REVIEW ARTICLE

Health risk due to the chronic use of formaldehyde in workplace settings and as a component of hair straightening products

Sebastián Vera M [1,a]; Sigrid Mennickent C* [1,a,b]; Carolina Gómez-Gaete [1,a,c]; Cristian Rogel C [2,a,d]

ABSTRACT

Formaldehyde is a chemical compound used as a precursor in various industrial processes and hair straightening products. It is classified as carcinogenic in humans. Considering the importance of the topic, this review aims to identify and characterize the health risks that formaldehyde chronic exposure involves and to describe the existing evidence of its main toxic effects as well as the risk factors during the application of this compound in the hair straightening process.

For this purpose, a literature review was carried out by using the PubMed database, limiting it to studies conducted between 2010 and 2020. A total of 126 publications were found, for which a relevance analysis was performed, and those that studied the effects after chronic inhalation of formaldehyde in humans were selected. Finally, this search resulted in 75 publications. Among the harmful effects of formaldehyde analyzed in each publication, those present in three or more publications were selected.

Based on the results obtained in this review, harmful effects of formaldehyde chronic exposure cannot be ruled out. There is evidence from the literature that corroborates the increase in genotoxic processes in humans, specifically in nasal epithelial cells and peripheral blood leukocytes. On the other hand, there is no robust epidemiological evidence that links chronic exposure to this compound and leukemia or nasopharyngeal cancer. Regarding reproductive toxicity, there are reports of miscarriages and low birth weight, even when the exposed subject is the future father. Other pathologies that have been linked to formaldehyde chronic exposure are renal damage, methemoglobinemia, asthma, dermatitis, tumors, skin irritation and burns, eye fatigue and pain, tearing, mood changes, fatigue, sore throat, rhinorrhea and headache.

On the other hand, the average concentration of formaldehyde to which a person could be exposed during a hair straightening treatment shows alarming values since it frequently exceeds the least restrictive exposure limits and can reach levels much higher than those experienced by the exposed subjects included in the reviewed epidemiological studies. It is important to have good ventilation and use products with formaldehyde concentrations within the allowed limit.

Keywords: Formaldehyde; Toxicity; Risk Factors; Hair Preparations (Source: MeSH NLM).

INTRODUCTION

Formaldehyde at room temperature is a colorless gas with a distinct pungent and suffocating odor, irritating to the eyes, nose and lungs [1]. Formalin, a 37 % to 40 % w/v aqueous solution of formaldehyde, is colorless, also has a pungent odor, and is irritating and toxic if ingested (National Institute for Occupational Safety and Health - NIOSH, 2007).

Formaldehyde in solution is also referred to as formalin or formol. There are also products initially free of formaldehyde but contain methylene glycol, which generates formaldehyde through a temperature-mediated chemical reaction, e.g., during the hair straightening process. Up to 47 % of the vaporized volume at 204 °C of a 37 % formalin solution (59 % methylene glycol) corresponds to formaldehyde [2,6].

Formaldehyde is used to manufacture explosives, fuels, resins, paint, adhesives, plastics, textiles, electronic products, plywood, disinfectants, as a preservative in agriculture and biological samples, and in the production of cosmetics [6,7,9-18].

As to hair straightening products, formaldehyde is used due to its ability to create covalent bonds between the amino acids of the keratin contained the hair fiber and the amino acids of the keratin contained in the product [2,3].

1 Universidad de Concepción, School of Pharmacy, Departamento de Farmacia (Department of Pharmacy). Chile.
2 Universidad de Concepción, School of Pharmacy, Departamento de Ciencia y Tecnología de los Alimentos (Department of Science and Food Technology). Chile.
[a] Pharmaceutical chemist; [b] Master in Pharmaceutical Sciences; [c] PhD in Pharmaceutical Technology and Biopharmacy; [d] PhD in Food Science.
*Corresponding author.

Formaldehyde is easily absorbed by mucous membranes and airways and reacts with macromolecules such as proteins and nucleic acids [19]. It is capable of producing covalent bonds between DNA and proteins or DNA-protein crosslinks (DPCs), which is one of the most harmful and least studied types of genetic damage, leading to steric hindrances in transcription and replication. If not repaired, DPCs can result in mutations, genomic instability and cell death. Hair straightening products are used to remove waves from the hair: after leaving them on for about 30 minutes, the hair is straightened with a curling iron heated to 230 °C. Formaldehyde can be released in high concentrations, posing a risk of allergic reactions or irritation of the eyes, skin and airways and, in some cases, more serious consequences [20].

Formaldehyde is classified as carcinogenic in humans [5]. In Chile, Supreme Decree No. 594, which establishes the basic sanitary and environmental conditions that all workplaces must comply with, sets an absolute allowable limit of 0.3 ppm for formaldehyde [21,22].

In July 2023, the European Commission adopted a new regulation aimed at safeguarding public health and environmental well-being. It intended to regulate the use of formaldehyde and formaldehyde-releasing agents. The regulation was prompted by the European Chemicals Agency (ECHA), which highlighted the inadequacy of current controls on formaldehyde exposure in consumer goods placed on the community market. The dossier revealed that formaldehyde-releasing substances could lead to concentrations that might exceed safe levels in indoor air, posing a potential risk to human health.

After a thorough evaluation, the commission established an emission limit of 0.062 mg/m³ for furniture, wood-based articles and composite products, and 0.080 mg/m³ for all other products [23].

