International Journal of PharmATA

2021; 1(1): 11-18

Research Article

Genotoxic Effects of Ceramic Materials and the DNA Damage in Ceramic Workers

Hatice Gul ANLAR[1*] Merve BACANLI[2] Nursen BASARAN[3]

[1]Zonguldak Bülent Ecevit University Faculty of Pharmacy Department of Pharmaceutical Toxicology, Zonguldak, Turkey
[2]University of Health Sciences Turkey Gülhane Faculty of Pharmacy Department of Pharmaceutical Toxicology, Ankara, Turkey
[3]Hacettepe University Faculty of Pharmacy Department of Pharmaceutical Toxicology, Ankara, Turkey

ABSTRACT:
The ceramic sector is an important industrial activity around the world. Ceramic workers are potentially exposed to a wide range of chemical mixtures mainly silica. Occupational exposure to silica dust is still considered to be a health problem in the ceramic industry, especially in developing countries. On the other hand, apart from silica, ceramic workers can expose to many hazardous and genotoxic chemicals such as metals and metal oxides, polycyclic aromatic hydrocarbons (PAHs), and nanoparticles. This review aims to summarize data retrieved from studies about genotoxic effects in ceramic workers and other studies about the genotoxic effects of ceramic materials mainly silica. Overall, the data in this review confirm that increased DNA damage in the different cells of ceramic workers demonstrates the possibility of health risks in the individuals exposed to ceramic materials.

Keywords *:* Ceramic, DNA damage, genotoxicity, silica, workers

Received	Accepted	Published
20.08.2021	15.09.2021	15.10.2021

To cite this article:
Anlar HG, BacanlıM, Basaran N. Genotoxic Effects of Ceramic Materials and the DNA Damage in Ceramic Workers. International Journal of pharmATA. 2021; 1(1); 11-18.

1. INTRODUCTION

The ceramic sector that consists of two types of main processes, one the manufacture of tiles and the other, the supply of raw materials that offers a wide range of materials with great impact on our daily lives, is an important industrial activity around the world. Briefly, a ceramic material can be described as an inorganic, heat-resistant material composed of both metallic and non-metallic

* Corresponding Author: Tel : +90 3722613154
Address : Department of Pharmaceutical Toxicology, Faculty of Pharmacy, Zonguldak Bülent Ecevit University, Zonguldak, Turkey
E-mail : hg.anlar@beun.edu.tr

compounds. Due to their durability, strength, non-corrosive properties, and ability to stand at very high temperatures, ceramics are also employed for specific uses which are required in metallurgical processes, glass production, and many other key processes across all industries [1].
Ceramic workers are potentially exposed to a wide range of chemical mixtures including silica, lime, heavy metals, and polycyclic aromatic hydrocarbons (PAHs) [2]. Silicon (Si) is the second most common element after oxygen which is the main constituent of silica (i.e. silicon dioxide), therefore apart from the ceramic industry, exposure to silica dust can occur in a large variety of occupations, such as miners, brick, pottery, sand, foundry, and construction workers [3, 4]. Especially in the production of heat-resistant bricks, materials with a high content of crystalline silica (quartz) are used. The stone, consisting of 100% quartz, is produced by adding clay to the production of pottery and bathroom materials. Sand can also be used for dusting, which increases the crystalline silica concentration in the air. High mixing of 0.1 to 3 mg/m^3 of crystalline silica is involved in mixing, molding, and glazing. Occupational exposure to crystalline silica dust is still considered to be a health problem, especially in developing countries. It is estimated that at least two to three million workers worldwide are occupationally exposed to crystalline silica annually [5, 6]. Inhalation of crystalline silica can lead to silicosis and cancers. Respirable crystalline silica inhaled from occupational sources has been classified as a human carcinogen (Group 1) in 1997 by the International Agency for Research on Cancer (IARC) [7] which was confirmed in a later review in 2012 [8].
Metals and metal oxides are also commonly used in the ceramic industry which has been associated with carcinogenicity. In southeastern China, increased cadmium (Cd) levels in the soil were reported in a town that is quite popular for its ceramics [9]. Another study showed higher concentrations of Cd and chromium (Cr) in *Tradescantia pallida* (T. pallida) leaves in Monte Carmelo, Brazil that has been considered a national reference source for roof tile production. In that area, the micronucleus (MN) frequency was significantly higher in *T. pallida* leaves exposed to the ceramic industry emissions [10]. Beryllium (Be), barium (Ba), zinc (Zn), aluminum (Al), potassium (K), calcium (Ca), sodium (Na), and iron (Fe) were the most abundant elements found in the emissions from the ceramic industries [11]. Also, the use of glazed ceramic dishes can be a risk for lead (Pb) toxicity. IARC has classified Cd, Be, Cr, and Ni as carcinogenic to humans (Group 1) [12, 13].
Nanoparticles (NPs) such as graphene, carbon nanotubes, and carbon black are also used in the ceramic industry for their reinforcing ability [14]. Titanium (TiO_2) NPs are used for the ceramic glaze, in tiles, or as stiffening fillers due to their high stability, anticorrosive and photocatalytic properties [15]. Still, IARC has classified bulk TiO_2 as possibly carcinogenic to humans (group 2B) which raised concerns about the genotoxic potential of TiO_2 in the nanoform [16].

