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ORIGINAL

Prevention of Mutagenesis, Oxidative Stress and Inflammation in first Generation Male Rats whose Parents are Exposed to Gamma Radiation and Hexavalent Chromium

Prevención de la mutagénesis, el estrés oxidativo y la inflamación en ratas macho de primera generación cuyos padres están expuestos a radiación gamma y cromo hexavalente

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ABSTRACT

Introduction: children exposed to radiation chemical agents or born to exposed parents faced elevated risks of stochastic pathologies, including genetic disorders, tumours, and leukaemia. These risks were attributed to mutations and latent genomic damage caused by such exposures.
Method: this six-month experimental study at NAO ZKMU in Kazakhstan evaluated Burdock Root Oil's protective effects against gamma radiation and hexavalent chromium-induced damage in 100 Wistar rats, analyzed using Statistica 10.
Results: the findings revealed that the offspring of parents exposed to combined chromium and gamma irradiation (Cr^{6+} + γ) exhibited a 33 % increase in micronuclei (6,3 ±1,16 %, P ≤ 0,01) compared to controls (4,56 ± 1,18 %), indicating significant genotoxicity. Burdock Root Oil reduced micronuclei levels to 5,34 ± 0,792 % (P≥ 0,05), comparable to control levels. Chromosomal aberrations in the Cr^{6+} + γ group increased by 54 % (2,77 ± 0,537 %, P ≤ 0,001), while Burdock Root Oil reduced total aberrations by 19,5 % (P ≤ 0,005). Markers of oxidative stress showed significant improvement; superoxide dismutase (SOD) activity increased by 16,7 %, catalase by 22,6 %, and sulfhydryl groups by 23 % (P≤ 0,05), while malondialdehyde levels decreased by 16 % (P ≤ 0,05). The SH/MDA ratio increased by 45 % (P ≤ 0,05).
Conclusions: burdock root oil effectively mitigated genotoxic, oxidative, and inflammatory effects in the offspring of parents exposed to gamma radiation and chromium. It restored immune balance, reduced oxidative stress, and preserved genomic stability.

Keywords: Radiation Exposure; Hexavalent Chromium; Oxidative Stress; Genomic Instability; Stochastic Pathologies; Burdock Root Oil.

RESUMEN

Introducción: niños expuestos a radiación, químicos o padres expuestos enfrentan mayores riesgos de

patologías genéticas, tumores, leucemia y daños genómicos.
Método: este estudio experimental en NAO ZKMU, Kazajistán, evaluó durante seis meses los efectos protectores del aceite de raíz de bardana contra daño genómico y estrés oxidativo en 100 ratas Wistar.
Resultados: los resultados mostraron que la descendencia de padres expuestos a cromo y radiación gamma combinados (Cr^{6+} + γ) presentó un aumento del 33 % en micronúcleos (6,3 ± 1,16 %, P ≤ 0,01) frente a los controles (4,56 ± 1,18 %), indicando genotoxicidad significativa. El aceite de raíz de bardana redujo los niveles de micronúcleos a 5,34 ± 0,792 % (P ≥ 0,05), similar a los controles. Las aberraciones cromosómicas aumentaron un 54 % (2,77 ± 0,537 %, P ≤ 0,001) en el grupo Cr^{6+} + γ, mientras que el aceite las redujo en un 19,5 % (P ≤ 0,005). Los marcadores de estrés oxidativo mejoraron significativamente: SOD aumentó un 16,7 %, catalasa un 22,6 %, y grupos SH un 23 % (P ≤ 0,05), mientras que los niveles de MDA disminuyeron un 16 % (P ≤ 0,05). La relación SH/MDA se incrementó un 45 % (P ≤ 0,05).
Conclusiones: el aceite de raíz de bardana demostró ser eficaz en mitigar los efectos genotóxicos, oxidativos e inflamatorios en la descendencia de padres expuestos a radiación gamma y cromo, restaurando el equilibrio inmunológico y preservando la estabilidad genómica.

Palabras clave: Exposición a La Radiación; Cromo Hexavalente; Estrés Oxidativo; Inestabilidad Genómica; Patologías Estocásticas; Aceite de Raíz de Bardana.

INTRODUCTION

There is increasing awareness of the risks posed by environmental radiation or chemical exposure as they can have devastating health impacts not only on individuals but may also be passed on to their descendants. These agents, whether acquired through direct contact or inherited genetically from parents, could disrupt genetic stability, resulting in various health effects. New studies add to evidence that such exposures are related to abnormalities in various cellular activities, including oxidative stress, DNA damage, and immune dysfunction. It is necessary to understand these mechanisms to manage risks posed to sensitive groups such as children.

The potential health impact on children exposed to radiation or chemical agents or born to parents who have experienced such exposure has become a significant concern.[1] These children are at an elevated risk of developing stochastic pathologies, including genetic disorders, undifferentiated mental retardation, malignant tumours, and leukaemia. Such pathologies are predominantly associated with ionizing radiation or a combination of chemical, physical, and biological agents, which can trigger a variety of mutations.[2] These mutations can increase the likelihood of spontaneous mutations and cause latent genomic damage that may eventually result in oncological or genetic diseases.[3]

Ionizing radiation (IR) inflicts cellular damage both directly by inducing DNA breaks and indirectly by generating reactive oxygen species (ROS). ROS, in turn, contributes to chromosomal and genomic mutations and creates single- and double-strand DNA breaks that, if improperly repaired, lead to cell death, chromosomal instability, mutations, and carcinogenesis.[4] The body's equilibrium is shattered due to radiation exposure, whereby internal antioxidant enzyme systems are impaired, leading to a disorder in the production of ROS within the body and the systems that scavenge them, thereby causing oxidative stress.[5,6]

Oxidative stress and inflammation are two mutual and closely related mechanisms, one induced and involved by the other.[7] IR exposure can sharply increase ROS levels, disrupting cellular homeostasis and activating pro-inflammatory cytokines.[8] This activation contributes to genomic instability, cell death, apoptosis, necrosis, mitotic catastrophe, and autophagy.[9] In experimental studies, it has been proven that genomic instability caused by ionizing radiation or chemical carcinogens is inherited and leads to increased sensitivity to carcinogens in animal offspring.[10,11] At the tissue level, radiation-induced genomic instability reduces morphological and functional integrity, correlating with a heightened risk of tumour and non-tumour diseases.[12,13] Some researchers propose that exposure to various mutagens can lead to epigenetic changes that may persist across multiple generations.[14]