In February 2023, the Agência Nacional de Vigilância Sanitária (ANVISA - National Health Surveillance Agency) of Brazil reported the recall of products for styling, braiding and setting hair due to reports of health issues, some serious, mainly affecting the eyes (even resulting in temporary blindness). Ninety percent of these effects required medical assistance. The marketing of all types of these products—not only those involved in the reports—was banned. Several compounds, including formaldehyde, were considered to be the cause of the health issues. At the local level, the Instituto de Salud Pública (ISP – Public Health Institute) conducted a review of the existence of these products in Chile, but it could not find their existence or imports [24].

The U.S. Occupational Safety and Health Administration (OSHA) has established an allowable limit of 0.75 parts of formaldehyde per million parts of air (0.75 ppm) for an 8-hour workday during a 40-hour workweek [25].

The objective of this study was to identify and characterize the health risks associated with chronic exposure to formaldehyde and hair straightening products that contain or produce formaldehyde.

SEARCH STRATEGY

A literature review was conducted using the PubMed database, restricted to studies between 2010 and 2020, and using the keywords formaldehyde, toxic effects and risk factors.

A total of 126 publications were found, which were then analyzed for relevance, selecting those that studied the effects of chronic formaldehyde inhalation in humans, resulting in 75 publications [1-75]. The effects present in three or more publications were selected from the harmful effects of formaldehyde analyzed in each publication.

The description of the risk factors involved in exposure to formaldehyde released by hair straightening products included the formaldehyde concentrations in these products and the volume of air around the users (dependent on the space where the treatment is performed) as the main variables to determine the maximum level of exposure [8,26-30,36,38].

To estimate the formaldehyde concentration in hair straightening products, the analytical results obtained by Pierce et al. [26] were used. Values between 1 m³ and 24 m³ were considered for the air volume. The minimum value represents the direct exposure around the stylist and client, and the maximum value represents the exposure for beauty salon attendees who are not in direct contact with the treatment [26].

To determine the amount of product used by each procedure, the simulation method by Stewart et al. was used, which considers a product volume of 30 ml and estimates the percentage of formaldehyde contained in the products that is released during the treatment, a value that varies depending on the consulted study. In this case, the most conservative estimate of 5.1 % is assumed [28].

The formaldehyde concentration in air was obtained from the formula: $c = (b/1.23)/v$, where c represents the formaldehyde concentration in ppm, b the amount of formaldehyde released in mg, and v the volume of air in the room [28].

The formaldehyde concentration in the product to be used is the most important factor in predicting whether its concentration in air will reach levels above the absolute allowable limit. The dimensions of the room also play an important role. According to these parameters, the stylist applying the treatment and the client could be exposed to concentrations even 460 times above the limit of 0.3 ppm.

The literature review also allowed describing the four most frequently studied toxic effects resulting from formaldehyde inhalation.

Genotoxicity-related studies

Bono et al., in 2010 [(30)], studied the relationship between formaldehyde in air and the formation of M_1dG adducts (a biomarker of oxidative stress and lipid peroxidation) in leukocyte DNA among pathology laboratory workers exposed to formaldehyde. Their results revealed a significant increase in the number of M_1dG adducts in pathologists compared to unexposed controls: 5.7 M_1dG adducts per 10^8 normal nucleotides (nn) and 2.4 M_1dG adducts per 10^8 nn, respectively ($p = 0.021$). They also underscore that increased levels of M_1dG adducts were detected only in workers exposed to more than 0.054 ppm of formaldehyde. However, the predictive value of early biomarkers is limited for estimating individual risk because the process from exposure to disease depends on numerous factors (genes, age, diet, lifestyle, etc.).

Santovito et al., in 2011 [(31)], evaluated the occurrence of chromosomal aberrations in peripheral blood lymphocytes from workers exposed to formaldehyde. They also analyzed the presence of inactive genotypes of the enzyme glutathione S-transferase (GST), which is responsible for the metabolic detoxification of environmental mutagens and carcinogens and their reactive metabolites. Their results indicated a significant increase (approximately three times) in the frequency of chromosomal aberrations per cell ($p < 0.001$) in the peripheral blood lymphocytes of workers exposed to formaldehyde (on average 0.059 ppm compared to controls exposed only to 0.030 ppm). Furthermore, they reported that genetic damage was not significantly influenced by the presence of inactive GST genotypes.

Kim et al., also in 2011 [(32)], reported damage to chromosomes and DNA in human peripheral blood cells, increased frequency of micronuclei in nasal epithelial cells after only eight weeks of exposure (0.41-0.80 ppm) and higher frequency of micronuclei in lymphocytes after one year of exposure, as well as increased sister chromatid exchange in individuals exposed to 0.5 ppm formaldehyde, compared to their control groups. In addition to this, the authors mention frequent chromosomal aberrations in peripheral blood lymphocytes of children exposed to formaldehyde in prefabricated schools. Concerning the possibility of carcinogenesis due to formaldehyde exposure, they indicate that formaldehyde undergoes chemical changes immediately after being absorbed; therefore, they consider it is unlikely that there are effects beyond the upper airways. Finally, they state that low levels of formaldehyde in air (< 1 ppm) may only have minimal or even nonexistent carcinogenic potential in humans.

