Chemical risk: state of the art of chemical substances exposure assessment

Riesgo químico: estado del arte sobre la evaluación a la exposición de sustancias químicas

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Keywords

Chemical risk; assessment; exposure; substances, effects.

Abstract

Given the ability of chemical substances to generate possible adverse effects on people's health, it is necessary to identify, collect and integrate all the information related to the dangers associated with these substances. Throughout the years, the definition of risk has had different interpretations, which has given rise to different alternatives for its evaluation and management. Currently, there are several equipment and tools used in chemical risk assessment. In the present study, a bibliographic review was carried out for different chemical scenarios where sixteen chemical risk assessment methodologies were analysed during the period 2003-2020 that correspond to both, qualitative and quantitative methods. In conclusion, the risk assessment methodologies have undergone changes over the years according to the needs and increasing complexity of the systems where they apply, artificial intelligence could also be a useful tool in chemical risk assessment.

Palabras clave

Riesgo químico; evaluación; exposición; substancias; efectos.

Resumen

Dada la capacidad que tienen las sustancias químicas de generar posibles efectos adversos sobre la salud de las personas, es necesario identificar, recopilar e integrar toda la información relacionada con los peligros asociados a estas sustancias. A lo largo de los años, la definición de riesgo ha tenido diferentes interpretaciones, generando diferentes alternativas y formas para su evaluación y gestión. Actualmente, existen variados instrumentos científicos y herramientas metodológicas que se utilizan en la evaluación del riesgo químico. En el presente estudio se realizó una revisión bibliográfica para diferentes escenarios químicos, donde se analizaron dieciséis metodologías relacionadas con la evaluación del riesgo químico. La revisión del estado del arte comprendió artículos científicos publicados durante el periodo 2003-2020, incluyendo tanto a métodos cualitativos como cuantitativos. Como conclusión principal se indica que las metodologías de evaluación de riesgos han experimentado cambios a lo largo de los años producto de factores como las necesidades y la creciente complejidad de los sistemas donde se aplican y de la inteligencia artificial; esta última pudiendo ser una herramienta útil en la evaluación de riesgos químicos.

Introduction

Chemicals are present in our environment in one way or another and many of these are used to improve the quality of life. Various chemicals used in industry and in everyday life have been classified as toxic and dangerous to health and the environment; however, most chemicals are not harmful to the environment or health, although some have the potential to produce adverse effects [1]. Studies have shown an association between the use of toxic chemicals and the risk of developing chronic diseases such as dermatitis, nasal septum perforations, respiratory diseases and ulcers [2].

Chemical agents can enter the through body by inhalation (through respiration), dermal (through the skin), digestive (ingestion of the chemical) and parental (through wounds or punctures) route [3, 4]. High environmental concentrations can increase the amount of chemical that enters the through body, as well as the time of prolonged exposure and favorable conditions in the subject, such as rapid breathing, skin lesions or damage to the body that do not allow its to eliminate correctly the chemical agent [3].

Due to the use and exposure to chemicals, it is important to know the level of occupational risk to which people are exposed. Occupational risk refers to the possibility that a worker may suffer some damage (illness, pathology or injury) due to certain facts or actions derived from them work [5,6]. From the point of view of seriousness, occupational risk assesses both the probability and the severity of the damage [5] and makes it possible to recognize and compensate for such damage, whether as accidents at work or occupational diseases [6]. Chemicals have various properties, which carry different types of risks [7]. Chemical risk is the ability of chemical substances to generate possible adverse effects on people's health. This depends on the conditions and routes of exposure to the chemical agent, as well as on its physicochemical and toxicological properties [8].

Occupational risk evaluation

The occupational risk assessment is used in industrial streams or in facilities that handle chemical products, to determine potential hazards in the tasks performed. Its main objective is always to eliminate and / or reduce risks to the lowest possible level [9]. Within the workplace, it is essential to identify, collect and integrate all the information related to the supposed dangers of a chemical agent, as well as to enter into dose-exposure-damage [10].

Risk has had various interpretations throughout the years, therefore, different definitions of risk can lead to different alternatives for its evaluation and management. This is why risk assessment methods have undergone continuous development over the years, because they are also capable of evolving in parallel with the increasing complexity of the systems where they are applied [11].

