

Evaluation of mutagenic activity of external factors

Evaluación de la actividad mutagénica de factores externos

Irina Dmitrievna Sitdikova <http://orcid.org/0000-0002-6835-402X>, DSc, Professor of KFU, Republican Center for Medical Prevention, Sar1002@mail.ru, 89503138892. The research area is the study of health problems in able-bodied population, ID Scopus 6506943645

Ilnur Nilovich Khalfiev, Candidate of Science, chief physician, 8432789651, rcmp.rt@tatar.ru. Scientific direction is the study of the cytogenetic effects of the technosphere factors; study of carcinogenic factors affecting the working-age population, development of models and systems that provide an assessment of the intermittent impact of risk factors. Orcid 0000-0002-4856-6177

Marina Konstantinovna Ivanova Doctor of Science, Professor of ISMA, 89127546222, sokol0872@rambler.ru. The research area is the study of various types of technogenesis on the processes of environmental stress, biomedical indicators, mathematical modeling. Orcid 0000-0002-4987-4127

Almas Azgarovich Imamov Doctor of Medical Sciences, Professor, Head of the Department of Kazan State Medical University, 420012, Kazan, Butlerova St., 49, the research area is the study of the mechanisms of influence of factors of industrial ecology and toxicology, profmed@mail.ru, Orcid 0000-0002-4834-6075

Dmitrii Vladimirovich Lopuchov Candidate of Medical Sciences, Associate Professor of the Department of Preventive Medicine and Human Ecology, Kazan State Medical University. Kazan State Medical Academy, Branch of Federal State Budgetary Educational Institution of Further Vocational Education "Russian Medical Academy of Continuous Professional Education", Ministry of Health of Russia. The research area is the study of the mechanisms of influence of factors of industrial ecology. profmed@mail.ru, Orcid 0000-0001-8896-969X

Svetlana Aleksandrovna Fadeeva Postgraduate student, Kazan Federal University. The research area is the study of factors of industrial ecology in terms of bioengineering. lana@mail.ru, ID Scopus 571191637033, Orcid 0000-0001-8209-831X

Milyausha Shamilevna Muzaffarova <https://orcid.org/0000-0003-1732-6974> Research area. Study of medical and industrial ecology. Analysis of the incidence of the population. Development and implementation of management solutions for the reduction and prevention of morbidity of the population from environmental influences. Tel. 89178618207, Email: shamilevnamed@mail.ru,

Ayrat Ravilevich Zamaliev Postgraduate Student, KFU, Center for Biology and Pedagogical Education / Department of Human and Animal Physiology. E-mail: AjRZamaliev@stud.kpfu.ru, zamaliev.ayrat@yandex.ru, ORCID: <https://orcid.org/0000-0001-8112-1020>, The research area is the study of health indicators of the population. email: roza.fomina2012@yandex.ru, ORCID: 0000-0002-4688-8901. SPIN-code: 8823-1597, AuthorID: 958550

Lilia Kazimovna Karimova <https://orcid.org/0000-0002-9859-8260> Chief Researcher, Department of Occupational Medicine, Ufa Research Institute of Occupational Medicine and Human Ecology, Professor, Doctor of Medical Sciences, 450106, Russia, Republic of Bashkortostan, Ufa, St. Kuvykina, 94, e-mail: iao-karimova@rambler.ru. The research area is the study of health problems in able-bodied population

Fomina Roza Vladimirovna Assistant of the Department of Instrumental Diagnostics with the Course of Phthisiology, I.N. Ulyanov Chuvash State University, Faculty of Medicine, address: 428017, Russia, Chuvash Republic, Cheboksary city, Moskovsky prospect, 45. email: roza.fomina2012@yandex.ru ORCID: 0000-0002-4688-8901. SPIN code: 8823-1597, AuthorID: 958550

