Potential Carcinogenic Risk of Formaldehyde Due To the Occupational Exposure in a Chemical Manufacturing Plant

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Abstract: Formaldehyde exposures are common and epidemiologically linked to cancer. Workers occupationally exposed to formaldehyde in industrial and medical fields have a significant probability of acquiring degenerative diseases. The main objective of this study was to determine formaldehyde in the occupational environment of a chemical manufacturing plant in Egypt and assess its risk for the exposed workers.

Formaldehyde was monitored in workplace environment of a chemical manufacturing plant. Formaldehyde concentration (mg m^{-3}) was determined and the exposure *(E)* for an individual worker due to intake process (inhalation), chronic daily intake *(CDI)* and carcinogenic risk *(CR)* were calculated for the different cases according to the US EPA Carcinogenic Assessment Section of the Integrated Risk Information System (IRIS).

Formaldehyde concentration was variable between different production departments with a range from 0.11 to 5.7 mg m^{-3}. The calculated exposure results were coincided with the high formaldehyde concentrations at the concerned departments. Formaldehyde cancer risks for all reported concentrations were greater than the acceptable cancer risk 1×10^{-6}. Consequently, inhalation exposure to formaldehyde has a critical influence on workers of this factory. The results prove that risk assessment estimation is a powerful assisting tool in developing abetment plans to reduce pollutants emission and improve air quality. The lack of quality epidemiological studies on exposed populations emphasizes the need for more extensive studies on formaldehyde and its related health effects in Egypt.

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1. Introduction

Formaldehyde (CH_2O; 1 ppm = 1.25 mg/m^3) is the simplest and most common aldehyde found in the environment. The atmospheric half-life is quite short (few hours), so it's main impact is relatively close to the source. The natural background concentration is <1 µg/m^3 with a mean of about 0.5 µg/m^3 (IARC, 1995). The IARC Monographs Programmer (IARC, 2004a), concluded that formaldehyde is carcinogenic to humans and classified it as an agent belonging to Group 1 (''carcinogenic to humans'') (IARC, 2004b) as there was "sufficient evidence" that formaldehyde causes nasopharyngeal cancer (NPC) in humans (IARC, 2006). The major anthropogenic sources affecting humans are in the indoor environment. People exposed to chemicals in workplaces (industries, laboratories, hospitals, and others) have an increased probability of acquiring degenerative diseases (USEPA, 1996a; 2002; ATSDR, 1999).

The toxicity of formaldehyde in humans has been the matter of several reviews (e.g. Ulsamer et al., 1985; Garnier et al., 1985; WHO, 1989; Smith, 1992). It is a strong irritant to the eyes, skin and upper respiratory tract. Burns and acute respiratory distress following heavy exposure have been reported. Exposure to formaldehyde may induce respiratory symptoms, acute partially reversible and chronic irreversible functional impairments of the lungs (Arts et al., 2008; Neghab et al., 2011). Epidemiological studies on the effects of chronic formaldehyde exposure consistently found respiratory and allergic effects at levels below 123 µg/m^3 (Krzyzanowski et al., 1990; Smedje et al., 1997; Garrett et al., 1999; Franklin et al., 2000; Smedje & Norbäck, 2001; Rumchev et al., 2002).

Formaldehyde is primarily used to produce glues for the manufacture of particleboard, veneers, wood furniture and other wood products. Formaldehyde is also used in the manufacture of various plastics, some fertilizers, resins used in foundry sand moulds, and some paints and varnishes. The textile industry uses these resins as finishers to make fabrics crease-resistant. Formaldehyde is mainly stored and sold as an aqueous solution at concentrations varying between 30% and 56% by mass.

Urea-formaldehyde (UF) and melamine-formaldehyde (MF) resins are the most commonly used amino resins. They are produced domestically by adding formaldehyde (CH_2O) to urea (NH_2CONH_2) or melamine ($C_3N_3(NH_2)_3$) to form methylol monomer units, and subsequent condensation of these units to form a polymer. UF are used in the production of home insulation and as adhesives in the production of particleboard, fiberboard, and interior plywood. Moreover, MF is widely used in the manufacture of molding compositions, laminating, adhesives, surface coating and other industrial applications (Pizzi, 1989; Sandler & Karo, 1994).