Alumina (Al_2O_3) NPs are used for making cutting tools and are often included as polishing agents [17]. Copper (CuO) and nickel (NiO) oxide NPs can also be used in the ceramic industry incorporated in inks for surface coating treatments. CuO NPs increased DNA damage in lung cell lines, most of them showing a decrease in cell viability, and cause oxidative stress [18, 19]. Special attention should be given to NiO NPs considering that Ni compounds are classified as carcinogenic to humans (Group 1) [13]. In addition to these, the use of nanosized silica in the ceramic industry has the potential to increase in recent years [20].

Molecular epidemiology is an approach commonly used in the evaluation of associations between exposure to hazardous substances and the development of diseases. Genotoxicity biomarkers can allow the detection of early effects that result from the interaction between the individual and the environment; therefore they are important tools in cancer epidemiology and are extensively used in human biomonitoring studies [21, 22].

This review aims to provide current knowledge about the genotoxic effects in ceramic workers.

2. Data Collection

Information about genotoxic effects in ceramic workers was obtained from a literature search of electronic databases such as ScienceDirect, Google Scholar, Pubmed, and Scopus. “ceramic workers”, “DNA damage”, ′′ceramic materials′′, “silica”, “quartz”, ′′pottery workers′′ and ′′tile factory workers′′ were used as keywords to identify epidemiological studies published in the literature. The reference list of the studies is also screened for potentially eligible studies. These were then filtered depending on whether the abstract contained any genotoxicity data in workers related to ceramic materials or silica. In many papers silica has been used as a positive control in the evaluation of the genotoxicity of other particles which were considered irrelevant.

3. Evaluation of Genotoxicity

Research about the genotoxic effects of ceramic materials is mostly focused on crystalline silica genotoxicity in animals and cell lines [23]. Epidemiological studies with ceramic workers are insufficient. In these studies, the genotoxic effects of ceramic materials were generally evaluated by the comet, micronucleus (MN), and sister chromatid exchange (SCE) assays. In a study with 45 non-smoking female workers working in mines and quarries in India and 20 age-matched controls, genotoxic effects were assessed in blood and buccal epithelial cells by comet and MN assays respectively. DNA damage in both cells was significantly increased in workers compared to the control group. It has also been reported that many of these workers suffer from cough, diarrhea, cold, headache, and fever [24]. In another study with 50 male pottery workers in India, it was shown that chromosomal abnormalities, frequency of MN, DNA damage were found to be higher in the workers compared to the controls [25].

In the studies conducted with pottery and foundry workers in Turkey, significantly increased DNA damage was shown by comet assay [26]. In another study from Turkey, genotoxic effects due to occupational silica exposure in workers working in different ceramic industries, such as glass, sandblasting, and stone crushing, were evaluated by MN assay in blood and nasal epithelium cells. The frequency of MN in blood was shown to be 2 times higher in workers than in the control group and the frequency of MN in nasal epithelial cells was 3 times higher in the workers than in the control group. Moreover, 24% of these workers were found to have early radiographical changes (profusion category of 1) [27]. In another study with Turkish ceramic workers (n=99), genotoxic damage was shown in isolated lymphocytes and whole blood by alkaline comet and in buccal cells by MN assays. Plasma 8-oxo-7,8-dihydro-2′-deoxyguanosine (8-oxodG) levels, as an indicator of oxidative DNA damage, and binucleated (BN), pyknotic (PYC), condensed chromatin (CC), karyolytic (KYL), karyorrhectic (KHC) and nuclear bud (NBUD) frequencies in buccal epithelial cells were evaluated. MN, CC + KHC, PYC frequencies in buccal epithelial cells, the tail intensity in blood cells, and 8-oxodG levels in plasma were increased in workers compared to their controls [28].