Costa et al., in 2013 [(33)], studied the occurrence of genotoxicity by measuring the frequency of cells with micronuclei, sister chromatid exchange and T-cell receptor mutations in peripheral lymphocytes of workers exposed to an average of 0.36 ppm formaldehyde. The percentage of micronuclei was 2.5 times higher, and the sister chromatid exchange per cell was 1.3 times greater, in both cases, particularly in exposed workers compared to the control group ($p < 0.05$). The frequency of mutations in T-cell receptors was not significantly altered when comparing both groups.

Costa, in 2015 [(40)], evaluated the effects of formaldehyde on peripheral blood lymphocytes of workers exposed to an average of 0.38 ppm, and detected chromosomal aberrations and DNA damage. According to the authors, their results confirm the genotoxic activity of formaldehyde at the structural level in chromosomes, as well as the risk of damage to peripheral blood lymphocytes. Lorenzoni et al., in 2017 [(41)], researched the potential mutagenic and cytotoxic effects of formaldehyde on the buccal epithelium cells of students exposed to 0.73 ppm of the compound during anatomy classes. The frequency of micronucleated cells in the students increased significantly from 0.05 % to 0.11 % after one month of exposure ($p = 0.034$), and then to 0.16 % after 3.5 months of exposure ($p = 0.017$).

Liang et al., in 2018 [(42)], evaluated the risk of carcinogenesis in workers in China exposed to formaldehyde by collecting air samples from different areas of public places. They obtained an average formaldehyde concentration of 0.46 ppm, with a maximum of 0.67 ppm, and cancer risk rates ranging from 4.7×10^{-5} to 1.57×10^{-4}. These values were above the acceptable range of 1×10^{-6} proposed by the U.S. Environmental Protection Agency (EPA). Of particular interest for this review was that, according to their study, the authors found that work in beauty salons had the highest cancer risk: 1.57 in 10,000 for men and 1.47 in 10,000 for women (1.57×10^{-4} and 1.47×10^{-4}, respectively), one order of magnitude above the hotel industry, shopping malls and cultural or entertainment centers, and two orders of magnitude above the acceptable risk of one in a million.

Zendehdel et al., also in 2018 [(43)], determined, in Iranian workers, a cumulative exposure between 2.4 and 1972 mg in one year, and estimated the level of formaldehyde exposure at which there is a 10 % excess risk of genetic damage at 0.08 ppm.

Aglan et al., in 2020 [(36)], found a significant increase in genotoxic markers in workers exposed to formaldehyde, and there was a positive correlation between the degree of increase and the duration of exposure.

Leukemogenicity-related studies

Zhang et al., in 2010 (44), conducted a cross-sectional study aimed to determine whether formaldehyde exposure alters hematopoietic function and causes leukemia-related chromosomal changes. They studied 43 workers exposed to formaldehyde (median of 1.28 ppm) and 51 controls in China. The effect of formaldehyde as an inhibitor of myeloid progenitor cell differentiation was studied by measuring the number of colonies formed in cultures of blood samples from volunteers, confirming a 20 % decrease in exposed workers. Although the decrease was not significant ($p = 0.10$), the inhibitory effect on the myeloid progenitor cell differentiation was supported by the results of hemograms, which showed a significant decrease in the total leukocyte count ($p = 0.0016$) and a significant decrease in the lymphocyte count ($p = 0.0002$) in exposed workers compared to the control group.

Bachand et al., also in 2010 (45), conducted a series of meta-analyses of epidemiological literature on the association between formaldehyde exposure and leukemia. The authors did not evidence a significant increased risk of leukemia between exposed individuals and controls, since the summary relative risk (RR) was 1.05 (95 % confidence interval [95 % CI]: 0.03-1.20) for cohort studies and the summary odds ratio *(OR)* was 0.99 (95 % CI: 0.71-1.37) for case-control studies.

Goldstein, in 2010 (46), published a review of the existing hematological and toxicological evidence, focusing particularly on confirming or refuting the findings of pancytopenia and chromosomal abnormalities in Chinese workers exposed to high formaldehyde concentrations as reported by Zhang et al. in 2010. According to Goldstein, it seems impossible that inhaled formaldehyde could penetrate the nasal mucosa and reach the bone marrow.

Gentry et al., in 2013 (47), conducted a review and reevaluation of the results obtained by Zhang et al. in 2010: inhaled formaldehyde and its metabolite, methanediol (methylene glycol), are unable to reach the bone marrow due to their rapid metabolism to formic acid, carbon dioxide and water, along with the homeostatic mechanisms that regulate their tissue levels. They concluded that it is questionable to use the results obtained by Zhang et al. (2010) as evidence to support the biological plausibility of formaldehyde as a causative agent of leukemia.

Coggon et al., in 2014 (48), followed up a British cohort of workers at six chemical factories in England and Wales where formaldehyde was produced or used, and compared mortality in these with that in the area during the period 1941-2012. They concluded that there was no significant increase in mortality among workers exposed to formaldehyde.

Checkoway et al., in 2015 (49), aimed to evaluate the association between formaldehyde exposure and mortality from acute myeloid leukemia and other lymphohematopoietic malignancies in a U.S. National Cancer Institute (NCI) cohort study of workers in formaldehyde industries. They did not observe an association between cumulative formaldehyde exposure and mortality.