Industrial releases of formaldehyde can occur at any stage during the production, use, storage, transport, or disposal of products with residual formaldehyde. Formaldehyde has been detected in emissions from chemical manufacturing plants (Environment Canada, 1997a; b; 1999). Formaldehyde occurs in occupational environments mainly as a gas, therefore exposure to formaldehyde in workers occurs mainly through inhalation of the gaseous form (Liteplo & Meek, 2003). Formaldehyde-containing particles can also be inhaled when paraformaldehyde or powdered resins are being used in the workplace (Arts et al., 2006; 2008; NICNAS, 2006). There is also a possibility of dermal exposure to liquid formaldehyde resins. In general, dermal exposure is small compared to inhalation because of the high vapour pressure and low skin permeability of formaldehyde (Collins et al., 2001).

Occupational exposure to formaldehyde by inhalation is mainly from three types of sources: thermal or chemical decomposition of formaldehyde based resins, formaldehyde emission from aqueous solutions (e.g. embalming fluids), or the production of formaldehyde resulting from the combustion of a variety of organic compounds (e.g. exhaust gases) (Goyer et al., 2006; NICNAS, 2006).

Formaldehyde exposures hazards to human health, through industrial activity or consumer products (such as resins, glues, insulating materials, and fabrics), are well known and differ depending on the duration of exposure (Ladeira et al., 2011). In the case of occupational exposure over several years, formaldehyde has been related to causing cancer of the nasopharynx. Carcinogenicity of formaldehyde is still controversial, but more recent analyses seem to find an elevated lung cancer risk in exposed workers in industry. Nasal cancer and malignant melanomas of the nasal cavity have also been reported (Marsh et al. 2007; Mauro Pala et al., 2008). Exposure concentrations are highly variable between workplaces. The reported mean concentrations in the air of factories producing formaldehyde-based resins vary from <1 to >10 ppm (<1.2 to >12 mg/m^3) (IARC, 1995).

To enhance the recognition of the potential health risk in indoor and occupational environments, the main objective of this study was to evaluate the human cancer risk due to formaldehyde inhalation in the workplace environment of a chemical manufacturing plant in Egypt.

2. Materials and methods

i. Sampling and analysis

Formaldehyde was monitored in workplace environment of a chemical manufacturing plant. Air samples were collected in glass bubblers with coarse fritted inlet. It is normally necessary to sample air for quite long period, to obtain sufficient formaldehyde for analysis and a pump capable of drawing at least 0.5 L/min for required time. A critical orifice, rotameter or a gas meter can be used to meter the flow.

Aldehydes in air are collected in 0.05% aqueous solution of 3-methyl-2-benzothiazolone hydroazone hydrochloride (MBTH). The resulting azine is then oxidized by ferric chloride-sulphamic acid to form a blue cationic dye in acid solution which can be measured at 628 nm (Perry & Young, 1977). The formaldehyde content (expressed as HCHO µg/ml) can be determined from the calibration plot. From 0.03 to 0.7 µg/ml of HCHO can be measured in the color developed solution. The reproducibility of the method is to within ± 5%.

ii. Health risk characterization

A- Exposure calculation

Workers could expose to formaldehyde vapor repacking during resin manufacture, production and end use. Workers are likely to be exposed by skin and eye contact during handling of formaldehyde solution such as manual operations and cleaning of the equipments. In this study, characterization of human health risks associated with exposure to formaldehyde is based upon analysis of the concentrations in air. The exposure ***(E)*** for an individual ***(i)*** due to intake process (inhalation) was calculated from the equation of the US EPA (1992a):

$$E_i = C_j IR_i t_{ij}$$

Where ***C*** is the concentration of the pollutant (µg/m^3), ***IR*** is the inhalation rate (m^3/h), ***t*** is the exposure time (h/day) and ***j*** is the microenvironment.