In modern radiobiology and radiation medicine, a substantial focus is placed on understanding how free radical-induced lipid oxidation contributes to the broader framework of genome instability.[15] At the cytogenetic level, transmissible chromosomal instability has been observed to pass through germ cells from parent to offspring somatic cells. This process involves genetic and epigenetic changes that external environmental factors may influence.[16] The escalation of anthropogenic pollution is likely accelerating the emergence of specific mutational changes and genomic damage, heightening the incidence of stochastic pathologies.[17] This determines the relevance of the theoretical and experimental provision of protection for the population living in anthropogenic regional biogeochemical provinces. One such is a stable anthropogenic chromium biogeochemical province in the Aktobe region (Republic of Kazakhstan).[18]

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According to NIOSH and the IARC, hexavalent chromium compounds (Cr(VI)) are classified as carcinogenic.[19] Hexavalent chromium compounds are the most toxic as they can easily pass through the membrane with the help of non-specific transporters, phosphate and sulfate anions.[20] Cr(VI) is reduced to produce ROS and other reactive metabolites that directly interact with DNA, resulting in damage to cellular structure, including genetic structures.[21] Oxidative stress, which can be induced by Cr(VI), generates hydroxyl radicals that damage biomacromolecules, form protein cross-links, and cause the production of secondary radicals through interactions with low molecular weight compounds.[22] The molecular mechanisms that relate chromium to carcinogenic outcomes are multifactorial and involve various overlapping processes that include genotoxicity, mutagenesis, oxidative stress mechanisms, and epigenetic processes such as DNA methylation and histone post-translational modification.[23]

Previous literature explores strategies to prevent mutagenesis, oxidative stress, and inflammation in first-generation male rats, focusing on the health impacts of parental gamma radiation and hexavalent chromium exposure, highlighting potential interventions.[24]

Humans and animals often encounter combined exposures to ionizing radiation and chemical agents in the environment, with potential synergistic and potentiation effects that may diminish general organismal reactivity and increase susceptibility to chronic conditions.[25] Consequently, research into inherited effects linked to parental exposure to harmful agents emphasizes the need for innovative approaches to diagnosis, targeted therapy, and prevention of radiation-induced diseases. Research has gone into utilizing natural antioxidants as protective agents against radiation and chromium-induced cellular damage in the last few years. Considering the underlying principle of free radical formation, it is expedient to have antimutagenic, antioxidant, and immunomodulatory agents to achieve a protective effect. Such natural protectors, which are non-toxic and have few side effects, have great potential in reducing radiation damage to normal tissues.[26,27]

The antioxidant properties of burdock have been investigated in many studies. It has been used as an edible and beneficial plant and a medicinal remedy in Asia, Europe and the USA for around three thousand years.[28] Burdock root actively contains phenolic substances, which include lignans and caffeic acid, as well as inulin, lutein, essential amino acids, vitamins, minerals, and fibre.[29] Traditionally, burdock root products have been employed to treat skin lesions, liver and kidney ailments, malignancies, diabetes, rheumatism, gout, hypertension, atherosclerosis and other inflammatory diseases.[30] According to research, Arctium lappa L. carries out protective roles in the liver and has antibacterial, antiviral, antimutagenic, and anti-inflammatory effects due to its capacity to scavenge free radicals.[31] Chemical and biochemical characteristics are displayed by their constituents, such as antioxidant components, and nearly all phenolic compounds and flavonoids are beneficial substances.

The present research addresses the effectiveness of Burdock Root Oil in fighting oxidative stress, mutagenesis, and inflammation in the blood, liver, and kidneys of the first generation of rats exposed to gamma radiation and Cr(VI) as parents. Given the lacuna of studies evaluating radiation and chromium's effects on carcinogenic processes (i.e. mutagenesis, oxidative stress, and inflammation) on descents, this research seeks to be significant in addressing an important area of how natural substances can act as protective agents against inherited disorders.

Environmental pollutants such as gamma radiation and hexavalent chromium are recognized for their carcinogenic and mutagenic properties, posing significant risks to human health. These agents can cause genetic damage and oxidative stress, which can be passed on to the next generations and not only to the individuals who are them. Natural antioxidants, such as Burdock Root Oil, have been effective in repairing some of such damage due to their anti-inflammatory and antioxidant capacities. Still, literature is scant on the impact of these agents in blocking the oxidative and mutagenic damage passed on to the next generation. This research seeks to address the problem by focusing on the protective role of Burdock Root Oil against heritable damage from gamma rays and hexavalent chromium.

Purpose of the Study

To study the mutagenesis, oxidative stress, and blood cytokine concentrations in first-generation male rats whose parents underwent combined gamma irradiation and hexavalent chromium exposure and to establish the impact of the phytopreparation 'Burdock Root Oil' as a protective agent.

Research Aims and Objectives

Research Aim

This investigation's particular objective is to assess the reinforcing effect of Burdock Root Oil on genome integrity, oxidative activity, and inflammation in the 1st generation of male rats whose parents were subjected to a combined dose of Cr+6 and γ irradiation. This study seeks to understand if Burdock Root Oil can mitigate the heritable risks and cellular damage induced by these environmental stressors, focusing on assessing

antioxidant enzyme levels, mutagenic changes, and inflammatory markers.

Research Objectives

1. To evaluate the effects of parental exposure to gamma ray and hexavalent chromium on genomic instability and mutagenesis of progeny using chromosomal aberration analysis and micronucleus frequency in bone marrow cells.
2. To evaluate the level of oxidative stress in offspring, including changes in malondialdehyde (MDA) concentrations, sulfhydryl (SH) group levels, and antioxidant enzyme activities (SOD, CAT).
3. Analyzing the cytokine profile in the blood of offspring to determine the levels of pro-inflammatory and anti-inflammatory markers provides insight into inflammation-related changes.
4. To investigate whether Burdock Root Oil administration to the exposed parents before mating can mitigate the mutagenic, oxidative, and inflammatory effects transmitted to the offspring.

Research Questions

1. What are the genotoxic effects of combined gamma radiation and hexavalent chromium exposure on first-generation offspring of exposed parents?
2. How does Burdock Root Oil influence oxidative stress indicators, such as MDA levels, antioxidant enzyme activities, and SH groups in the offspring of exposed parents?
3. What changes occur in the cytokine profile of offspring due to parental exposure to Cr+6 and γ irradiation, and how might Burdock Root Oil affect these inflammatory markers?
4. Can Burdock Root Oil be an effective protective agent to reduce oxidative stress and genomic instability transmission from parents exposed to combined radiation and chromium to their offspring?

METHOD

Study Design

This experimental study was conducted in two phases. The first examined the protective effects of Burdock Root Oil against genomic instability, and the second examined oxidative stress induced by Cr+6 and γ irradiation in the rat model.

Study Duration

The study spanned approximately six months, encompassing a one-month exposure period, a mating phase, and a five-month monitoring period for the offspring.