Mundt et al., in 2017 (50), reevaluated the study conducted by Zhang et al. in 2010 (44), with particular focus on hematotoxicity indicators. Values for blood parameters were lower for exposed workers compared to controls; however, the differences in total granulocyte, platelet and leukocyte counts were greater for workers exposed to formaldehyde concentrations < 1.3 ppm than for those exposed to concentrations ≥ 1.3 ppm.

Allegra et al., in 2019 (51), conducted a literature review to evaluate the associations between cumulative and peak formaldehyde exposure and the occurrence of myeloid leukemia. Their analysis revealed that, with the exception of Zhang et al. (2010) (44), none of the included studies suggested a causal relationship.

Reproductive toxicity-related studies

The review by Duong et al. (52) and that by Kim et al. (32) highlighted that, in a Finnish cohort, formaldehyde exposure was significantly associated with an increase in delayed conception, with a fecundability ratio (FR) for female workers exposed to average formaldehyde levels of 0.33 ppm (FR = 0.64, 95 % CI: 0.43–0.92).

In the case of spontaneous abortions, among the 12 publications that studied this effect, only one Finnish publication yielded results that significantly associated the risk of spontaneous abortions with formaldehyde exposure, with an *OR* of 3.5 (95 % CI: 1.1-11.2) among female laboratory workers exposed to formaldehyde levels between 0.01 and 7 ppm when compared to a control group. For both the occurrence of congenital malformations and preterm deliveries, the publications reviewed by the authors showed no significant differences when comparing groups exposed to formaldehyde and control groups. Finally, Doung et al. (52) performed a meta-analysis, which indicated a significant increase only for the RR of spontaneous abortions (1.76; 95 % CI: 1.20-2.59; $p < 0.002$) following chronic formaldehyde exposure.

Wang et al., in 2012 (53), conducted a study in China comparing the reproductive outcomes of a group of 302 men occupationally exposed to formaldehyde and a control group. Their results revealed a significant increase in the delayed conception among the wives of exposed workers (*OR* = 2.828; 95 % CI: 1.081–7.224; *p* = 0.034). The study also showed a significant increase in the risk of spontaneous abortion (*OR* = 1.916; 95% CI: 1.103–3.329; *p* = 0.021, respectively).

Haffner et al., in 2015 (54), concluded that avoiding formaldehyde exposure during pregnancy is associated with a lower RR of low birth weight, congenital malformations and spontaneous abortions.

Nasopharyngeal cancer-related studies

Bachand et al., in 2010 (45), conducted a meta-analysis, reporting a summary *OR* across all studies of 1.22.

Coggon et al., in 2014 (48), conducted a follow-up of a British cohort of workers at six factories that used or produced formaldehyde. They found no evidence of excess deaths from nasopharyngeal cancer.

Bono et al., in 2016 (30), conducted a cross-sectional study to compare the frequency of M_1dG adducts in nasal epithelial cells of workers exposed to formaldehyde compared to controls. The frequency of M_1dG adducts in workers exposed to average formaldehyde levels of 0.172 ppm was two times higher than the frequency in the control group (exposed to 0.029 ppm), respectively. The authors state that M_1dG adducts constitute a potential mechanism for formaldehyde-induced toxicity in nasal carcinomas.

Other studies

Cases of renal damage (7,9) and methemoglobinemia (12) have also been reported with the use of hair straightening products.

Chang et al. (56) studied the relationship between hair product use and uterine cancer in 33,947 volunteers aged 35 to 74 years, between 2003 and 2009. The women had used hair products for at least 12 months. After an average follow-up of 10.9 years, 378 cases of uterine cancer were identified. Although no statistically significant relationship was established between the use of hair products and uterine cancer, a stronger association was observed with frequent use of these cosmetics (more than four times in 12 months).

Other diseases mentioned as related to formaldehyde exposure are asthma, dermatitis, cancers of various organs, tumors, skin irritation and burns; eye irritation, fatigue and pain; tearing, mood changes, general fatigue, throat irritation, rhinorrhea, headache (55-75).

Researchers at the U.S. National Institute of Environmental Health Sciences (NIEHS)—which is part of the National Institute of Health (NIH)—found in the Sister Study, conducted on 46,709 women, that those who used permanent hair dyes and chemical straighteners had a higher risk of developing breast cancer than those who did not use them. Many hair products contain endocrine disruptors and carcinogens that may be relevant to breast cancer. In the abstract of their study, the experts explained that products used predominantly by Black women may contain more hormonally active compounds. The study analyzed data from women aged 35 to 74 years, enrolled between 2003 and 2009, who had used these chemicals for at least one year and had a sister with breast cancer (75).

CONCLUSIONS

Based on the results obtained in this review, harmful effects from chronic formaldehyde exposure cannot be ruled out. There is literature evidence that confirms the increase in genotoxic processes in humans, specifically in nasal epithelial cells and peripheral blood leukocytes.

Regarding reproductive toxicity, there are reports of spontaneous abortions and low birth weight, even when the exposed individual is the future father. Consequently, it is advisable to avoid formaldehyde exposure for both parents prior to conception.