In this study, the different concerned departments in the factory were selected to calculate the exposure ***(E)***, of which the exposure time ***(t)*** was based upon residence time for the staff; a mean residence time of 8 hrs (the official working time) was considered.

Table 1. Exposure parameters used in calculation

Parameters	Value	Reference
Inhalation rate (m^3 day^{-1})	15	US EPA (1989a)
Exposure time (h)	48000	Site assumption
Body Weight (kg)	70	Site assumption
Life time (h)	525600	Site assumption
HCHO Unit Risk Factor (μg m^{-3})	1.3E-5	US EPA (2003)

Indoor inhalation rates were estimated for an average person (IR = $0.63m^3/h$) according to EPA exposure factors (US EPA, 1990).

B- Evaluation of the cancer risk

The cancer risk was estimated by the chronic daily intake (CDI) multiplied by the slope factor according to the USEPA Carcinogenic Assessment Section of the Integrated Risk Information System (IRIS) (US EPA, 1992a; 1996a; 2004a). The Slope Factor is an estimate of an upper-bound probability of an individual developing cancer as a result of a lifetime exposure to a particular level of a potential carcinogen (US EPA, 1996b). On the basis of weight, the slope factor is expressed as [milligrams of substance per kilogram body weight per day (mg kg^{-1} day^{-1})] (US EPA, 1992a).

The CDI can be derived from the following equation (US EPA, 1992b; US EPA, 1996a):

Chronic Daily Intake (mg/kg/day) =

$$\frac{\text{Contaminant Concentration} \times \text{InhalationRate} \times \text{ExposureTime}}{\text{Body Weight} \times \text{LifeTime}}$$

In the current study, certain assumptions were made to estimate the risk, e.g. the amount of air breathed, exposure time and average body weight. To facilitate the estimate of the cancer risk, USEPA suggests standard values of 15 m^3 air breathed per day and an average body weight of 70 kg for man (US EPA, 1990; 1997 a; b). In Egypt, employees spend an average of 8 h day^{-1} and average 300 days of work in a year. Thus, 2400 h of annual exposure and 4800 h of lifetime exposure (equivalent to 20 years of exposure) were considered. Default values of other parameters are shown in **Table 1.** For carcinogenic potency, a slope factor of 0.0455 $(mg/kg/day)^{-1}$ for formaldehyde was used according to the IRIS system (US EPA, 1992 a; b; 1996 a; 2003; 2004a). The inhalation cancer risk of formaldehyde is the output of the multiplication of daily intake and slope factor.

C- Calculation uncertainty

There are several uncertainties in the public health risk characterisations. The objective of the uncertainty analysis was to evaluate the variation or the imprecision of the output or predicted variable (Abdel-Latif, 2001). Uncertainties to the risk characterisation are due to limited information for air monitoring data and lack of perfect knowledge. In addition, uncertainties are inherent in the assumptions and approximations used in modelling in order to estimate the likely exposure to the agent. Generally, uncertainty can be reduced by obtaining better information. The interpretation of risk studies is not an easy one as uncertainty implies that a non-optimal choice might be chosen and quite different outcome might actually obtained instead of the expected one.

3. Results and Discussion

Formaldehyde mean concentration in environment of all departments of the investigated factory was measured and the results are listed in **Table 2**. Formaldehyde concentrations in different departments ranged between 0.11 to 5.7 mg/m^3, and concentrations in many workplace departments exceeded the Egyptian limit value of 0.37 mg/m^3 (EEAA, 1994). The current formaldehyde concentrations of different investigated sites were higher than the regulatory standards for formaldehyde in various jurisdictions as well as the recommendations of independent or governmental organizations that are interested in workers' health and safety (Cavalcante, 2006; Zhang, 2009).