Natalia Denisovna Rotanova Student of Kazan State Medical University. The research area is the environmental aspects that form morbidity of the population. 89503456709, Ronan@mail.ru, ORCID:0000-002-6299-7104

Received/Recibido: 12/24/2021 Accepted/Aceptado: 03/19/2022 Published/Publicado: 04/25/2022 DOI: <http://doi.org/10.5281/zenodo.6662020>

Abstract

Petrochemical enterprises dominate the system of the economic potential of our country. These enterprises, according to Russian legislation, are classified as carcinogenic. The technological process of this industry has excellent potential for improvement, which is predominantly expressed in the areas of technological, sanitary, and technical labor protection. However, according to the technical regulations, it is challenging to achieve complete industrial safety, which forms the list of problems of carcinogenic industrial facilities. Hence, the main objective of the present study is to evaluate the mutagenic activity of external factors. To accomplish that aim, experimental research is conducted. The results of this research can serve as a starting point in developing preventive measures to reduce the level of mutagenic hazard at carcinogenic enterprises.

Keywords: mutagenic hazard, genotoxicity test, working area, petrochemical enterprise, chromosomal and chromatid aberrations

Resumen

Las empresas petroquímicas dominan el sistema del potencial económico de nuestro país. Estas empresas, según la legislación rusa, están clasificadas como cancerígenas. El proceso tecnológico de esta industria tiene un excelente potencial de mejora, que se expresa predominantemente en las áreas de protección tecnológica, sanitaria y técnica laboral. Sin embargo, de acuerdo con los reglamentos técnicos, es un desafío lograr una seguridad industrial completa, que forma parte de la lista de problemas de las instalaciones industriales cancerígenas. Por lo tanto, el objetivo principal del presente estudio es evaluar la actividad mutagénica de factores externos. Para lograr ese objetivo, se lleva a cabo una investigación experimental. Los resultados de esta investigación pueden servir como punto de partida en el desarrollo de medidas preventivas para reducir el nivel de riesgo mutagénico en empresas cancerígenas. Palabras clave: riesgo mutagénico, prueba de genotoxicidad, área de trabajo, empresa petroquímica, aberraciones cromosómicas y cromátidas.

Currently, almost all carcinogenic substances are proven to be mutagens¹⁻³. However, the mechanism of development of tumor states as a result of mutagenic effects follows different scenarios⁴⁻⁶.

Scientific cooperation of geneticists, oncologists, and ecologists is necessary and can reveal additional mechanisms and patterns in studying this phenomenon^{7,8}.

The cooperation is also interesting in matters of antimutagenesis, anticarcinogenesis. The mechanism of direct and long-term effects of exposure to harmful substances of this direction is described⁹⁻¹¹.

The issue is about the formation of gene mutations and chromosomal aberrations¹²⁻¹⁴.

There is evidence that newly emerging mutations cause at least 50% of spontaneous abortions; at least 25% of congenital malformations result from new mutations of all types; 15% of perinatal mortality is the result of the effect of the mutation process^{15,16}.

Therefore, this study primarily intends to assess the mutagenic activity of external factors.

To meet the aim of the study, experimental research was carried out in several stages:

- air sampling from working areas (186 samples), the initial matrix was 1090 x 14;
- experiments for a short-term test for evaluating the mutagenic activity of the samples taken. Method: "Short-term test for chromosomal and chromatid aberrations in the experiment with *Crepis capillaris* by bioindication of the mutagenic background of the external environment No. 05-485, 2003"²⁻⁵;
- counting of chromosomal and chromatid aberrations^{17,18};
- determination of the type of violations (multiple deletions, translocations, separation of small and large chromosome arms, acentric deletion, etc.)^{19,20};
- identification of points with the highest level of mutagenic activity^{21,22};
- qualitative and quantitative analysis of the air environment^{23,24};

- the study of causal relationships in the "Characteristics of substances - the level of induced mutagenesis"²⁵⁻²⁷
- statistical processing of the material with the use of parametric and non-parametric statistical methods^{11,12}.