Concerning the relationship of formaldehyde with other diseases whose association is frequently researched, studies on this topic face difficulties in detecting significantly increased risk in the exposed population. For this reason, there is controversy with the decision of agencies such as the International Agency for Research on Cancer (IARC) or the National Toxicology Program (NTP) to classify formaldehyde as a carcinogen in humans, a controversy that is evidenced by research linking formaldehyde to nasopharyngeal cancer and leukemia. The latter is of particular interest as several authors believe that the relationship between formaldehyde and the onset of leukemia was strongly influenced by the study of Zhang et al. (2010) (44), on which subsequent reviews have detected protocol flaws and proposed mechanisms for which there is little or no biological evidence supporting their plausibility.

On the other hand, the average formaldehyde concentrations to which a person could be exposed during a hair straightening treatment present alarming values as they exceed many times the least restrictive exposure limits and can reach levels much higher than those experienced by the exposed individuals included in the epidemiological studies reviewed. In this regard, the primary recommendation is, in the first place, to avoid the use of hair straightening products containing formaldehyde. If they are used, it is preferable to choose those with less than 0.025 % of this compound, so as not to exceed the allowable limit of 0.3 ppm (8,10-11, 13-18).

In conclusion, there is consistent evidence to link chronic exposure to formaldehyde with increased genotoxic processes in humans and with an increased risk of unfavorable reproductive outcomes, primarily spontaneous abortions. There is no robust epidemiological evidence linking chronic exposure to this compound and leukemia or nasopharyngeal cancer. Regarding its use as a hair straightening product, it is advisable to perform this procedure in well-ventilated areas and to use products with formaldehyde concentrations within the allowable limit.

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BIBLIOGRAPHIC REFERENCES

1. Agency for Toxic Substances and Diseases Registry; 2011. Available from: https://www.atsdr.cdc.gov/index.html.
2 Drahl C. Cross-linkers, redox chemistry, or high pH, all in the name of beauty [Internet]. Chemical & Engineering News; 2010. Available from: https://cen.acs.org/articles/88/i45/Hair-Straighteners.html.
3. Golden R, Valentini M. Formaldehyde and methylene glycol equivalence: Critical assessment of chemical and toxicological aspects. Regul Toxicol Pharmacol [Internet]. 2014;69(2):178-86.
4. Detcheberry M, Destrac P, Meyer X-M, Condoret J-S. Phase equilibria of aqueous solutions of formaldehyde and methanol: improved approach using UNIQUAC coupled to chemical equilibria. Fluid Phase Equilib [Internet]. 2015;392:84-94.
5. ARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Chemical agents and related occupations. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. World Health Organization, International Agency for Research on Cancer; 2020.
6. National Center for Biotechnology Information; 2020. Available from: https://www.ncbi.nlm.nih.gov/.
7. Abu-Amer N, Silberstein N, Kunin M, Mini S, Beckerman P. Acute kidney injury following exposure to formaldehyde-free hair-straightening products. Case Rep Nephrol Dial [Internet]. 2022;12(2):112-6.
8. Henault P, Lemaire R, Salzedo A, Bover J, Provot G. A methodological approach for quantifying aerial formaldehyde released by some hair treatments-modeling a hair-salon environment. J Air Waste Manag Assoc [Internet]. 2021;71(6):754-60.
9. Mitler A, Houri S, Shriber L, Dalal I, Kaidar-Ronat M. Recent use of formaldehyde-'free' hair straightening product and severe acute kidney injury. Clin Kidney J [Internet]. 2021;14(5):1469-71.
10. Asare-Donkor NK, Kusi Appiah J, Torve V, Voegborlo RB, Adimado AA. Formaldehyde exposure and its potential health risk in some beauty salons in Kumasi metropolis. J Toxicol [Internet]. 2020;2020:1-10. 11. Aglan MA, Mansour GN. Hair straightening products and the risk of occupational formaldehyde exposure in hairstylists. Drug Chem Toxicol [Internet]. 2020;43(5):488-95.