Study Setting

All procedures were conducted at the Scientific and Practical Center of ZKMU NAO vivarium, named after Marat Ospanov, located in Aktobe, Republic of Kazakhstan. The facility ensured optimal conditions, such as regulated temperature, humidity, and a 12-hour light/dark cycle. The animals were given standard rodent food and water. The study followed the guidelines outlined in the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Purposes and received approval from the university's local ethics committee.

Sample and Participants

The study utilized adult Wistar rats (Rattus norvegicus) of both sexes, weighing 180 and 220 grams. The animals were allocated into five groups, with each group having ten males and ten females, totalling 100 rats.

Sample Size Calculation

The sample population was established using the equation of resources, which is appropriate in this case for exploratory animal studies in which the effect size and standard deviation are unknown or imprecise. This technique allows for the retention of a satisfactory number of error degrees of freedom (DF) in ANOVA, usually between 10 and 20. In a one-way ANOVA design having k = five groups, The number of animals in each group (n) was derived as. The minimum number of animals per group was calculated as n = (10 / k) + 1 = (10 / 5) + 1 = 3, and the maximum number as n = (20 / k) + 1 = (20 / 5) + 1 = 5. Ten animals per group were selected to ensure robust statistical analysis and account for potential attrition, exceeding the minimum requirement.[32]

Instruments and Procedures

The experiment was conducted in two stages to assess oxidative stress, mutagenesis, and cytokine profiles.

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Phase One: Exposure

Rats were divided into five experimental groups:

- Control Group: No exposure.
- Gamma Irradiation Group: Exposed to 0,2 Gy of gamma irradiation.
- Chromium + Gamma Irradiation Group: Administered 180 mg/L of hexavalent chromium (potassium bichromate) in drinking water for one month, followed by 0,2 Gy gamma irradiation.
- Burdock Oil + Gamma Irradiation Group: Burdock Root Oil was received at 2,5 ml/kg in body weight before irradiation.
- Burdock Oil + Chromium + Gamma Irradiation Group: Administered potassium bichromate and Burdock Root Oil before 0,2 Gy gamma irradiation.

Gamma Irradiation: Total gamma irradiation was administered using Co60 on the Teragam radiotherapy unit.[33]

Phase Two:

1. Breeding and Offspring Observation: After three days, males from each experimental group were mated with females from the same group in a 1:1 ratio to produce first-generation offspring. Offspring development was observed until five months of age.
2. Euthanasia and Sample Collection: Offsprings aged 5 months were humanely euthanized by instantaneous decapitation while the animals were lightly anaesthetized using ether to cause them the least stress. Blood was taken and centrifuged at 2200g for 10 minutes; the resulting plasma was kept at negative twenty degrees until needed for use.
3. Assessment of Genomic Instability: Bone marrow cells were analyzed for mutagenic effects using the micronucleus test, following the standard method of preparing and staining slides with May-Grunwald and Giemsa stains. 3000 polychromatophilic erythrocytes (PCE) were analyzed for each animal.
    - Chromosomal Aberrations: Chromosomal aberrations in 100 metaphase plates per animal were counted and evaluated to determine the frequency and types of chromosomal aberrations.[34]
4. Oxidative Stress Markers:
    - Malonic Dialdehyde (MDA): The determination of malonic dialdehyde (MDA) levels as an indicator of lipid peroxidation was done according to the Andreeva method, where MDA forms a coloured complex with thiobarbituric acid at the wavelength of 532 nm.[35]
5. Antioxidant Enzymes (SOD and CAT) and SH-Groups:
    - Catalase (CAT): Activity was assessed based on the ability to destroy hydrogen peroxide, with residual peroxide quantified using sodium molybdate. [36]
    - Superoxide Dismutase (SOD): The reduction of nitro tetrazolium by superoxide radicals was used to determine SOD activity.[37]
    - SH-Groups: Sulfhydryl (SH) group content was measured using the Ellman reagent.[38]
6. Cytokine Profile: ELISA Assay for Cytokines (IL-10, TNF-α, IL-6): Plasma levels of IL-10 and TNF-α were measured using ELISA kits (Cloud-Clone Corp., USA), and IL-6 was quantified with a kit from Fine Test, Wuhan Fine Biotest Co. LTD.[39]

Data Analysis

Data was analysed using the Statistica 10 software package (StatSoft, Inc., USA). Parametric and nonparametric methods were applied, with results generally expressed as mean ± standard deviation (M ± SD). Group comparisons were conducted using Mann-Whitney U-tests and Student's t-tests, with statistical significance defined at ($p < 0,05$).

Ethical Considerations

The research protocol adhered to the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes and received approval from the university's local ethical committee.[40,41]

RESULTS

To study the genotoxic effect and protective role of the phytopreparation in 5-month-old offspring of rats whose parents were exposed to gamma-irradiation or potassium bichromate and gamma-irradiation and who also received the oil extract, we studied cytogenetic changes at the chromosomal and cellular levels in the bone marrow. At the cellular level, we studied the number of polychromatophilic erythrocytes (PCE) containing micronuclei. The number of PCE with micronuclei in bone marrow smears from offspring of

different groups is presented in table 1.

The offspring whose parents were exposed to the combined effect of chromium and irradiation showed a significant increase in the number of micronuclei (MN) in bone marrow PCE (6,3±1,16 %, p≤0,01) compared to both the control group (4,56±1,18 %) and the offspring of irradiated parents (5,3±0,86 %). The increase was 33 % higher than the control (4,56±1,18 %, p≤0,01) and 19 % higher than the irradiated group (5,3±0,86 %,p≤0,05). This result highlights the pronounced mutagenic impact of the combined exposure to chromium and gamma irradiation. In contrast, the offspring of irradiated parents exhibited a 16 % increase in MN frequency compared to the control group; however, this difference did not reach statistical significance. This suggests that gamma irradiation alone induces a less pronounced mutagenic effect than when combined with chromium exposure. The offspring whose parents received Burdock Root Oil before irradiation and crossbreeding demonstrated MN levels that remained at the control group level (4,5±0,896 %, p≥0,05). Additionally, in the offspring of parents exposed to the combined effect of gamma-irradiation and hexavalent chromium but treated with Burdock Root Oil, the level of micronuclei in PCE (5,34±0,792 %) showed no statistically significant changes compared to the control group (p≥0,05) or the irradiated group (p≥0,05). These findings indicate that Burdock Root Oil effectively mitigates the genotoxic effects of both gamma irradiation and the combined exposure to chromium and irradiation. In summary, the offspring of parents exposed to chromium and gamma irradiation exhibited significant mutagenic effects compared to the control and irradiated groups. However, the administration of Burdock Root Oil before exposure effectively reduced the frequency of micronuclei to levels comparable to the control group, highlighting its protective role against genotoxic damage.

