourth step, the hazard factor for each substance was determined. The hazards posed by a chemical depend on its toxicity and exposure pattern. The hazard rate (HR) was determined by the lethal dose and lethal concentration of the chemical, which are shown in Table 1 and the rat inhalation LC50 was used. In the fifth stage, a detailed inspection was carried out of the units according to their work tasks. In the sixth step, information on the duration of exposure and its repetition was collected, and the level of exposure was determined according to the amount, repetition, intensity, and duration of exposure. In this study, air sampling and monitoring results were obtained through the company's annual measurement results and documentation available in the company.

In the seventh step, the exposure coefficient to chemicals was determined. Based on the results of air sampling and monitoring, the weekly time-weighted average of exposure was estimated using equation (1).

$$E=(F\times D\times M)/W$$

E is the weekly exposure amount (PPM or mg/m3), F is the frequency of exposure per week, M is the intensity of exposure (PPM or mg/m3), W is the average working hours per week (40 hours), and D is the average duration of each exposure (hours). Therefore, the exposure coefficient (ER) is compared with the long-term permissible exposure values from the exposure value (E) obtained from the above relationship, and then the exposure coefficient (ER) is determined by Table 2.

In the eighth step, the risk rating (RR) is calculated using Equation 2 and based on the ratings obtained in the fourth (HR) and seventh steps (ER) and finally the hazard of each chemical and its ranking are determined using Table 3; this ranking was used to prioritize corrective actions to reduce risk in the factory.

$$RR=\sqrt{HR \times ER}$$

Table 1. Determination of hazardous rate using acute chemicals toxicity [20].

HR	LC50 intake by inhalation in rats (mg L^{-1}) aerosols and particulate matter during 4 hrs.	LC50 intake by inhalation in rats (mg L^{-1}) gases and vapors during 4 hrs.	LD50 intake by the skin (mg/kg body weight of rats)	LD50 intake orally (mg/kg body weight of rats)
1	LC50 > 5	LC50 > 20	LD50 > 2000	LD50 > 2000
2	1 < LC50 < 5	2 < LC50 < 20	400 < LD50 < 2000	200 < LD50 < 2000
3	0.25 < LC50 < 1	0.5 < LC50 < 2	50 < LD50 < 400	25 < LD50 < 200
4	LC50 < 0.25	LC50 < 0.5	LD50 < 50	LD50 < 25

Table 2. Exposure Rating [20].

E / PEL	Exposure Rating (ER)
< 0.1	1
0.1 to < 0.5	2
0.5 to < 1.0	3
1.0 to < 2.0	4
≥ 2.0	5

PEL: Permissible Exposure level

Table 3. Risk Ranking [20].

Risk Rating	Rank
0-1.7	Insignificant
1.7-2.8	low
2.8-3.5	Medium
3.5-4.5	High
4.5-5	Very High

Table 4. Chemical hazard assessment results for different parts of the factory

Unit	Number of people exposed	Chemical substance	HR	ER	RR	Rank
Laboratory	10	Phenol	3	1.98	2.43	Low
		Formaldehyde	4	2.27	3.01	Medium
		Sodium hydroxide	3	3.37	3.17	Medium
		Sulfuric acid	4	3.07	3.5	High
		Hydrochloric acid	3	2.49	2.73	Low
Production line	80	Methanol	2	3.37	2.59	Low
		Hexanol	3	3.07	3.03	Medium
Foil printing	10	Benzene	5	2.68	3.6	High
		Xylene	3	2.44	2.7	Low
		Toluene	3	2.68	2.8	Medium

In the ninth stage, corrective actions were taken based on the results of the researchers' suggestions to implement control strategies, and then in the tenth and eleventh stages of the research, the documentation and re-evaluation process was carried out.

RESULTS

After completing the above steps, all the required data were collected. The results of the initial steps showed that in three parts of the factory, including the laboratory, Production line and foil printing, 10 chemicals were identified: phenol, formaldehyde, sodium hydroxide, sulfuric acid, hydrochloric acid, methanol, hexanol, benzene, xylene and toluene. In total, 100 people were in contact with various chemicals in different parts of the factory. According to the results in Table 4, 80% of the chemicals identified in the factory were at the second and third levels (low, medium) and 20% of the compounds were at the fourth level (High). In the laboratory unit which had 10 employees, phenol had the lowest risk (2.43) and sulfuric acid had the highest risk (3.5); in the factory production line which had 80 employees, methanol had the lowest risk (2.59), while hexanol had a medium risk (3.03). In the foil printing unit which had 10 employees, benzene had the highest risk (3.6), whereas xylene had the lowest risk (2.7).