Occupational exposure limit values

Exposure limit values are a form of evaluation criterion, defined as magnitudes of reference values for the concentrations of the different chemical agents and they are the value of a magnitude can be compared the reality to be evaluated. In the Latin American context, the exposure values used in the USA are used more specifically for TLVs, which are, according to the time metric, divided into several types as the following; [7]

- TLV-TWA. Time-weighted average. A normal day of 8 hours and 40 hours per week is estimated, with a daily exposure in which workers do not suffer adverse effects. Generically when speaking of TLV, reference is made to TLV-TWA
- TLV-C. Ceiling value is a concentration that must not be exceeded at any time
- TLV-STEL. Exposure limits for short periods of time. It is defined as the concentration to which workers can be exposed for a short period of time without having any type of adverse effect. The TLV-STEL is a complement to the time-weighted average (TWA). It is estimated as the 15-minute time-averaged mean exposure that does not have to be exceeded during the day.

International and national regulations

International regulations

In 1970, the Occupational Safety and Health Act was enacted in the United States. Under this law, the Occupational Safety and Health Administration (OSHA) and the National Institute for Occupational Safety and Health or NIOSH (National Institute for Occupational Safety and Health) are created, which works together with OSHA to carry out investigations and offer recommendations for work-related injuries and illnesses, with the aim of promoting a safe and healthy workforce [7,12].

National regulations

The Political Constitution, in its articles 21 and 50, establishes that the right to life and health of persons is a fundamental right, where the State has an inexorable obligation to ensure their protection. Derived from this duty of protection, the General Regulation on Occupational Safety and Hygiene was created, where risk factors are analyzed according to the measures that must be taken to avoid damage to the health of workers. Chapter V of dangerous substances establishes in relation to the permissible limits of these substances, that this will be carried out in accordance with the provisions of the International Labor Organization [13,14].

Methodologies to assess chemical risk

Among the chemical risk assessment methods are; the British model COSHH Essentials, the French model from the Institut National de Recherche et de Sécurité (INRS) [15], Chemical Risk Management (CHARM) [14], Stoffenmanager, ECETOC TRA Targeted Risk Assessment, Advanced REACH Tool (ART) [16], New Approach Methodologies (NAM) [17], Critical Task Exposure Screening (CTES) [18], Artificial Intelligence for Chemical Risk Assessment [19], Lung function tests [20], SQCRA Method [31] [33], PBPK Model for Modified Ethanol [20], Chem-SAM, UOW and SQCRA Methods [21], Chemical Health Risk Assessment (CHRA) [22], Exposure to Ultrafine Particles [23], Application of PBPK models in support of derivation of toxicity reference values for 1,1,1-trichloroethane [24], Assessment of hazards and risks of industrial chemicals in the occupational context in Europe: some current problems [25].

Control of Dangerous Substances for Health (COSHH Essentials)

N.P. Vaughan., *et al.* [26] made a comparison between the target concentration ranges in the air taking into account the initial classification that COSHH essentials made to 111 substances that had a current Occupational Exposure Limit (OEL) based on health in Great Britain and extended it to a wide range of substances (over 95%, 850 substances) that did not yet have a recognized OEL. The exercise included substances with OEL published by nine international organizations; and the threshold levels (DNEL) assigned by registrants in the EU: Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). It was concluded that when comparing the 8-hour TWA OELs for 850 substances extracted from nine bodies and a limited number of DNELS, the target concentration ranges of C-E in air remain valid [26].

Chemical Risk Management (CHARM) and Control of Dangerous Substances for Health (COSHH Essentials)

M. Kim, *et al.* [27] carried out a chemical risk assessment of 59 carcinogenic, mutagenic and reprotoxic substances (CMR). During their study they used the COSHH Essentials (UK) and the CHARM (South Korea) methods separately. Among the results obtained with these two methods is that the identified risk level was much lower for CHARM than for COSHH Essentials; the risk assessment was high for both, but the exposure assessment was low for both. CHARM determines the level of exposure based on measurements of the chemical work environment. COSHH Essentials assesses exposure levels using physical properties and general handling, and assesses the hazard using the H-phrases or R-phrases. It has been judged to be more conservative than CHARM [27].