For an objective comparative scientific analysis, control and experimental groups have been formed. The control conditions were zones free of industrial air pollution. The working zones of a petrochemical enterprise's permanent workplaces were considered experimental conditions.

Characteristics of the mutagenic background of the control area:

- Number of metaphases - 1060
- Number of aberrations - 8
- Type of aberrations - deletions

Characteristics of the mutagenic background of working areas:

- Plate shop, job - vulcanizer; number of metaphases - 1073; number of aberrations - 20; type of aberration - deletion, multiple lesions; reliability criterion (in comparison with control) - 1.09; level of significance (in comparison with control) - (P < 0.05);
- Continuous vulcanization section, job - extrusion machine operator; number of metaphases - 1027; number of aberrations - 23; type of aberrations - deletions, isochromatid deletions; reliability criterion (in comparison with control) - 1.54; level of significance (in comparison with control) - (P < 0.05);
- Molding section, job - molding vulcanizer; number of metaphases - 2037; number of aberrations - 22; type of aberration - deletion, multiple deletions; reliability criterion (in comparison with control) - 1.89; level of significance (in comparison with control) - (P < 0.05);
- Lead press section, job - lead press operator; number of metaphases - 1118; number of aberrations - 28; type of aberration - deletion, dicentric, acentric ring with microfragments; reliability criterion (in comparison with control) - 2.1; level of significance (in comparison with control) - (P < 0.05);
- Preparatory production, job - roller dyer; number of metaphases - 1014; number of aberrations - 21; type of aberration - deletion, multiple deletions; reliability

- criterion (in comparison with control) - 1.92; level of significance (in comparison with control) - (P <0.05);
- Calendar line, job - callender machine operator; number of metaphases - 1082; number of aberrations - 24; type of aberration - deletion, multiple deletions, dicentric; reliability criterion (in comparison with control) - 1,57; level of significance (in comparison with control) - (P <0.05);
 - mechanical rubber mixture feed section, job - roller; number of metaphases - 1074; number of aberrations - 26; type of aberration - deletion, multiple deletions, translocations; reliability criterion (in comparison with control) - 2.63; level of significance (in comparison with control) - (P <0.05);
 - Non-molded production section, job - machine operator; number of metaphases - 1074; number of aberrations - 26; type of aberration - deletion, multiple deletions, translocations; reliability criterion (in comparison with control) - 2.63; level of significance (in comparison with control) - (P <0.05);
 - mechanical rubber mixture feed section, job - roller; number of metaphases - 1072; number of aberrations - 23; type of aberration - deletion, multiple deletions, isochromatid deletions; reliability criterion (in comparison with control) - 2.21; level of significance (in comparison with control) - (P <0.05);
 - Lead press section, job - machine operator; number of metaphases - 1087; number of aberrations - 27; type of aberration - deletion, isochromatid deletions, acentric ring with microfragments; reliability criterion (in comparison with control) - 1.95; level of significance (in comparison with control) - (P <0.05);
 - Technical plate section, job - roller; number of metaphases - 1082; number of aberrations - 32; type of aberration - deletion, multiple deletions, translocations; reliability criterion (in comparison with control) - 2.08; level of significance (in comparison with control) - (P <0.05);

In parallel with the experiment and study of the air in the working areas with the use of "Short-term test for chromosomal and chromatid aberrations in the experiment with *Crepis capillaris* by bioindication of the mutagenic background of the external environment" a qualitative and quantitative chemical analysis of air was conducted. Our study identified a set of substances released into the air of working zones, such as vapors of carbon dioxide, gasoline, hydrocarbons, ethyl acetate, chromium, benzopyrene. The analysis found that the highest levels (statistically significant) of mutagenic activity are characteristic of the following areas: technical plates, continuous vulcanization, brake, mechanical rubber mixture feed, non-molded production, calendar line, preparatory production, press-leaded, molding equipment. Among the jobs that involve contact with conditions of high mutagenic activity, the following are noted: a roller operator, a calendar operator, a roller-dyer, and a lead press operator.