The Occupational Safety and Health Administration (OSHA) has established the permissible exposure limit (PEL) of 0.75 ppm as 8-h time-weighted average (8 h TWA) and the short-term (15 min) exposure limit (STEL) of 2 ppm (OSHA, 2002). In this perspective, the American Conference of Governmental Industrial Hygienists (ACGIH) recommended threshold limit value (TLV) is 0.3 ppm as an 8 h TWA (ACGIH, 2000, 2002). The National Institute for Occupational Safety and Health (NIOSH) recommends much lower exposure limits of 0.016 ppm (8 h TWA) and 0.1 ppm (STEL) (NIOSH, 2011). Moreover, The TWA limit of Japan has approved to be 0.1 ppm (JSOH, 2007).

Formaldehyde levels in different workplaces were reported in many studies worldwide. For example, it was reported a variable formaldehyde mean concentration from 1 to 10 ppm (1.2 to 12.3 mg/m^3) in the air of factories that produce formaldehyde based resins (Stewart et al., 1987). Also, emitted formaldehyde from processing phenol-formaldehyde resins in Poland was found in the range of 0.07–0.197 mg/m^3 (Pośniak et al., 2001). In a recent study carried out at a local Iranian melamine-formaldehyde resin producing factory, mean value of formaldehyde concentration for exposed workers was found to be 0.78 ppm (Neghab et al., 2011). Moreover, Tang et al. (2009) concluded that a person working in an industrial workplace in China can be exposed occupationally to average formaldehyde levels at 0.58 mg/m^3 per hour per day. All these studies indicated that occupational exposure to emitted formaldehyde during the industrial processes might be dangerous for human health due to its carcinogenicity.

Table 2. Concentration of formaldehyde (mg/m^3), calculated daily exposure (mg/m^3), estimated human daily intake (mg/kg/day), and calculated carcinogenic risk

Measuring Site	HCHO Concentration mg/m^3	daily exposure (mg/m^3)	daily intake (mg/kg/day)	Inhalation carcinogenic risk
Mills Plant1	2.08	10.48	4.07E-02	1.85E-03
Mills Plant2	5.7	28.73	1.12E-01	5.08E-03
Extruder 1	1.8	9.07	3.52E-02	1.60E-03
Extruder 2	0.2	1.01	3.91E-03	1.78E-04
Resin Plant 1	2.4	12.10	4.70E-02	2.14E-03
Resin Plant 2	3.8	19.15	7.44E-02	3.38E-03
Laboratory	0.82	4.13	1.60E-02	7.30E-04
Products Store	0.11	0.554	2.15E-03	9.79E-05
Mixers	0.44	2.22	8.61E-03	3.92E-04
Reactor	1.69	8.52	3.31E-02	1.50E-03
Phenol Plant	0.16	0.806	3.13E-03	1.42E-04

People exposed to chemicals, mainly in workplaces have an increased probability of acquiring degenerative diseases (US EPA, 1996b; 2002; ATSDR, 1999). Exposure (*E*) was calculated at different workplaces in the factory taking into account the official working time and the average residence time for staffs during which the occupational exposure to formaldehyde occur **(Table 2)**. The highest calculated exposure was for mills plant 2 and resin plant 2 followed by resin plant 1 and mills plant 1. The calculated exposure results were coincided with the high formaldehyde concentrations at the concerned departments. Occupational epidemiologic studies showed an increased risk of nasopharyngeal and sino-nasal cancer in workers exposed to high concentrations of formaldehyde (IARC, 1995; Environment Canada, 2001).

The same trend was reported for the calculated formaldehyde chronic daily intake and human cancer risks shown in **Table 2**. Daily intake ranges were 2.15E-03 - 1.12E-01, while formaldehyde cancer risks ranged from 9.79E-05 to 5.08E-03. The estimated risk for all reported concentrations were greater than the acceptable cancer risk $1{\times}10^{-6}$ (1 in 1000,000) (US EPA, 1989b), representing a very high human formaldehyde risk.

Consequently, inhalation exposure to formaldehyde has a critical influence on workers and staff of this factory. The risk might represent the high-end estimates (increased chance of developing cancer) for an individual if he continuously breathed air containing formaldehyde for 70 years (life expectancy).