Simplified Chemical Risk Assessment Methodology (INRS) and Control of Hazardous Substances for Health (COSHH Essentials)

A. Segura & A. R. Maurí [15] made a comparison of the risk assessment in a research laboratory at the University of Valencia, Spain, where a wide variety of chemical agents are used, usually in small quantities. The researchers used simplified chemical inhalation risk assessment methods (COSHH Essentials and INRS-based method). During fieldwork, information was collected on agents used, quantity, mode of use, frequency of use, working temperature and collective and individual protection used. Likewise, the information has been supplemented with the necessary data, R and H phrases, environmental limit value and boiling temperature. The main conclusion of the research is that both methods can be a simple resource to plan prevention in work environments with chemical risk. The INRS-based method contemplates more risk determinants than COSHH Essentials, but the disparate characteristics of both methods should determine the best choice for each situation; or even, as the results of this study suggest, its complementary use [15].

Stoffenmanager, ECETOC TRA v3. and ART

N. Savic, *et al*. [16] investigated the degree of consistency for evaluating the risk of exposure to vapors from volatile liquids, powders and abrasive solids, and for non-volatile liquids mixtures. During the study, the Stoffenmanager, ART and ECETOC TRA v3 risk assessment tools were applied separately. In this analysis the translation rules between the models defined in TREXMO were used to generate 319,000 different situations of *in silico* exposure in ART, Stoffenmanager and ECETOC TRA v3. The estimates of the three models were calculated and the correlation and coherence between them were investigated. The main conclusions are that the best correlated pair was Stoffenmanager-ART (R, 0.52-0.90), while the ART-TRA and Stoffenmanager-TRA correlations were the lowest (R, 0.36-0.69) or no correlation was found. In general, the models were more consistent for vapors than for powders and solids, near fields than for far fields and indoors than for outdoor exposure [16].

New approach methodologies for exposure science

Wambaugh, J.F. *et al*, [17] theoretically analyzed several NAMs (New approach methodologies for exposure science) that are applied around the research that is currently carried out in collaboration with the ExpoCast project ('Exposure forecast') of the Environmental Protection Agency of the States United (EPA), to characterize the routes of exposure. It describes how these NAMs can be combined with hazard information to establish exposure models, chemical priorities, including the identification of highly exposed or susceptible populations taking into account human variability in exposure. Finally, the great importance of current advances in high performance methods for hazard identification is concluded. Together, these new approaches allow for greater certainty about the environment in which we are exposed and its impact on public health [17].

Critical Task Exposure Screening (CTES)

E. Tjoe-Nij, *et al*. [18] conducted a Critical Task Exposure Screening (CTES) study at a global chemical company where they evaluated 5 tasks using three chemicals: trimethylamine (three tasks), isopropanol (one task), and paramethoxyphenol (one task). To carry out the study, information was collected on the chemical agents studied (toxicological data, including the occupational exposure limits (OEL), the occupational exposure band (OEB) and the vapor pressure), they specified the concentrations of the substance and the tasks and their duration were described. For each substance, inhalation risk scores (which were compared with results obtained using the ART 1.5 model), skin hazards with warnings for local and systematic adverse effects, and status of CMR effects were obtained. Trimethylamine presented the task with the highest risk. The main conclusion of this study is that CTES is an easy-to-use and reliable tool that allows establishing priorities and focusing on the most critical scenarios, in addition that the ART 1.5 model can be included effectively in detection tools such as the one described [18].

Artificial Intelligence for the Evaluation of Chemical Risks

C. Wittwehr, *et al*. [19] conducted an assessment of how, and to what extent, artificial intelligence can support chemical risk assessment. These scientists believe that the use of artificial intelligence can improve various areas, among which are the identification and prioritization of problems, improvement of the evidence base (adding, interpreting and processing useful information), discovery of knowledge (joining information from different sources), evaluation process in a neutral, coherent and transparent way, and through the construction of cognitive and decision-making models. In conclusion, it is recommended that further exploration of these issues in conjunction with the global collaboration of various disciplines materialize into executable plans for pilot projects, in order to improve the effectiveness and efficiency of the chemical risk assessment process [19].