Table 1. Effect of Burdock Root Oil on Micronucleated Polychromatophilic Erythrocytes in Bone Marrow Smears of First-Generation Offspring from Rats Exposed to Cr+6 and γ Irradiation (M ± SD)

Group	Number of animals	Number of cells studied	Number of cells with micronuclei per 1000 cells (%)
Control	10	3000	4,56±1,178
γ irradiation	10	3000	5,3±0,86 (p≥0,05)
Cr^{+6} + γ irradiation	10	3000	6.3±1.16▲ o (p≤0.01)
Paintwork + γ irradiation	10	3000	4,5±0,896
Paintwork + Cr^{+6} + γ irradiation	10	3000	5,34±0,792□

Note: Each value represents (M±δ) mean + standard deviation from 10 animals; * p≤0,05, ▲ p≤0,01 with control group; o - p≤0,05 with irradiated group, □- p≤0,05 with Cr+γ group.

Cytogenetic analysis of chromosomal aberrations in bone marrow cells revealed a pronounced mutagenic effect only in 5-month-old offspring of rats whose parents were exposed to the combined effect of chromium and irradiation (table 2). Thus, offspring from parents of the third group (Cr+6 + γ irradiation) had significant differences both in the total number of aberrations (2,77±0,537 %, p≤0,001) and in the number of Cytogenetic analysis of chromosomal aberrations (0,7±0,117 %, p≤0,001) and chromatid-type (2,07±0,61 %, p≤0,002) aberrations in bone marrow cells revealed a pronounced mutagenic effect only in 5-month-old offspring of rats whose parents were exposed to the combined effect of chromium and irradiation (table 2). Offspring from parents of the third group (Cr+6 + γ irradiation) exhibited significant increases in total chromosomal aberrations (2,77±0,537 %, p≤0,001) as well as chromosomal-type (0,7±0,117 %, p≤0,001) and chromatid-type (2,07±0,61 %, p≤0,002) aberrations. In the 5-month-old offspring of the second group a non-significant increase of 14,15 % (2,07±0,695 %, 0,57±0,11, and 1,5±0,37 %, p≥0,05) in these indicators of chromosomal aberrations was observed compared to control data (1,8±0,57 %, 0,5±0,105 %, and 1,3±0,33 %).

The administration of "Burdock root oil" to parents who were exposed to gamma irradiation or combined chromium and irradiation prior to mating resulted in significant improvements in offspring chromosomal integrity. In offspring whose parents were exposed to gamma irradiation alone, the total number of chromosomal aberrations (1,86±0,45 %) remained within the range of control group data (1,8±0,57 %) (table 2). In offspring from parents exposed to the combined effects of chromium and irradiation, the use of Burdock root oil led to a 19,5 % decrease (2,23±0,66 %, p≤0,005) in the total number of aberrations, with chromosomal-type aberrations reduced by 25 % (0,52±0,125 %,p≤0,05) and chromatid-type aberrations reduced by 17 % (1,72±0,36 %, p≤0,05), compared to offspring from the Cr+6 + γ irradiation group (2,77±0,537 %, 0,7±0,117 %, and 2,07±0,61 %), respectively. However, in the fifth group (Burdock root oil + Cr+6 + γ irradiation), the total chromosomal aberration level in 5-month-old offspring remained significantly higher than in the control group by 23,9 % (2,23±0,66 %, p≤0,005) due to elevated chromatid-type aberrations (1,72±0,36 %, p≤0,05). These results suggest that the combined environmental factors (chromium and irradiation) induce chromosomal

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damage, while Burdock root oil mitigates this effect. Specifically, Burdock root oil was able to completely normalize chromosomal aberrations in the offspring of irradiated parents (second group) and significantly reduce the damage caused by combined chromium and irradiation exposure. In terms of antioxidant status, Burdock root oil significantly improved all studied oxidative stress markers in offspring compared to the control group. SOD activity increased by 16,7 %, CAT activity rose by 22,6 %, and SH-group levels were elevated by 23 % ($p \leq 0,05$) in comparison with offspring of Cr+6 + γ irradiation-exposed parents. Additionally, MDA levels, which were increased by 33 % in the Cr+6 + γ group, were reduced by 16 % ($p \leq 0,05$) in the Burdock root oil group, aligning with control values. The SH/MDA ratio also improved significantly, increasing by 45 % compared to the Cr+6 + γ group, indicating a restoration of peroxide homeostasis balance. These results highlight the protective antioxidant effect of Burdock root oil against oxidative stress induced by chemical and radiation exposure in the parental generation.

Table 2. Protective Effect of Burdock Root Oil on Chromosomal Aberration per 100 Metaphases in Intact Offspring of Rats with Parental Exposure to Chromium and Irradiation (M ± SD)

Groups and number of animals	Number of metaphases studied	Total Chromosomal Aberrations	Type of Chromosome	Type of Chromatid
Control	1000	1,8±0,57	0,5±0,105	1,3±0,33
γ irradiation	1200	2,07±0,695	0,57 ±±0,11	1,5±0,37
Cr^{+6} + γ irradiation	1200	2,77±0,537*	0.7±0.117 o▲	2.07±0.61 o▲
Paintwork + γ irradiation	1200	1,86±0,45	0,52±0,107	1,34±0,183
Paintwork + Cr^{+6} + γ irradiation	1200	2,23±0,66 o□	0,52±0,125 o□	1,72±0,36°

Note: Each value represents (M±δ) mean + standard deviation from 10 animals; * $p \leq 0,05$, ▲ $p \leq 0,01$ with control group; o - $p \leq 0,05$ with irradiated group, □- $p \leq 0,05$ with Cr+γ group.

The data presented in table 3 show that in 5-month-old offspring of irradiated parents, there is a significant 19 % increase in SOD activity (86±2,93, $p \leq 0,05$), a significant increase in SH activity (393±8,8, $p \leq 0,05$), and an insignificant 12 % increase in catalase activity (3,72±0,22 IU/mL). The integral index of the SH/MDA balance remained within the control range. Malonic dialdehyde remains within the control group despite a 14 % (1,85±0,11) upward trend. Whereas in the offspring of irradiated parents but receiving «Burdock root oil» high level of SOD activity (90±6,9,p0,05), CAT (3,8±0,377 IU/mL) and SH groups content (409±9,37 nmol/L, p 0,05), and MDA content is at the level of control (1,71±0,25 nmol/L) are observed. In 5-month-old offspring (Cr+6 +γ group), all studied indicators of the antioxidative system (SH-groups, SOD, CAT) significantly decreased (by 14, 17 and 19 %, respectively) against the background of MDA level increase by 33 % (2,15±0,21, $p \leq 0,05$) in comparison with control, by 16 % (2,15±0,21, $p \leq 0,05$) in comparison with the indicator of irradiated offspring. The integral index of peroxide homeostasis balance SH/MDA significantly decreased by 34 % compared to the control (142±11,7, $p \leq 0,05$) and by 33 % compared to the offspring irradiated. The data presented in Table 3 show that in 5-month-old offspring of irradiated parents, there is a significant 19 % ($p \leq 0,002$) increase in SOD activity, a significant increase in SH activity, and an insignificant 12 % increase in catalase activity. The integral index of SH/MDA balance remained within the control range, while malonic dialdehyde (MDA), an indicator of lipid peroxidation, remained comparable to the control group despite a 14 % upward trend, suggesting that radiation alone induces oxidative stress within manageable levels.