Overall, based on these results, it can be stated that:

- application of a short-term test for chromosomal and chromatid aberrations in the experiment with *Crepis capillaris* by bioindication of the mutagenic background under the influence of industrial factors of ecology objectively evaluates the severity of induced mutagenesis;
- the priority pollutants of a petrochemical industrial facility are vapors of carbon dioxide, gasoline, hydrocarbons, ethyl acetate, chromium, and its compounds, benzopyrene;
- reliably high levels by types of aberration were noted for multiple deletions, isochromatic deletions, displacement of the chromosome bridge to the periphery, forming acentric chromosomes with micro fragments;
- production sections with a high level of mutagenic activity were identified - sections of technical plates, continuous vulcanization, brake, mechanical rubber mixture feed, non-molded production, calendar line, preparatory production, press-lead plating, and molding;
- jobs that involve contact with high mutagenic activity have been identified - a roller operator, a calendar operator, a roller-dyer, and a lead press operator.

Conclusions

Our study made it possible to assess the level of mutagenic activity that forms at an industrial facility with a petrochemical profile and identify priority pollutants areas with a reliably high level of genotoxicity and describe the range of occupations that are in the group of high reproductive risk. At the same time, the results show a range of areas in the study of this problem. Prospective studies include the development and construction of models based on methods of mathematical modeling, which allow identifying and assessing risk factors in modern petrochemical industrial facilities^{21, 22, 23}.

The ability to predict and manage risk factors is the basis for developing management mechanisms to minimize and eliminate occupational mutagenic hazards and prevent occupational and occupationally-related pathology.

Source of funding: self-funded.

Conflict of interest: there is none.

Acknowledgments: not applied.