Due to the lack of similar studies, the obtained current data were compared with other previous studies carried out at different occupational locations. For example, it has reported a highest formaldehyde cancer risk for office workers in China (1.25E-04) (Li et al., 2008), which is similar to the finding of Wu et al. (2003) who found a cancer formaldehyde risk range of 2.06E-04 – 1.75E-03 inside offices in Taiwan. It has suggested also that formaldehyde cancer risks in offices are generally higher than other environments due to the common high formaldehyde levels in offices environment (Dingle et al., 2000; Cheong & Chong, 2001; Li et al., 2008).

Table 3 shows that exposures risks of formaldehyde in the current study was higher than the corresponding values recorded in different workplaces worldwide (Báez et al., 2003; Feng et al., 2004; Lü et al., 2006). Furthermore, the current estimated risk due to formaldehyde exposures was much higher than key estimates of the human carcinogenic risk for occupational formaldehyde exposure (for non-smokers) suggested by Chemical Industry Institute of Toxicology (CIIT) (NICNAS, 2006). The occupational respiratory carcinogenic risk of formaldehyde to humans using CITT model, was about 0.05 and 50 in 1 million with exposure concentration of 0.12 and 1.2 mg/m^3 HCHO, respectively.

Integrated Risk Information System (IRIS) presently classifies formaldehyde in carcinogenicity group B1 (probable human carcinogen), with an inhalation unit risk of (1.3E-5 µg/m^3)$^{-1}$; http://cfpub.epa.gov/ncea/iris/index.cfm?fuseaction=iris.showQuickView&substance_nmbr=0419; (last updated on September, 2011).

Table 3. Comparison of exposure risks of formaldehyde in the indoor air with the current study

Parameter	Formaldehyde		
	Mean	Risk (mean)	Reference
Office			
C (µg/m^3)	26.2	3.4E-4	Báez et al. (2003)
E (µg/day)	132		
Ballroom			
C (µg/m^3)	33.1	4.4E-4	Feng et al. (2004)
E (µg/day)	124		
Hospital			
C (µg/m^3)	8.3	1.1E-4	Lü et al. (2006)
E (µg/day	41.8		
Maximum			The current study
C (µg/m^3)	5700	5.08E-03	
E (µg/day)	28728		
Minimum			
C (µg/m^3)	100	8.90E-05	
E (µg/day)	504		

C: Concentration, E: Exposure

Cancer risks for formaldehyde should be viewed as preliminary, in coincidence with Báez et al. (2003) who emphasized that parameters such as the ventilation rate, time spent outside and inside houses and offices, transportation media, the duration and type of physical activity, i.e. work, rest, and light-to-moderate activity, were not determined, and because of insufficient data. Besides, there are other limitations such as uncertainties in the estimation of unit risks and reference concentrations (Caldwell et al., 1998).

Conclusions

Although carcinogenic effects due to formaldehyde are well documented in the literature, there is also a need to determine or examine the health impact of inhalation exposure to formaldehyde in Egyptian workers. Based on the current study, monitoring should be conducted where a workplace assessment indicates a potential risk to health due to hazardous chemical. Formaldehyde-free products should be considered for replacing high level formaldehyde products in industry whether possible.

Main scientific uncertainties in the risk assessment process used included measurement uncertainties and exposure scenario uncertainties (USEPA, 2004b). Concerning measurements uncertainties in the current study, the concentrations used were based on short-term measurements and potential daily variations over prolonged periods are ignored. Exposure time, inhalation rate, body weight and calculation method are the scenario uncertainties because the assumptions used in this study were based on information of international survey which could not represent the accurate characteristics in Egypt.

Given these results, preventive actions must prioritize environmental safety conditions for workers. In general, reduction of exposure to formaldehyde in this occupational setting may be achieved through adequate control means. Effective ventilation is a critical control measures to maintain exposure level below the national exposure standard. Workplaces with elevated levels of formaldehyde should institute engineering controls to maintain workers occupational exposure as low as possible. Where elevated exposure is not prevented, workers should wear appropriate protective gloves and respiratory devices.

It is strongly recommended to conduct epidemiological studies on formaldehyde's health effects, as well as extensive investigations on the characteristics of formaldehyde-exposed populations to confirm the findings of this study.

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