12. De Vere F, Moores R, Dhadwal K, Karra E. A severe case of methaemoglobinaemia in a Brazilian hairdresser. BMJ Case Rep [Internet]. 2020;13(1):e232735.
13. Pexe ME, Marcante A, Luz MS, Fernandes PHM, Neto FC, Sato APS, et al. Hairdressers are exposed to high concentrations of formaldehyde during the hair straightening procedure. Environ Sci Pollut Res Int [Internet]. 2019;26(26):27319–29.
14. Hadei M, Hopke PK, Shahsavani A, Moradi M, Yarahmadi M, Emam B, et al. Indoor concentrations of VOCs in beauty salons; association with cosmetic practices and health risk assessment. J Occup Med Toxicol [Internet]. 2018;13(1):30.
15. Blessy A, John Paul J, Gautam S, Jasmin Shany V, Sreenath M. IoTbased air quality monitoring in hair salons: Screening of hazardous air pollutants based on personal exposure and health risk assessment. Water Air Soil Pollut [Internet]. 2023;234(6):336.
16. Sankaran G, Tan ST, Shen J, Gutiérrez R, Ng LC, Sim S. Assessment of indoor air quality in air-conditioned small business units with no mechanical ventilation. Atmos Environ (1994) [Internet]. 2023;299(119645):119645.
17. Ricklund N, Bryngelsson I-L, Hagberg J. Occupational exposure to volatile organic compounds (VOCs), including aldehydes for Swedish hairdressers. Ann Work Expo Health [Internet]. 2023;67(3):366–78.
18. Kaikiti C, Stylianou M, Agapiou A. TD-GC/MS analysis of indoor air pollutants (VOCs, PM) in hair salons. Chemosphere [Internet]. 2022;294(133691):133691.
19. Sullivan J, Krieger G. Clinical environmental health, and toxic exposures. USA: Lippincott Williams & Wilkins; 2001.
20. Klages-Mundt NL, Li L. Formation and repair of DNA-protein crosslink damage. Sci China Life Sci [Internet]. 2017;60(10):1065–76.
21. Ajalla Puente KG, Sandoval Polanco C, Nitu M, Sancho Prades AM. Revisión de la relación existente entre la exposición ocupacional al formaldehído y leucemia. Med Segur Trab (Madr) [Internet]. 2013;59(230):112–23.
22. Biblioteca del Congreso Nacional. Decreto 594 aprueba reglamento sobre condiciones sanitarias y ambientales básicas en los lugares de trabajo [Internet]. Chile: Biblioteca del Congreso Nacional; 2021. Available from: https://www.bcn.cl/leychile/navegar?idNorma=167766&idVersion=2019-06-20&idParte=8643227.
23. Diario Oficial de la Unión Europea. Reglamento (UE) 2023/1464 de la comisión de 14 de julio de 2023 por el que se modifica el anexo XVII del Reglamento (CE) n° 1907/2006 del Parlamento Europeo y del Consejo en lo que respecta al formaldehído y a los liberadores de formaldehído [Internet]. Diario Oficial de la Unión Europea; 2023. Available from: https://eur-lex.europa.eu/legal-content/ES/TXT/PDF/?uri=CELEX:32023R1464.
24. Instituto de Salud Pública. El Instituto de Salud Pública analiza información de seguridad de productos para modelar el cabello y entrega recomendaciones [Internet]. Chile: Instituto de Salud Pública; 2023. Available from: https://www.ispch.cl/wp-content/uploads/2023/03/Scan09-03-2023-170447.pdf.
25. ATSDR, Agencia para sustancias tóxicas y el registro de enfermedades. ToxFAQsTM Formaldehído (Formaldeyde) [Internet]. ATSDR; 2016. Available from: https://www.atsdr.cdc.gov/es/toxfaqs/es_tfacts111. html.
26. Pierce JS, Abelmann A, Spicer LJ, Adams RE, Glynn ME, Neier K, et al. Characterization of formaldehyde exposure resulting from the use of four professional hair straightening products. J Occup Environ Hyg [Internet]. 2011;8(11):686–99.
27. Monakhova YB, Kuballa T, Mildau G, Kratz E, Keck-Wilhelm A, Tschiersch C, et al. Formaldehyde in hair straightening products: rapid 1H NMR determination and risk assessment. Int J Cosmet Sci [Internet]. 2013;35(2):201–6.
28. Stewart M, Bausman T, Kumagai K, Nicas M. Case study: Formaldehyde exposure during simulated use of a hair straightening product. J Occup Environ Hyg [Internet]. 2013;10(8):104–10.
29. Galli CL, Bettin F, Metra P, Fidente P, De Dominicis E, Marinovich M. Novel analytical method to measure formaldehyde release from heated hair straightening cosmetic products: Impact on risk assessment. Regul Toxicol Pharmacol [Internet]. 2015;72(3):562–8.