1. Gurvich VB. Evaluation of the carcinogenic risk to human health from inhalation exposure to chemical factors when justifying the sanitary protection zones of industrial enterprises. *Ural Medical Journal*. 2011; 10: 5-7.
2. Zaitseva NV. et al. The effect of toxic burden on the course of pregnancy, childbirth and the postpartum period of female workers in chemical production and living in an environmentally destabilized region. Proceedings of the interregional scientific-practical conference, "Topical issues of health improvement and rehabilitation of pregnant women and gynecological patients in sanatorium-resort conditions". - Perm2008:158-171.
3. Ailamazian EK. The main problems and applied significance of environmental reproduction. *Obstetrics and female diseases*. 2005;2: 4-10.
4. Zaridze DG, Ilicheva SA, Shangina OV. Carcinogenicity of ecotoxicants in cohort studies of industrial populations. *Hygiene and sanitation*. 2003; 6: 71-73.
5. Kavitskii R.E. Mechanisms of carcinogenesis and factors of anticarcinogenesis. *Problems of Oncology*. - 2005. - No. 6. - p. 32-35.
6. Amirov NKh, Sitdikova ID, Khasanov RSh. Aspects of industrial ecology in the formation of a malignant process. *Kazan: KSMU*. 2003: 33 p.
7. Amirov NKh, Sitdikova ID. Carcinogenic and mutagenic effects of factors of the production environment. *Kazan Medical Journal*. 2003; 80(1):13-16.
8. Vekker IR, Setko NP, Antonenko BN. The role of environmental factors in perinatal pathology (review). *Hygiene and Sanitation*. 2001;3:29-31.
9. Zaitseva NV, Dolgikh OV, Nurislamova TV. Diagnostic aspects of identification of dangerous aliphatic chlorinated hydrocarbons for people's health. *Hygiene and Sanitation*. 2006;1:66-67.
10. Lipatov Gla. et al. About the development of programs to reduce the carcinogenic hazard of industrial enterprises. *Ural medical journal*. 2008;11: 92-94.
11. Setko AG. et al. Assessment of the risk to public health under the multi-environment exposure to chemicals in the zone of influence of petrochemical enterprises. *Ural Medical Journal*. 2010; 11: 44-46.
12. Sitdikova ID, Ivanova MK, Vaziev IK. Modern technogenesis (medical and ecological aspects). *Kazan*.2009: 106 p.
13. Ronsmans C, Graham WJ, Lancet Maternal Survival Series steering group. Maternal mortality: who, when, where, and why. *The lancet*. 2006 Sep 30;368(9542):1189-200. [https://doi.org/10.1016/S0140-6736\(06\)9380-X](https://doi.org/10.1016/S0140-6736(06)9380-X).
14. Paoletti P. Application of biomarkers in population studies for respiratory non-malignant diseases. *Toxicology*. 2001; 101(1): 99-105.
15. Boev VM, Kuksanov VF, Fast VV. Chemical carcinogens of the habitat and malignant neoplasms. - M.: Medicine. 2002: 90-123.
16. Antonov AV. Assessment of health risk as a way to reduce congenital and hereditary pathology in children. *Hygiene and Sanitation*.2006;3: 4-6.
17. Jayaratne A. Application of a risk management system to improve drinking water safety. *J. Water Health*. 2008;6(4):547 - 557.
18. Hasson LE, Nyren O, Bergstrom R. Nutrients and gastric cancer risk. A population-based case-control study in Sweden. *Int. J. Cancer*. 2004;57(5): 638-644.
19. Bochkov NP. Human ecological genetics. *Occupational medicine and industrial ecology*. 2004;1: 1-6.
20. Euripidou E, Murray V. Public health impacts of floods and chemical contamination. *J. Public. Health (Oxf)*. 2004;26(4):376 - 383. Es una revisión de literatura It is a literature review
21. Zheng T. et al. Breast cancer risk associated with congeners of polychlorinated biphenyls. *Am. J. Epidemiol*. 2001; 152(1):P.50.
22. Zaridze DG. Men TKh. Priority areas of anti-cancer fight. *Russian Journal of Oncology*. 2001;38: 1066-1073.
23. Ivanova MK. Assessment and management of risk factors of carcinogenic and mutagenic hazard in technogenesis: Author's abstract, Doctor of Medicine, - Kazan.2012: p. 39.
24. Chabla-Inga MF, Mesa-Cano IC, Ramírez-Coronel AA, Jaya-Vásquez LC. Diabetes como factor de riesgo de mortalidad intrahospitalaria en pacientes con COVID-19: revisión sistemática. *Archivos Venezolanos de Farmacología y Terapéutica*. 2021;40(3):240-7. <https://doi.org/10.5281/zenodo.5038351>.
25. Md CE, Verdugo EE, Vilema EM, Riera BR, Espinosa MY, de la Rosa SA, Alverca CY, Quintanilla SB. Aspectos clínicos de la covid-19 en los pacientes con cáncer. *Síndrome Cardiometabólico*. 2020;10(1):43-7. <http://doi.org/10.5281/zenodo.4531504>.
26. Od EG, Od AM, MgSc AM, MgSc JV, Mgsc RV, Od JO, Od PP, MgSc CE, Zambrano AD, MgSc MD, Inv ZD. Nivel de estrés radicular en premolares superiores y presión ejercida en tejidos adyacentes: un modelo mecánico en 3D. *Archivos Venezolanos de Farmacología y Terapéutica*. 2021;40(9):942-5. <http://doi.org/10.5281/zenodo.5838992>.
27. Martínez-Santana MC, Miquireno RC, Cáceres YD, Ochoa WR, Gómez FJ. Bienestar social en mujeres víctimas del conflicto armado en la fundación humildad extrema en Cúcuta. *Archivos Venezolanos de Farmacología y Terapéutica*. 2020;39(8):976-85. <https://doi.org/10.5281/zenodo.4543972>.