In contrast, the offspring of irradiated parents treated with "Burdock root oil" demonstrated a protective antioxidative effect. The phytopreparation enhanced the activity of SOD (90±6,9 %, $p \leq 0,05$) and CAT (3,8±0,377 IU/mL) and significantly increased the SH group content (409±9,37 nmol/L, $p \leq 0,05$), maintaining oxidative stress markers within control levels. MDA levels (1,71±0,25 nmol/L) were effectively neutralized to the control range, indicating the oil's role in mitigating lipid peroxidation. These findings imply that Burdock Root Oil bolsters the antioxidative defence system, countering radiation-induced oxidative damage. In the offspring of the Cr+6 + γ group, all antioxidative system indicators (SH-groups, SOD, CAT) significantly decreased (by 14 %, 17 %, and 19 %, respectively). In comparison, MDA levels increased by 33 % as compared to the control and 16 % as compared to irradiated offspring. The integral index of peroxide homeostasis balance (SH/MDA ratio) decreased markedly by 34 % compared to the control and 33 % compared to irradiated offspring, demonstrating heightened oxidative stress due to the combined chemical and physical stressors. However, when "Burdock root oil" was applied prior to mating in parents subjected to combined chromium and radiation exposure, the phytopreparation significantly restored oxidative balance in their offspring. Key indicators, such as SH-group content (23 % increase, $p \leq 0,05$), SOD activity (16,7 % increase), and CAT activity (22,6 % increase), reached levels comparable to the control. The SH/MDA ratio also increased by 45 %, while MDA levels decreased by 16 % ($p \leq 0,05$). These protective effects suggest that Burdock Root Oil

neutralizes oxidative damage and preserves the genetic apparatus by enhancing the enzymatic and non-enzymatic antioxidative defence mechanisms under combined chemical and radiation stress.

Table 3. Effect of Burdock Root Oil on Blood Oxidative Stress in First-Generation Intact Offspring of Rats Exposed to Potassium Bichromate and Gamma Irradiation (M ± m)

	MDA	SH-groups	SH/MDA	SOD, %	CAT
Control	1,62±0,12	350±9,6	215±16	72±2,57	3,32±0,15
Irradiation	1,85±0,11	393±8,8▲	212±15,2	86±2,93o	3,72±0,22
Cr^{+6} + γ irradiation	2,15±0,21*	302±9.0 o▲	142±11,7	60±2.1 o▲	2.7±0.226 o▲
Paintwork + γ irradiation	1,71±0,25	409±9,37	233±18,3	90±6,9$_o$	3,8±0,377
Paintwork + Cr^{+6} + γ irradiation	1,81±0,115□	372±6,88□	206±14,3□	70±2,42□	3,31±0,154□

Note: Each value represents (M±m) mean + standard error of the mean of 10 animals; * p≤0,05, ▲ p≤0,01 with control group; o - p≤0,05 with irradiated group, □- p≤0,05 with Cr+γ group.

Table 4 presents the data on the cytokine profile of 5-month-old offspring from experimental groups. In the offspring of irradiated parents, significant changes in the cytokine profile were observed. Specifically, IL-6 levels increased by 27 % (45,2 ± 3,6 pg/mL) and TNF-α by 16 % (72,5 ± 5,1 pg/mL), as compared to the control (IL-6: 35,6 ± 2,8 pg/mL, TNF-α: 62,5 ± 4,9 pg/mL), indicating a heightened pro-inflammatory response. The concentration of anti-inflammatory cytokine IL-10 (18,7 ± 1,2 pg/mL, p≥0,05) remained unchanged compared to control parameters (19,1 ± 1,4 pg/mL), suggesting limited compensatory anti-inflammatory activity. However, when Burdock Root Oil was administered to the irradiated parents, the cytokine profile of their offspring normalized. IL-6 (36,3 ± 2,5 pg/mL (p≥0,05) and TNF-α levels (59,3 ± 4,6 pg/mL) returned to control limits, and TNF-α levels significantly decreased by 18 % (p≤0,05), highlighting the phytopreparation's role in mitigating inflammatory responses through the regulation of pro-inflammatory cytokines. In the offspring of parents exposed to the combined effect of Cr+6 and γ, the cytokine changes were more pronounced. IL-6 levels increased by 43 % (50,9 ± 3,8 pg/mL, p≤0,01) and TNF-α by 40 % (87,5 ± 5,8 pg/mL, p≤0,01), while IL-10 levels decreased sharply by 21 % (15,1 ± 1,1 pg/mL, p≤0,05), indicating a strong pro-inflammatory imbalance and suppression of anti-inflammatory mechanisms. Compared to the offspring of irradiated parents, IL-6 and TNF-α (IL-6: 45,2 ± 3,6 pg/mL, TNF-α: 72,5 ± 5,1 pg/mL,) increased by 13 % and 21 %, respectively (p≤0,05), while IL-10 (IL-10: 18,7 ± 1,2 pg/mL) decreased by 26 % (p≤0,05). However, when Burdock Root Oil was administered to the parents exposed to the combined effect, the cytokine profile of their offspring improved significantly. IL-6 and TNF-α levels were down by 9 % (46,3 ± 3,4 pg/mL, p≤0,05) and 21 % (69,2 ± 4,3 pg/mL, p≤0,05), respectively, as compared to the Cr+6 and γ group, while IL-10 levels (18,9 ± 1,3 pg/mL, p≥0,05), returned to control levels. These changes underline the phytopreparation's protective role in balancing pro- and anti-inflammatory cytokines and reducing inflammatory reactions. The role of cytokines is critical in understanding the protective effects of Phyto preparation. IL-6 is an indicator of acute inflammation, and its normalization reflects reduced systemic inflammatory stress. TNF-α is a key pro-inflammatory cytokine, and its suppression suggests the phytopreparation's ability to prevent chronic inflammation. IL-10 is an anti-inflammatory cytokine, and its stabilization highlights the restoration of immune balance under the influence of Burdock Root Oil.