30. Bono R, Munnia A, Romanazzi V, Bellisario V, Cellai F, Peluso MEM. Formaldehyde-induced toxicity in the nasal epithelia of workers of a plastic laminate plant. Toxicol Res (Camb) [Internet]. 2016;5(3):752–60.
31. Santovito A, Schilirò T, Castellano S, Cervella P, Bigatti MP, Gilli G, et al. Combined analysis of chromosomal aberrations and glutathione S-transferase M1 and T1 polymorphisms in pathologists occupationally exposed to formaldehyde. Arch Toxicol [Internet]. 2011;85(10):1295–302.
32. Kim K-H, Jahan SA, Lee J-T. Exposure to formaldehyde and its potential human health hazards. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev [Internet]. 2011;29(4):277–99.
33. Costa S, García-Lestón J, Coelho M, Coelho P, Costa C, Silva S, et al. Cytogenetic and immunological effects associated with occupational formaldehyde exposure. J Toxicol Environ Health Part A [Internet]. 2013;76(4–5):217–29.
34. Choi Y-H, Kim HJ, Sohn JR, Seo JH. Occupational exposure to VOCs and carbonyl compounds in beauty salons and health risks associated with it in South Korea. Ecotoxicol Environ Saf [Internet]. 2023;256(114873):114873.
35. Dugheri S, Massi D, Mucci N, Berti N, Cappelli G, Arcangeli G. Formalin safety in anatomic pathology workflow and integrated air monitoring systems for the formaldehyde occupational exposure assessment. Int J Occup Med Environ Health [Internet]. 2021;34(3):319–38.
36. Aglan MA, Mansour GN. Hair straightening products and the risk of occupational formaldehyde exposure in hairstylists. Drug Chem Toxicol [Internet]. 2020;43(5):488–95.
37. Kangarlou MB, Fatemi F, Dehdashti A, Iravani H, Saleh E. Occupational health risk assessment of airborne formaldehyde in medical laboratories. Environ Sci Pollut Res Int [Internet]. 2023;30(17):50392–401.
38. Pierce JS, Abelmann A, Spicer LJ, Adams RE, Glynn ME, Neier K, et al. Characterization of formaldehyde exposure resulting from the use of four professional hair straightening products. J Occup Environ Hyg [Internet]. 2011;8(11):686–99.
39. Abdu H, Kinfu Y, Agalu A. Toxic effects of formaldehyde on the nervous system. International Journal of Anatomy Physiology [Internet]. 2014;3(3):50–9.
40. Costa S, Carvalho S, Costa C, Coelho P, Silva S, Santos LS, et al. Increased levels of chromosomal aberrations and DNA damage in a group of workers exposed to formaldehyde. Mutagenesis [Internet]. 2015;30(4):463–73.
41. Lorenzoni DC, Pinheiro LP, Nascimento HS, Menegardo CS, Silva RG, Bautz WG, et al. Could formaldehyde induce mutagenic and cytotoxic effects in buccal epithelial cells during anatomy classes? Med Oral Patol Oral Cir Bucal [Internet]. 2017;22(1):58–63.
42. Liang X, Zhang J, Song W, Wang K, Zhang B. Formaldehyde exposure in indoor air from public places and its associated health risks in Kunshan City, China. Asia Pac J Public Health [Internet]. 2018;30(6):551–60.
43. Zendehdel R, Vahabi M, Sedghi R. Estimation of formaldehyde occupational exposure limit based on genetic damage in some Iranian exposed workers using benchmark dose method. Environ Sci Pollut Res Int [Internet]. 2018;25(31):31183–9.
44. Zhang L, Ji Z, Guo W, Hubbard AE, Galvan N, Xin KX, et al. Occupational exposure to formaldehyde, hematotoxicity and leukemia-specific chromosome changes in cultured myeloid progenitor cells – response. Cancer Epidemiol Biomarkers Prev [Internet]. 2010;19(7):1884–5.
45. Bachand AM, Mundt KA, Mundt DJ, Montgomery RR. Epidemiological studies of formaldehyde exposure and risk of leukemia and nasopharyngeal cancer: a meta-analysis. Crit Rev Toxicol [Internet]. 2010;40(2):85–100.
46. Goldstein BD. Hematological and toxicological evaluation of formaldehyde as a potential cause of human leukemia. Hum Exp Toxicol [Internet]. 2011;30(7):725–35.
47. Gentry PR, Rodricks JV, Turnbull D, Bachand A, Van Landingham C, Shipp AM, et al. Formaldehyde exposure and leukemia: critical review and reevaluation of the results from a study that is the focus for evidence of biological plausibility. Crit Rev Toxicol [Internet]. 2013;43(8):661-70.
48. Coggon D, Ntani G, Harris EC, Palmer KT. Upper airway cancer, myeloid leukemia, and other cancers in a cohort of British chemical workers exposed to formaldehyde. Am J Epidemiol [Internet]. 2014;179(11):1301-11.
49. Checkoway H, Dell LD, Boffetta P, Gallagher AE, Crawford L, Lees PS, et al. Formaldehyde exposure and mortality risks from acute myeloid leukemia and other lymphohematopoietic malignancies in the US National Cancer Institute cohort study of workers in formaldehyde industries. J Occup Environ Med [Internet]. 2015;57(7):785-94.
50. Mundt KA, Gallagher AE, Dell LD, Natelson EA, Boffetta P, Gentry PR. Does occupational exposure to formaldehyde cause hematotoxicity and leukemia-specific chromosome changes in cultured myeloid progenitor cells? Crit Rev Toxicol [Internet]. 2017;47(7):592-602.
51. Allegra A, Spatari G, Mattioli S, Curti S, Innao V, Ettari R, et al. Formaldehyde exposure and acute myeloid leukemia: A review of the literature. Medicina (Kaunas) [Internet]. 2019;55(10):638.
52. Duong A, Steinmaus C, McHale CM, Vaughan CP, Zhang L. Reproductive and developmental toxicity of formaldehyde: a systematic review. Mutat Res [I[Internet].net]. [Internet]. 2011;728(3):118-38.
53. Wang H-X, Zhou D-X, Zheng L-R, Zhang J, Huo Y-W, Tian H, et al. Effects of paternal occupation exposure to formaldehyde on reproductive outcomes. J Occup Environ Med [Internet]. 2012;54(5):518-24.
54. Haffner MJ, Oakes P, Demerdash A, Yammine KC, Watanabe K, Loukas M, et al. Formaldehyde exposure and its effects during pregnancy: Recommendations for laboratory attendance based on available data: formaldehyde exposure and its effects during pregnancy. Clin Anat [Internet]. 2015;28(8):972-9.
55. Bono R, Munnia A, Romanazzi V, Bellisario V, Cellai F, Peluso MEM. Formaldehyde-induced toxicity in the nasal epithelia of workers of a plastic laminate plant. Toxicol Res (Camb) [Internet]. 2016;5(3):752-60.
56. Chang C-J, O'Brien KM, Keil AP, Gaston SA, Jackson CL, Sandler DP, et al. Use of straighteners and other hair products and incident uterine cancer. J Natl Cancer Inst [Internet]. 2022;114(12):1636-45.
57. Molina Aragonés JM, Bausà Peris R, Carreras Valls R, Carrillo Castillo A, Fiblà Nicolau F, Gaynés Palou E, et al. Toxicidad del formaldehido en trabajadores profesionalmente expuestos. Revisión bibliográfica. Arch Prev Riesgos Labor [Internet]. 2018;21(3):128-57.
58. Cammalleri V, Pocino RN, Marotta D, Protano C, Sinibaldi F, Simonazzi S, et al. Occupational scenarios and exposure assessment to formaldehyde: a systematic review. Indoor Air [Internet]. 2022;32(1).
59. Luque Flores ER, Saravia Cardozo M del C, Ortuño Numbela CX, Quispe Arancibia LJ, Teran Alvarez TM, Gomez Terrazas J. Exposición al formol y posible sintomatología en estudiantes de medicina. Re Ci Sa UNITEPC [Internet]. 2020;7(1):18-24.
60. Abdu H, Kinfu Y, Agalu A. Toxic effects of formaldehyde on the nervous system. International Journal of Anatomy and Phisiology [Internet]. 2014;3(3):50-9.
61. Pourtaghi GH, Bahrami A, Shaban I, Taheri E, Pirmohamadi Z, Health Research Center, et al. Exposure risk assessment of formaldehyde in four military hospitals in Tehran. J Occup Hyg Eng [Internet]. 2020;7(1):21-30.
62. Zendehdel R, Vahabi M. Formaldehyde carcinogenicity risk assessment using benchmark doses approach based on genotoxic effects in occupational exposure. JCHR [Internet]. 2022;12(1):7-13.