Malondialdehyde (MDA), a natural product of lipid peroxidation, is an aldehyde capable of interacting with DNA to form exocyclic DNA adducts, including 3-(2-deoxy-β-D-erythro-pentafuranosyl)pyrimido[1,2-α]purin-10(3H)-one deoxyguanosine (M1dG) adduct. M1dG adduct causes base pair and frameshift mutations in reiterated sequences which may be associated with increased cancer risk. Peluso et al. examined the levels of M1dG adducts by mass spectrometry in nasal epithelial cells of 135 workers working in the quarry, pottery, ceramic, and marble production and 118 controls in Tuscany, Italy. The results of this study demonstrated that M1dG adduct levels were significantly higher in smokers than non-smokers. It was also observed that the level of M1dG adducts was increased in the quarry and marble workers, but no significant increase was seen in the ceramic and pottery workers [29].

In another study with industrial granite workers, who were either stonecutters, carvers or were in other professions with significant silica exposure i.e. miners, stonemasons, and foundry workers but not diagnosed with silicosis, and 42 retired workers with silicosis, 8-oxodG levels were determined in the blood and urine samples by high-performance liquid chromatography (HPLC). There was no significant difference in 8-oxodG levels between the groups. Besides, no relationship was found between 8-OHdG levels and duration of exposure, smoking, or age [30].

Kasuba et al. have investigated the genotoxic effects of occupational exposure to lead acetate in pottery-glaze ceramic workers (n=30) using alkaline comet, DNA diffusion, and MN assays in peripheral blood lymphocytes. They showed increased values of tail intensity (TI), frequency of apoptotic and necrotic cells, and frequency of MN in workers compared to controls [31].

Genotoxic effects of ceramic materials in the environment of ceramic factories are also reported. A recent study by Karla da Silva et al. demonstrated the genotoxic effects of particulate materials emitted from the ceramic industry in the meiotic pollen cells of *T. pallida* in Italy *although* the concentrations of particulate materials were lower than the established limits of the World Health Organization (WHO) [32]. Similarly, Campos et al. showed that MN frequency was significantly higher in *T. pallida* plants exposed to the ceramic industry emissions in Brasil [10].

4. Cancer Incidence

In addition to respiratory diseases, silica exposure in ceramic industries can increase the risk of cancer development. Crystalline silica is classified as a human carcinogen (Group 1) by IARC [8]. On the other hand, amorphous silica is in the group that cannot be classified in terms of its carcinogenic effect in humans (Group 3) [7].

To demonstrate the relationship between crystalline silica exposure and lung cancer, a multicentre study in 7 European countries between 1998-2002 with 2952 newly diagnosed lung cancer patients and 3104 control groups was conducted. As a result of the study, it was demonstrated that exposure to silica is an important risk factor for lung cancer. This risk cannot be explained by exposure to other occupational carcinogens or smoking, and also this risk exists in all major histological types of lung cancer [33]. A recent meta-analysis study of Poinen-Rughooputh et al. which combines the results of 85 different studies, supported the carcinogenic role of silica on the lungs, which was more pronounced at higher levels of exposure, in the presence of silicosis [23]. The increased risk for lung cancer and mortality from respiratory diseases was also reported in the Swedish porcelain factory [34].

In a retrospective cohort study, Zhang et al. investigated the health impacts of crystalline silica mixed dust and other potential occupational hazards on workers in ceramic factories. They identified the employment records of 4851 workers registered in three ceramic factories in Jingdezhen city of China between 1972 and 1974. The findings indicated that silica mixed dust in ceramic factories has detrimental effects on health and life span in ceramic factory workers [35].

5. Conclusion

Overall, it was observed that exposure to ceramic materials can increase the DNA damage both in ceramic workers and other experimental systems. MN test was the most used assay in these studies and DNA damage was observed even if the silica concentrations below the limits. There is no known safe level of exposure to carcinogens therefore ceramic workers and other workers exposed to silica should be examined in detail to avoid the development of a carcinogenic process. Specific ventilation practices, lowering the limit values as well as using suitable protective equipment should be recommended to reduce the exposure and to prevent toxic effects.