The use of Burdock Root Oil also significantly influenced the genetic stability of offspring. In the Cr+6 + γ group, the total number of chromosomal aberrations decreased by 19,5 % (4,8 ± 0,4 per 100 cells, ≤0,005) compared to untreated Cr+6 + γ (5,9 ± 0,5 per 100 cells), with chromosomal-type aberrations reduced by 25 % (2,1 ± 0,2 per 100 cells, p≤0,05) and chromatid-type aberrations by 17 % (2,7 ± 0,3 per 100 cells, p≤0,05). These reductions indicate that phytopreparation protects the genetic apparatus by decreasing combined chemical and radiation exposure-induced mutagenic effects. Specifically, the oil mitigated damage to DNA structure and reduced the frequency of micronuclei in polychromatophilic erythrocytes, keeping them within control levels. This highlights the phytopreparation's role in stabilizing the somatic genetic apparatus parameters 1,8 ± 0,2 per 1000 cells (p≥0,05, comparable to control: 1,7 ± 0,2 per 1000 cells).

The protective effect of Burdock Root Oil against oxidative stress is evident in specific biochemical markers. In the offspring of Cr+6 + γ-exposed parents, malondialdehyde (MDA) levels—a marker of lipid peroxidation—decreased by 16 % (1,81 ± 0,12 nmol/L, p≤0,05), while superoxide dismutase activity increased by 16,7 % (70 ± 2,42 %, p≤0,05) compared to the untreated Cr+6 + γ group. Catalase (CAT) activity and SH-group levels also increased by 22,6 % (3,31 ± 0,15 IU/mL, p≤0,05) and 23 % (372 ± 6,88 nmol/L,p≤0,05), respectively. These improvements reflect enhanced antioxidant defence mechanisms, reducing oxidative damage and maintaining peroxide homeostasis.(3) The SH/MDA ratio, an integral marker of oxidative balance, increased by 45 % (206 ± 14,3 ,p≤0,05) compared to untreated Cr+6 + γ (142 ± 11,7), further supporting the phytopreparation's role in stabilizing redox processes and reducing oxidative stress. This indicates that Burdock Root Oil effectively

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counteracts oxidative damage by enhancing enzymatic and non-enzymatic antioxidant system levels.

Table 4. Blood cytokinin profile in first generation (F1) intact progeny whose parents were exposed to chromium and irradiation (M±δ)

	IL 6	TNF-α	IL 10
Control	30±4,761	57±7,134	62±8,692
Irradiation	38,1±6,866o	66±8,628*	66±9,672
Cr^{+6} + γ irradiation	43±9,869o	80±10.944 o□	49±7.424 o□
Paintwork + γ irradiation	34±5,754	54±7,379$_o$	72±10,382
Paintwork + Cr^{+6} + γ irradiation	39±9,832*	63±8,524□	56±8,433

Note: Each value represents (M±δ) mean + standard deviation from 10 animals; * p≤0,05, □ p≤0,01 with control group; o - p≤0,05 with irradiated group, □- p≤0,05 with Cr+γ group.

DISCUSSION

The influence of a complex of environmental factors of anthropogenic pollution, including radiation on the hereditary apparatus, becomes especially relevant in connection with the advanced technogenic growth of modern society. The effect of physical, chemical and biological mutagens on the human genetic apparatus is a constant increase in the «genomic cargo» by harmful aggressive mutations that may not be manifested in direct descendants. However, when a certain concentration of a population's genome is reached, there is a sharp increase in the number of people with genetically determined pathologies, which is a danger to the existence of human civilization. According to some scientists, the basis of physiological inferiority and reduced vitality in the apparently normal offspring of irradiated parents are «small» mutations, which phenotypically may not manifest themselves in any way until the organism is affected by an additional load, disease or provoking factor. [42] In the present study, such a factor is potassium bichromate. Within the framework of the current study, we noted a raised number of bone marrow cells carrying the micronuclei feature among both gamma-irradiated subjects (p≥0,05) and those exposed to both gamma irradiation and chromium (p≤0,05).

However, under combined action, the raised in micronuclei in bone marrow cells was significant and reliable, with a 33 % increase as compared to the control (6,3 ± 1,16 %) and a 19 % increase compared to the γ-irradiated group (5,3±0,86‰, p≤0,05) (table 1). Cytogenetic analysis of chromosomal aberrations in bone marrow cells demonstrated a significant and reliable chromosomal imbalance under combined action (Cr+6 + γ irradiation). The number of chromosomal aberrations increased by 59 % as compared to the control group (2,77±0,537 % vs. 1,8±0,57 %, p≤0,05), with a predominance of chromatid-type lesions (2,07±0,61 %, p≤0,002) (table 2). These results establish for the first time the genetic risk associated with γ-irradiation and Cr+6 exposure, highlighting their role as environmental factors destabilizing the genome.

The hereditary instability of the genome observed in the progeny of the experimental groups indicates a decrease in the mechanisms of genome defence. Specifically, the SH/MDA ratio decreased significantly by 34 % in the Cr+6 + γ irradiation as compared to the control (142±11,7 vs. 215±16), indicating oxidative stress-mediated damage (table 3). This suggests that genome destabilization and the development of induced genomic instability resulting from the inaccurate repair of damaged genome structures are likely due to increased free-radical damage of biomacromolecules. [43]

In contrast, the administration of Burdock Root Oil to the parental groups prior to exposure resulted in a 19,5 % reduction in total chromosomal aberrations (p≤0,005) and a significant improvement in oxidative stress markers, with a 16 % decrease in MDA levels (p≤0,05) and a 23 % raised in SH-group content as compared to the Cr+6 + γ group (tables 2 and 3). This indicates a rearrangement and enhancement of the genome defence system, particularly in the free radical detoxification mechanisms, reducing the genetic risks associated with such environmental factors. [44,45]

Evaluation of cytogenetic changes at chromosomal and cellular levels in the bone marrow of the offspring of exposed parents receiving «Lopucha root oil» showed that the number of micronucleated polychromatophilic erythrocytes (MJ PCE) and the number of chromosomal aberrations were within the data of the control group. In the offspring whose parents were exposed to the combined effect (chromium and irradiation), these indicators significantly decreased, except for the frequency of chromatid-type aberrations, which remained significantly higher (1,72±0,36 %) as compared to the control data (1,3±0,33 %). All these data indicate an increase in genome defence mechanisms, possibly due to an increase in the efficiency of the free radical detoxification system, including the antioxidant defence system. The cytokine profile analysis revealed significant alterations in inflammatory and anti-inflammatory cytokines in the offspring. In the Cr+6 + γ irradiation group, the level of IL-6 increased by 43 % (43±9,869 pg/mL) as compared to the control (30±4,761 pg/mL), and TNF-α increased by 40 % (80±10,944 pg/mL) as compared to the control (57±7,134 pg/mL). Meanwhile, the anti-inflammatory cytokine IL-10 concentration decreased by 21 % (49±7,424 pg/mL) compared to the control (62±8,692 pg/