Lung function tests

Y. Mehrifar, *et al.* [20] carried out a cross-sectional study in an Iranian shipbuilding factory, with the purpose of determining the incidence of respiratory symptoms and lung function, in welders exposed to the effect of toxic gases and metallic fumes resulting from the SMAW, GMAW and FCAW welding processes. For this study, 60 welders and 45 factory administrative employees were selected. The toxic gases evaluated are CO, NO, NO2, O3 and CO2, regarding the toxic fumes, the total smoke and six metals (Cr, Mn, Mg, Cu, Fe and Al) were evaluated. All contaminants were taken from the respiratory tract of welders and analyzed using standard methods suggested by the American National Institute for Occupational Safety and Health (NIOSH). A pulmonary function test (PFT) was also performed using calibrated MIR spirometry. In conclusion, it was determined that welding, especially of the GMAW type, is related to the production of large amounts of metal gases and fumes and drastically deteriorates lung function in welders [20].

SQCRA method

S. Karimi Zeverdegani, *et al.* [28] carried out a cross-sectional study in an Iranian steel factory in order to assess the risk of exposure to gases produced by the PAW, SAW and GTAW welding types. To do this, the researchers used the Semi-Quantitative Chemical Risk Assessment (SQCRA) method proposed by the Occupational Safety and Health Division of the Singapore Ministry of Human Resources. During fieldwork the concentration of O3 ,CO, NO, NO2 and CO2 was obtained by means of direct reading instruments known as real-time instruments, including detector tubes (GASTEC Corporation, Japan) and piston pump (Gastec GV-100- S-TR, GASTEC Corporation, Japan). The main conclusion of the study is that there should be greater control in the welding processes, for which the use of respiratory protection equipment and extraction ventilation is recommended [28].

H. Dazi, *et al.* [29] carried out a cross-sectional study in one of the petrochemical industry complexes, in a special area of Assaluyeh, Iran, workers are exposed to various dangerous chemical factors. During the evaluation, the SQCRA method and spirometry were also used through a series of experiments in pulmonary function tests (PFTS). Information was collected on the toxic and / or dangerous effects of chemical reagents, vapor pressure or particle size of the chemical, OT / PEL radio, safety measures, amount of material used per week and amount of time worked per week. Of the materials used by workers 48.14% present a low chemical risk, 29.62% medium chemical risk, 18.51% high chemical risk and 3.7% very high chemical risk [29]. Similarly, M. H. Beheshti *et al*. [30] used the SQCRA method in the operating unit of an Iranian petrochemical company with high amounts and exposure to various chemical contaminants. The results obtained indicate that 81% of the chemicals used have a moderate or high chemical risk [30].

PBPK model for modified ethanol

A. Maier, *et al*. [31] conducted a safety assessment using a Weight-Of-Evidence (WOE) approach using a Physiologically Based Pharmacokinetic (PBPK) model, in order to assess the potential adverse effects on development and reproduction related to the use of alcohol-based hand sanitizers (ABHS) in healthcare workers. Two different application scenarios were evaluated: hand hygiene application (small amounts with several applications per day) (modeled after a description made by the US FDA and data found in the open literature) and surgical application (higher amount and fewer applications per day) (conditions based on studies by Kramer *et al*, 2017 and on an alternative typical product use scenario). The model considered the skin compartment to allow simulation of dermal exposures and the inclusion of the hepatic form and urinary excretion of ethyl glucuronide, used as a biomarker for ethanol exposures. The study concluded that the use of ABHS by healthcare workers is safe, even under hypothetical conditions of the worst use scenarios [31].

Chem-SAM, UOW and SQCRA methods

S. Karimi Zeverdegani, *et al.* [21] made a comparison of the risk assessment in a chemical laboratory using three different methodologies; the Chemical Risk Management Self-Assessment Model (Chem-SAM), the University of Wollingong (UOW) Risk Assessment method and the Semi-Quantitative Chemical Risk Assessment (SQCRA) method. During fieldwork, information was collected regarding chemical toxicity, exposure, risk controls, chemical reactions, etc. Compiled the data indicated by each methodology, a statistical analysis was performed using SPSS (Version 20.0, IBM Corporation, Armonk, NY, USA) and a graph was drawn with the Excel software. The main conclusion of the research is that the three methodologies presented similar results on the level of risk of exposure at the evaluated site [21].