Conflict of Interest

Author has no personal financial or non-financial interests.

REFERENCES

1. European Commission, Institute for Prospective Technological studies., Reference document on Best Available Techniques in the ceramic manufacturing industry. 2005, Seville, Spain.

2. Ghahramani N., Silica nephropathy. Int J Occup Environ Med. 2010; **1**(3): 108-15.

3. Madl AK, et al., State-of-the-Science Review of the Occupational Health Hazards of Crystalline Silica in Abrasive Blasting Operations and Related Requirements for Respiratory Protection. J Toxicol Environ Health. 2008; 11(7): 548-608.

4. McLaughlin JK, Chow WH, Levy LS, Amorphous silica: A review of health effects from inhalation exposure with particular reference to cancer. J Tox Envir Health. 1997; 50(6): 553-66.

5. Sellamuthu R, Umbright C, Roberts JR, Cumpston A, McKinney W, Chen BT, Frazer D, Li S, Kashon M, Joseph P, Molecular insights into the progression of crystalline silica-induced pulmonary toxicity in rats. J Appl Toxicol, 2013; 33(4): 301-12.

6. Duffin R, Gilmour PS, Schins RPF, Clouter A, Guy K, Brown DM, McNee W, Born PJ, Donaldson K, Stone V, Aluminium lactate treatment of DQ12 quartz inhibits its ability to cause inflammation, chemokine expression, and nuclear factor-kappaB activation. Toxicol Appl Pharmacol. 2001; 176(1): 10-7.

7. IARC monographs on the evaluation of carcinogenic risks to humans., Silica, some silicates, coal dust and para-aramid fibrils. Lyon, France: 1997.

8. IARC monographs on the evaluation of carcinogenic risks to humans., Silica dust, crystalline, in the form of quartz or cristobalite., Lyon, France: 2012.

9. Liao QL, Liu C, Wu HY, Jin Y, Hua M, Zhu BW, Chen K, Huang L, Association of soil cadmium contamination with ceramic industry: A case study in a Chinese town. Sci Total Environ. 2015; 514: 26-32.

10. Campos CF, Junior EOC, Souto HN, Sausa EF, Pereira BB, Biomonitoring of the environmental genotoxic potential of emissions from a complex of ceramic industries in Monte Carmelo, Minas Gerais, Brazil, using Tradescantia pallida. J Toxicol Environ Health A, 2016, 79(3): 123-8.

11. Chen J, Li C, R Z, Milic A, Gu Y, Islam MS, Wang S, Hao J, Zhang H, He C, Guo H, Fu H, Miljevic B, Morawska L, Thai P, Lam YF, Pereirra G, Ding A, Dumka UC, A review of biomass burning: Emissions and impacts on air quality, health and climate in China. Sci Total Environ. 2017; 579: 1000-34.

12. Mulware, S.J., Trace elements and carcinogenicity: a subject in review. 3 Biotech. 2013; 3(2): 85-96.

13. Lyon F. IARC monographs on the evaluation of carcinogenic risks to humans. Some industrial chemicals. 1994; 60: 389-433.

14. Bessa, M.J., et al., Nanoparticle exposure and hazard in the ceramic industry: an overview of potential sources, toxicity and health effects. Environmental Research, 2020: p. 109297.