63. Yahyaei E, Majlesi B, Naimi Joubani M, Pourbakhshi Y, Ghiyasi S, Rastani J, et al. Asian occupational exposure and risk assessment of formaldehyde in the pathology departments of hospitals. Pac J Cancer Prev [Internet]. 2020;21(5):1303-9.
64. Jalali M, Moghadam SR, Baziar M, Hesam G, Moradpour Z, Zakeri HR. Occupational exposure to formaldehyde, lifetime cancer probability, and hazard quotient in pathology lab employees in Iran: a quantitative risk assessment. Environ Sci Pollut Res Int [Internet]. 2021;28(2):1878-88.
65. Adamović D, Čepić Z, Adamović S, Stošić M, Obrovski B, Morača S, et al. Occupational exposure to formaldehyde and cancer risk assessment in an anatomy laboratory. Int J Environ Res Public Health [Internet]. 2021;18(21):11198.
66. Protano C, Buomprisco G, Cammalleri V, Pocino RN, Marotta D, Simonazzi S, et al. The carcinogenic effects of formaldehyde occupational exposure: A systematic review. Cancers (Basel) [Internet]. 2021;14(1):165.
67. Gonzalez-Gil G, Kleerebezem R, Lettinga G. Formaldehyde toxicity in anaerobic systems. Water Sci Technol [Internet]. 2000;42(5-6):223-9.
68. Inci M, Zararsız I, Davarci M, Gorur S. Toxic effects of formaldehyde on the urinary system. Turk Urol Derg [Internet]. 2013;39(1):48-5.
69. Kang DS, Kim HS, Jung J-H, Lee CM, Ahn Y-S, Seo YR. Formaldehyde exposure and leukemia risk: a comprehensive review and networkbased toxicogenomic approach. Genes Environ [Internet]. 2021;43(1):13.
70. Yu G, Chen Q, Liu X, Guo C, Du H, Sun Z. Formaldehyde induces bone marrow toxicity in mice by inhibiting peroxiredoxin 2 expression. Mol Med Rep [Internet]. 2014;10(4):1915-20.
71. Bernardini L, Barbosa E, Charão MFF, Brucker N. Formaldehyde toxicity reports from in vitro and in vivo studies: a review and updated data. Drug Chem Toxicol [Internet]. 2022;45(3):972-84.
72. Latorre N, Silvestre JF, Monteagudo AF. Dermatitis de contacto alérgica por formaldehído y liberadores de formaldehído. Actas Dermosifiliogr [Internet]. 2011;102(2):86-97.
73. Tasdemir R, Acar E, Colak T, Hunc F, Bamac B, Kir HM, et al. Investigation of possible oxidative damage caused by formaldehyde exposure in the rat's heart and aorta tissue. Int J Morphol [Internet]. 2021;39(4):1042-7.
74. Dahlgren J, Roback R, Dominguez M, Byers V, Silver D, Faeder E. Case report: Autoimmune disease triggered by exposure to hair straightening treatment containing formaldehyde. Open J Rheumatol Autoimmune Dis [Internet]. 2013;03(01):1-6.
75. Russo T. Un caso de intoxicación crónica por formaldehido. MedULA [Internet]. 1999;8:1-4.
76. Eberle CE, Sandler DP, Taylor KW, White AJ. Hair dye and chemical straightener use and breast cancer risk in a large US population of black and white women. Int J Cancer [Internet]. 2020;147(2):383-91.

Corresponding author:
Sigrid Mennickent C.
Address: Departamento de Farmacia, Facultad de Farmacia, Universidad de Concepción, Chile.
Telephone: +56 412 204 523
E-mail: smennick@udec.cl

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ORCID iDs

Sebastián Vera M	https://orcid.org/0009-0008-3839-2229
Sigrid Mennickent C	https://orcid.org/0000-0001-9312-873X
Carolina Gómez-Gaete	https://orcid.org/0000-0003-2080-9870
Cristian Rogel C	https://orcid.org/0000-0002-6602-9821