Chemical Health Risk Assessment (CHRA)

S. N Hunadia, A. Bakar, SR Sheikh & N. Anuara [22] carried out a Chemical Health Risk Assessment (CHRA) on the use of chemical agents in thirteen teaching and research laboratories of the Department of Chemistry and Process Engineering (JKKP) at the National University of Malaysia. To obtain the Risk Rating (RR), the Exposure Rating (ER) and the Hazard Rating (HR) were evaluated, also, the duration of exposure, the degree of presence, release and chemical absorption of the agent were studied. The final risk rating for all laboratories tested was C3, indicating that the department needs to identify measures, precautions, monitoring requirements, or health surveillance to maintain controls and decrease exposures. As part of the results, the university's security committee carried out monthly inspections of the evaluated sites for periodic monitoring and control [22].

Exposure to ultrafine particles

G. Buonanno *et al.* [23] carried out an evaluation on the influence on activity and time patterns on the levels of exposure to ultrafine particles present in certain activities and everyday microenvironments in central Italy (southern Lazio, in the macrozone Frosinone) during the summer and winter. Twenty-four non-smoking couples (12 in summer and 12 in winter) were selected, consisting of a man who works full time and a woman who only performs domestic chores, belonging to urban, suburban and rural areas. A mobile experimental device consisting of two portable UFP counters (NanoTracer, Philips) equipped with GPS tracking was placed on each person. During this research, information was collected on the concentration of the number of particles, the surface area of particles deposited in the lung, and the mean diameter of the particle number size distributions. An average concentration of higher number of particles was observed in women both in summer and winter, although mostly in the latter due to a reduction in indoor ventilation and outdoor inversion phenomena. Regarding the deposition of particles in the alveolar surface area, this was higher in women only in winter [23].

Application of PBPK models to support the derivation of toxicity reference values for 1,1,1-trichloroethane

L.Yasoung *et al.* [24] developed a review of the published literature of the PBPK models, for the extrapolation of doses, routes, and species, specifically for 1,1,1-trichloroethane and thus assess their applicability in the derivation of reference values in various durations of exposure. The experimental part included a multi-step reconstruction, testing, and evaluation of the PBPK models. The most adaptable model was found to be that published by El Reitz *et al*. (1988). It is concluded that the analysis shows that in the case of 1,1,1-trichloroethane toxicity, PBPK modeling can provide a scientifically credible alternative to the frequently used predetermined extrapolations in risk / health assessments [24].

Assessment of hazards and risks of industrial chemicals in the occupational context in Europe: some current problems

S. Fairhurst, conducts a study on industrial chemicals within the framework of the European continent, as well as existing regulations, indicate the limitations for the correct identification of risks and hazards as well as the existing gaps in the regulation of dangerous chemicals, as part of the investigation, two routes of classification of dangerous substances are proposed; Self-classification by suppliers and adherence to specific decisions of the European Union imposed by regulators. It is concluded that there are numerous scientific problems. that they remain unsolved, where knowledge and understanding is inadequate; There are many problems to discuss and considerable room for further improvement in the topic of chemicals management [25].

Conclusions

In total, sixteen methods applied during the years 2003 to 2020 were analyzed in different chemical scenarios such as laboratories, companies, steel, naval and petrochemical industries.

Among the most widely used methodologies are the Semi-Quantitative Chemical Risk Assessment method, the Physiologically Based Pharmacokinetic model and the British COSHH Essentials model.

Most of the methods use qualitative or quantitative systems or direct measurements by means of equipment such as ultrafine particle monitoring equipment, spirometers and direct reading instruments in real time.

Among the shortcomings of the methodologies are the difficulty in obtaining representative and truthful information, its little applicability to different exposure scenarios and the different criteria by analysts at chemical risk.

Among the advantages of the studied methods are the possibility of carrying out *in-silico* studies, which avoids the need to experiment in humans; they allow obtaining a reliable level of risk without the need to carry out environmental measurements; In addition, they provide a hierarchy of risk based on a general criterion.

The methods agree that the risk assessment needs to be carried out according to a systematic analysis where the objectives and steps to be followed are determined according to the needs, conditions and characteristics required by the researcher or analyst.

Artificial intelligence is viewed as a tool that could provide results with greater precision and accuracy, as well as offering efficiency in the chemical risk assessment process.

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