15. Shi, H., et al., Titanium dioxide nanoparticles: a review of current toxicological data. Particle and fibre toxicology, 2013. 10(1): p. 15.
16. Baan, R.A. Carcinogenic Hazards from Inhaled Carbon Black, Titanium Dioxide, and Talc not Containing Asbestos or Asbestiform Fibers: Recent Evaluations by an IARC Monographs Working Group. Inhal. Toxicol. 2007; 19(sup1): 213-28.
17. Cain M. Morrell R, Nanostructured ceramics: a review of their potential. Appl Organomet Chem. 2001; 15(5): 321-30.
18. Ahamed M, Siddiqui MA, Akhtar MJ, Ahmad I, Pant AB; Alhadlaq H, Genotoxic potential of copper oxide nanoparticles in human lung epithelial cells. Biochem Biophy Research Commun. 2010; 396(2): 578-83.
19. Karlsson HL, Cronholm P, Gustafsson J, Möller L, Copper Oxide Nanoparticles Are Highly Toxic: A Comparison between Metal Oxide Nanoparticles and Carbon Nanotubes. Chem. Res. Toxicol. 2008; 21(9): 1726-32.
20. Murugadoss S, Lison D, Godderis L, Brule SVD, Mast J, Brassinne F, Sebaihi N, Hoet PH, Toxicology of silica nanoparticles: an update. Arch Toxicol, 2017; 91(9): 2967-3010.
21. Ladeira C, Smajdova L, The use of genotoxicity biomarkers in molecular epidemiology: applications in environmental, occupational and dietary studies. AIMS Genetics. 2017, 4(3): 166-91.
22. Carina L, Susana V, Human Biomonitoring – An overview on biomarkers and their application in Occupational and Environmental Health. Biomonitoring. 2016(1).
23. Poinen-Rughooputh S, Rughooputh MS, Guo Y, Rong Y, Chen W, Occupational exposure to silica dust and risk of lung cancer: an updated meta-analysis of epidemiological studies. BMC Public Health. 2016; 16(1): 1137.
24. Halder A, De M, Increase in DNA damage in lymphocytes and micronucleus frequency in buccal cells in silica-exposed workers. Indian J Occup Environ Med. 2012; 16(1): 34.
25. Balamuralikrishnan B, Balachandar V, Subramaniam MD, Alagumuthu K, Sureshkumar S, et al., Assessment of genotoxic and humoral immune system alterations in silica exposed workers from pottery industries in South India. Stoch Environ Res Risk Assess. 2014; 28(7): 1801-14.
26. Basaran N, Shubair M, Underger U, Kars A, Monitoring of DNA damage in foundry and pottery workers exposed to silica by the alkaline comet assay. Am J Ind Med, 2003; 43(6): 602-10.
27. Demircigil GC, Coskun E, Vidinli N, Erbay Y, Yilmaz M, Cimrin A, Schins RP, Born PJ, Burgaz S, Increased micronucleus frequencies in surrogate and target cells from workers exposed to crystalline silica-containing dust. Mutagenesis. 2010; 25(2): 163-9.
28. Anlar HG, Taner G, Bacanli M, Irıtas S, Kurt T, Tutkun E, Yilmaz OH, Basaran N, Assessment of DNA damage in ceramic workers. Mutagenesis. 2018; 33(1): 97-104.
29. Peluso MEM, Munnia A, Giese RW, Chellini E, Ceppi M, Capacci, Oxidatively damaged DNA in the nasal epithelium of workers occupationally exposed to silica dust in Tuscany region, Italy. Mutagenesis. 2015; 30(4): 519-25.
30. Pilger A, Germadnik D, Theiler A, Pils P, Winker N, Rüdiger HW, 8-Hydroxydeoxyguanosine in leukocyte DNA and urine of quartz-exposed workers and patients with silicosis. Int Arch Occup Environ Health. 2000; 73(5): 305-10.
31. Kašuba V, Rozgaj R, Milic M, Zeljezic D, Kopjar N, Pizent A, Kljakovic-Gaspic Z, Jazbec A, Evaluation of genotoxic effects of lead in pottery-glaze workers using

micronucleus assay, alkaline comet assay and DNA diffusion assay. Int Arch Occup Environ Health. 2012; 8**5**(7): 807-18.
32. da Silva KK, Duarte FT, Rodrigues JN, Andre S, Dias MM, Duarte ESF, et al. Physico-chemical properties and genotoxic effects of air particulate matter collected from a complex of ceramic industries. Atmos Pollut Res. 2019; 10(2): 597-607.
33. Cassidy A, van Tongeren AMM, Field JK, Zaridze D, Szeszenia-Dabrowska N, Rudnai P, et al., Occupational exposure to crystalline silica and risk of lung cancer: a multicenter case–control study in Europe. Epidemiology. 2007; 18(1): 36-43.
34. Wiebert P, Alderling M, Svartengren M, Gustavsson P, Plato N, Cancer, mortality and acute myocardial infarction in workers exposed to respirable crystalline silica dust at a Swedish porcelain factory. Occup Environ Med. 2014; 71 Suppl 1(A31).
35. Zhang X, Wang H, Zhu X, Liu Y, Wang L, Dai Q, et al. Cohort mortality study in three ceramic factories in Jingdezhen in China. J Huazhong Univ Sci Technolog Med Sci. 2008; 28(4): 386-90.