DISCUSSION

In the company's laboratory unit, which had 10 employees, sulfuric acid had the highest risk (3.5). Sulfuric acid is highly corrosive and contact with it causes severe burns, blisters, and permanent scars and inhaling its vapors can damage the respiratory tract and lungs [20-22]; for this reason, laboratory operators must work with sulfuric acid with extreme caution, requiring strict adherence to exposure limits, use of appropriate personal protective equipment, and implementation of engineering controls to ensure safety [23, 24]. Considering the exposure of the factory laboratory personnel to sulfuric acid and their medical records, it is mandatory to pay attention to spirometry tests in this unit during periodic examinations. Mongkol Racha and colleagues conducted a study at power plants. The results showed that while industrial health assessments over the past three years reported atmospheric concentrations of sulfuric acid below standard levels, health risk assessments highlighted these chemicals as unacceptable but manageable risks to worker health, and that assessment of this compound was required [14].

In factory production line, which had 80 employees, methanol had the lowest risk (2.59), whereas hexanol had a medium risk, having the potential for acute toxicity and respiratory irritation [25]. The study by Nelson B et al. demonstrated moderate acute toxicity for hexanol with irritant potential and indicated the need for handling controls and exposure limits to ensure worker safety, all of which should be implemented as a perventive measure in the plant in our study [26].

On the other hand, in the foil printing unit, which had 10 employees, the chemical compound benzene had the highest risk (3.6), while xylene had the lowest risk (2.7). According to a review of the medical records of employees in the foil printing department, 20% of them were exposed to anemia, which could be caused by exposure to benzene. Peter J. Boogaard's study showed that benzene is one of the substances recognized by international organizations as a carcinogen and that exposure to it, even at low concentrations, can cause leukemia, which is consistent with the results of this study [27]. A study by Kahforoushan et al. titled "Evaluating the Risk of Exposure to Chemicals in an Automobile Tire Manufacturing Plant Using a Semi-Quantitative Risk Method" showed that 5% of employees suffered from anemia and iron deficiency due to exposure to benzene [5]. The results of a study by Anggi Isnani Parinduri et al. showed that benzene, as an ink solvent in the printing industry, causes damage to the hematopoietic system (bone marrow), which can pose a risk of reducing the number of blood cell elements, including a decrease in hemoglobin levels [28]. In this study, 10 percent of all workers were exposed to benzene, and that was only in the foil printing unit, but this compound was the most dangerous and hazardous chemical among the 10 chemicals identified, and great attention needs to be paid to the safety and health issues of workers in the foil printing unit.

The foil printing unit also contained toluene and xylene in addition to benzene, which had medium and low risk levels, respectively. The results of a study by A Blanc-Lapierre et al. suggest that combined exposure to benzene, toluene, xylene (BTX) is associated with higher risks of prostate cancer [29]. A study by Zhang et al. showed that exposure to BTX had positive combined effects on reducing monocyte counts, red blood cell counts, and hemoglobin concentrations, exacerbating the effects of benzene-induced anemia [30]. Therefore, it is essential to pay attention to anemia and prostate problems during periodic examinations of employees working in the foil printing unit.

CONCLUSION

This research aimed to investigate the risk of exposure to chemicals used in a pharmaceutical factory in Guilan city. In this study, two compounds, sulfuric acid in the laboratory section and benzene in the foil printing section, had the highest risk, which requires the implementation of engineering and management controls in these two units. It is recommended that special attention be paid to the foil printing unit of this factory so that, if possible, simultaneous exposure of personnel to benzene, toluene, and xylene is avoided, and engineering-management control methods are also implemented, including increasing the number of workers, reducing exposure hours, and measuring and monitoring material leaks.

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Conflict of Interest
The authors declare no conflict of interest.

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Study Conception or Design: N.SKH, JV
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AI Statement
The authors confirm that no AI tools or services were used during the preparation of this work.

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