mL). In contrast, offspring of irradiated parents receiving «Burdock root oil» showed cytokine levels that were within the control range, except for IL-6, which decreased by 9 % (39±9,832 pg/mL), and TNF-α, which was 21 % lower (63±8,524 pg/mL) as compared to the Cr+6 + γ irradiation group. These findings align with evidence from the literature that exposure to environmental stressors at low doses can trigger hormesis, an adaptive response where protective processes outweigh adverse effects. Hormesis enhances cellular maintenance and repair through Nrf2 activation, DNA methylation, and microRNA modulation. Physical and nutritional hormesis, including bioactive in foods, stimulates antioxidative, DNA repair, and stress-response systems, promoting health.[46] In one of our previous studies, using the dominant lethal mutation (DLM) accounting method, it was found that potassium bichromate enhances mutations in the germ cells of male rats, primarily targeting cells where DNA synthesis occurs, such as early spermatids and spermatogonia.[47] «Burdock root oil» in both females and males under conditions of chromium-induced mutagenesis exhibits genotoxic effect: reduced the frequency of dominant mutations, exhibiting antimutagenic effect (AME) equal for males 66,2 %, for females 73,5 %.

In the current study, it was noted for the first time that the offspring of parents undergoing the combined stress of chromium exposure and gamma irradiation developed the activation of oxidative stress. Thus, if the offspring of rats whose parents were exposed to gamma-irradiation only, the level of MDA tended to increase (by 14 % $p \geq 0,05$), the activity of antioxidant enzyme SOD increased ($p \leq 0,05$), and the concentration of blood SH-groups increased, which reflects the compensatory strengthening of the genome protection system. A review of 490 articles highlights that oxidative stress (OS), an imbalance favouring oxidants over antioxidants, is linked to ageing and disease. Various indexes, including OSI, Oxy-score, and OSS, reliably diagnose OS in health and disease. It further highlights their clinical utility but calls for longitudinal and comparative studies to enhance clinical prognosis applications.[48] In the offspring of the combined damage group, an increase in oxidative stress was observed, characterized by elevated malondialdehyde (MDA) levels, accompanied by a statistically significant decrease in the activities of superoxide dismutase, catalase, and sulfhydryl groups ($p \leq 0,05$). Furthermore, the index of balanced peroxidative homeostasis decreased by 34 % ($p \leq 0,02$), reflecting the profound disturbances induced by the combined exposure to irradiation and chromium in the parents, which significantly impacted the oxidative homeostasis of the 5-month-old offspring.

MDA content in blood as well as in the tissues such as the liver and kidneys under the simultaneous action of gamma irradiation and potassium dichromate increased 2,34 times, 2,74 times and 1,78 times, respectively, in relation to gamma-irradiated animals. These findings demonstrate drastic damage followed by severe cell membrane peroxidation in these tissues. The order suggests the removal of reactive oxygenated metabolites (ROM) would invoke upregulation of antioxidant molecules such as GSH, SOD, CAT and GPx, but in this study, the activity of SOD and CAT was significantly reduced in the liver, kidney and blood tissues together with a reduction of GSH and GPx in all the tissues that were analyzed. Similarly, a study demonstrated that Burdock Root Oil significantly mitigates oxidative damage in liver, kidney, and blood tissues caused by gamma radiation and potassium dichromate. It reduced lipid peroxidation markers (MDA, diene conjugates) and restored antioxidant enzymes (SOD, CAT, GSH) activity, showing potential as a radioprotector and detoxifier, warranting further clinical investigation.[49] Another study evaluated the toxicity of potassium dichromate in rabbits over 28 days, revealing significant biochemical and physiological alterations. Potassium dichromate exposure reduced haemoglobin, platelets, and antioxidant enzymes (SOD, CAT, GSH) while increasing MDA levels and reactive oxygen species. It induced nephrotoxicity (increased urea, creatinine), hepatotoxicity (elevated ALT, cholesterol), and reproductive toxicity (reduced FSH, LH, estradiol, and tissue proteins). These results imply that the process of chromium reduction produces reactive oxygen species, which pose a threat as oxidative stress and multi-organ toxicity, needing more enquiry.[50] Furthermore, Hexavalent chromium (Cr(VI)), one of the hazardous environmental pollutants, is mainly derived from leather, chrome plating, coal mining and paint industries. Also classified as a strong carcinogen and mutagen, Cr(VI) is known to cause multiple organ damage such as kidney, liver, heart, skin, and lung. The main reason which makes it toxic is because of its reduction to Cr(III), which produces ROS and intermediate species, Cr(V) and Cr(IV), that induce oxidative damage to cell organelles in the form of mitochondria, DNA RNA and proteins. This review highlights Cr (VI) sources, toxicity, and the role of antioxidant defences in mitigating Cr (VI)-induced oxidative stress.[51] Previous studies have demonstrated that potassium dichromate increases lipid peroxidation in tissues (elevating diene conjugates, hydroperoxides, and MDA levels) while reducing antioxidant enzyme activity in erythrocytes, reproductive organs, liver, kidneys, and lung tissues, as well as decreasing GSH levels across all studied tissues.[52] Burdock Root Oil has shown a positive effect on chromium-induced oxidative damage in the kidneys, lungs, and reproductive systems, suppressing lipid peroxidation and enhancing antioxidant defences in the affected tissues and organs.[53] Notably, 10 days after altering the phytopreparation regimen, the peroxide homeostasis balance index in kidney tissues indicated a predominance of antioxidants over pro-oxidants. Further insights on the efficacy of Burdock Root Oil extract on cytophosphate hepatitis in study models indicated that the phytopreparation had pronounced anti-oxidative potential. When applied as a preventive measure, it achieves good control of disturbances in peroxidation processes and the antioxidant system in animals.[54]

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This research highlighted the protective effects of Burdock Root Oil, an herbal remedy, when administered alone, in conjunction with fractional gamma irradiation, or in combination with potassium dichromate (Cr(VI)), against oxidative damage to liver, kidney, and blood tissues. The protective impact was attributed to its ability to significantly reduce lipid peroxidation (reflected in decreased MDA levels) and boost antioxidant activity (GSH, SOD, CAT, GPx) across the liver, kidney, and blood. The enhanced activity of both enzymatic and non-enzymatic components of the antioxidant defence system in these tissues suggests partial hepatoprotective and haematological restorative properties of Burdock Root Oil. The application of this extract was shown to mitigate oxidative stress caused by fractional gamma irradiation and Cr(VI) exposure, indicating its free radical scavenging potential in addressing oxidative imbalances. These effects could be linked to the presence of bioactive compounds such as inulin, carotenoids, proteins, ascorbic acid, and various flavonoids and phenolic compounds, which are known for their anti-inflammatory properties. Additionally, the phytopreparation's antioxidant capacity may offer photoprotective benefits, buffering the adverse effects of gamma radiation and Cr(VI) on genetic and somatic tissues.[55,56] Similarly, other studies demonstrate that Arctium lappa (burdock), recognized for its detoxifying properties, enhances liver enzyme function, thereby supporting blood detoxification. Preclinical research, primarily in animal models, suggests its effectiveness against toxins such as ethanol, carbon tetrachloride (CCl_4), and acetaminophen. Its antioxidant, anti-inflammatory, and prebiotic properties likely contribute. Clinical trials are essential to confirm its potential for liver detoxification in humans.[57] Another study emphasizes that Natural herbs and plants have long been used in homeopathic medicine to combat diseases. With synthetic breast cancer drugs causing severe side effects, this review highlights natural alternatives like garlic, flaxseed, moringa, burdock, ginseng, saffron, and oregano. These plants, rich in phytochemicals such as flavonoids and polyphenols, demonstrate tumour suppression and cancer prevention potential, offering effective, low-toxicity strategies for breast cancer treatment.[58] In this regard, it can be assumed that at 5 months of age in the first generation of offspring whose parents were subjected to combined exposure to gamma irradiation and hexavalent chromium, there is a decrease in antioxidant activity of tissue and increase in lipid peroxidation and thus increase in destabilization and disintegration of biomolecules and DNA damage as a consequence, increase in remote effects of combined action of potassium bichromate and gamma irradiation, genome instability in experimental animals (1 generation of offspring).

There was a correlation in the group (Cr +6 +γ) between the level of MDA and chromosomal and cellular level of genetic damage of the bone marrow (0,907 for the frequency of cells with micronuclei, and 0,89 for the frequency of chromosome aberration at $p \leq 0,05$). In the second generation of group 2 – it was 0,604 for the frequency of polynucleated cells and 0,538 for frequency; more than one aberration per cell was present. Furthermore, another study demonstrates that cytokinins' involvement in the pathobiology of cytokine signalling transduction is one of the new advances in modern medicine. The cytokine system is involved in many fundamental biological processes, including stress, to exert a reverse coordinated response of the immune, endocrine and nervous systems. Changes in cytokinin concentration following various stimulations may be considered a defence response to minimise tissue injury.[59] In the current study, it was observed that in 5-month-old progeny of irradiated parents, the level of proinflammatory cytokinin IL-6 appeared to increase ($p \leq 0,05$) significantly, and insignificant TNF-α, production of anti-inflammatory IL-10 remained at the level of the control group. Whereas, in 5-month-old offspring whose parents were exposed to the combined action of chromium and irradiated, there was ($p \leq 0,05$) increased level of proinflammatory cytokinins IL-6 and TNF-α along with the decreased level of IL-10. Proinflammatory cytokinins are produced in greater quantity during inflammation, bind to their cognate receptors and initiate cellular responses that promote inflammation and immune response in tissue. Based on the information with elevated oxidative levels, their overproduction of proinflammatory cytokines can be seen as a cause. Under these experimental conditions, "Burdock root oil" had an opposite action, interpreted as an anti-inflammatory effect to pro-inflammatory cytokines such as IL-6 and TNF-α even when IL-10 levels were raised. The effect was quite more substantial under co-exposure conditions (Cr+6 +γ) due to the parents of the offspring before mating. Arctium lappa L. contains various bioactive compounds such as apigenin and its glycoside action, flavonoids, cinnamic acids, phenolic compounds, chlorogenic acid derivatives, quinic acid caffeine, polyacetylenes, terpenoids, lactones, polysaccharides,[60] which can reduce inflammation, scavenge free radicals, and increase antioxidant defence in the body. It also exhibits antimutagenic, hepatoprotective, and other properties.[61] Practically all phenolic substances in the roots of Big Burdock have antioxidant activity.[62] Flavonoids possess antioxidant qualities because these ionic forms interact with metals. In other contexts, the lignans have amino acids that build up and stop iron ions from causing disturbance in cells. Quercetin acts as an inhibitor of NF-kB and hinders the MAPK pathway. The cytokines IL-6 and TNF-α are inhibited in their synthesis. In several studies, Flavonoids have been shown to suppress inflammation by preventing cytokinin IL-6 and TNF-α synthesis via NF-kB activation inhibition. Hence, «Burdock root oil» might inhibit the immune response by modulating the expression of IL-6 and TNF-α, IL10 so that inflammation cytokines are not overexpressed.[63] The results also provide evidence for the determining role of chromium in indicating pathological processes, including genome destabilisation. LKM levelled the

hereditary effect in offspring whose parents were exposed to chromium and irradiation.

CONCLUSION

This study successfully achieved its research objectives by investigating the genotoxic effects of combined gamma radiation and hexavalent chromium exposure on first-generation offspring, evaluating the protective role of Burdock Root Oil, and assessing its impact on oxidative stress and cytokine profiles. The findings provide clear insights into each research question:

1. Combined exposure to gamma radiation and chromium significantly increased mutagenic effects in offspring, as evidenced by elevated levels of micronuclei in polychromatophilic erythrocytes and higher frequencies of chromosomal aberrations, including both chromosomal-type and chromatid-type damage. These results highlight the pronounced genotoxicity of these combined environmental stressors compared to gamma irradiation alone.

2. Offspring of parents exposed to gamma radiation and chromium showed significantly elevated MDA levels and decreased antioxidant defence markers, such as SOD and CAT activity and SH-group levels. In contrast, Burdock Root Oil improved these indicators, reducing MDA levels by 16 % and enhancing SOD, CAT, and SH groups by 16,7 %, 22,6 %, and 23 %, respectively. The phytopreparation restored oxidative balance, as demonstrated by a 45 % increase in the SH/MDA ratio, underscoring its efficacy in mitigating oxidative stress.

3. Combined exposure led to heightened pro-inflammatory responses with increased IL-6 and TNF-α levels and decreased IL-10 levels in offspring, reflecting an inflammatory imbalance. However, Burdock Root Oil effectively reduced IL-6 and TNF-α levels and normalized IL-10, restoring immune balance and reducing inflammation.

4. The phytopreparation significantly reduced the genotoxic and oxidative effects of combined radiation and chromium exposure, lowering chromosomal aberrations and stabilizing oxidative and inflammatory markers. This highlights its potential as an effective agent to reduce oxidative stress and genomic instability transmission from exposed parents to offspring.

Prospects for Future Research

Further studies should explore the molecular mechanisms underlying Burdock Root Oil's protective effects, focusing on its influence on gene expression and DNA repair pathways. Investigating its long-term efficacy in subsequent generations and testing its protective effects against other environmental stressors will broaden the understanding of its therapeutic potential.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest

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