

Effect of Burdock Root Oil on Oxidative Stress Induced by Isolated and Combined Use of Gamma Radiation and Hexavalent Chromium

Marat Iztleuov¹, Yerbolat Iztleuov^{1*}, Samat Saparbayev¹,
Assem Temirbayeva¹, Raushan Medeuova¹, Zarina Aleuova²,
Irina Ismailova¹ and Nauryzbai Imanbayev¹

¹West Kazakhstan Marat Ospanov Medical University. Aktobe, Kazakhstan.

²West Kazakhstan M. Utemisov University.

*Corresponding Author E-mail: ermar80@mail.ru

<https://dx.doi.org/10.13005/bpj/2382>

(Received: 10 December 2021; accepted: 02 March 2022)

They studied the effect of the herbal medicine "Burdock root oil" on oxidative damage to liver, kidney and blood tissues. The experiment was performed on 50 non-linear white male rats weighing 180-220 g, divided into 5 groups. The first group - control; animals of groups II and III were subjected to fractional gamma irradiation for five days (0.6 G/day; dose rate 1 Gr/min (60Co)). The total dose was 3 Gr. Animals of the fourth and fifth groups were exposed to a combination of gradiation (as in groups I and III) and potassium dichromate (Cr+6). Potassium dichromate was administered intraperitoneally daily at a dose of 2.8 mg/kg of body weight (0.1LD50) for 5 days (0.5LD50). Rats of groups 3 and 5 received Burdock root oil at a dose of 2.5 ml/kg of body weight intragastrically for 14 days prior to the experimental exposure. Fractional exposure, combined exposure g-radiation, gamma radiation and Cr+6 led to an increase in malondialdehyde and diene conjugates in blood plasma, liver and kidney tissues. Under g-irradiation, the activity of superoxide dismutase enzymes (SOD) and catalase (CAT) in red blood cells compensation increased significantly against the background of a decrease in the level of SH-groups in blood plasma. In liver and kidney tissues, all studied enzymes and reduced glutathione (GSH) levels decreased. Under the conditions of combined exposure g-radiation and potassium dichromate - all the studied indicators of antioxidant protection decreased. The introduction of Burdock root oil before isolated and combined exposure provided significant antioxidant protection in the studied tissues. Conclusion: it can be assumed, that the "Burdock root oil" it is a potential drug that can be used as a radiation protector, in conditions of combined influence of a physical and chemical agent-a detoxifier. In our opinion, the antioxidant potential of the herbal medicine justifies the continuation of further research in clinical practice.

Keywords: Antioxidant Potential; Combined Effect of Gamma Irradiation and Cr; Fractional Gamma Irradiation; Herbal Medicine "Burdock Root Oil"; Liver, Kidney, Blood; Oxidative Damage.

Ionizing radiation causes physiological, biochemical, and morphological changes. Which depend on the absorbed dose, duration of exposure, post-exposure interval, and dose fractionation.

Radiation can initiate a series of targeted reactions that increase the levels of reactive oxygen species. Since human tissues contain up to 80% water, new radiation damage occurs due to water-borne

free radicals that occur when water is exposed to radiation. This leads to oxidative stress and biological damage^{1,2}. Many pathological conditions are associated with either high levels of free radicals or reduced ability to absorb free radicals^{4,6}. The negative effects of ionizing radiation in biological systems are caused by the generation of reactive oxygen species. This contributes to radiation-induced oxidative stress, which leads to damage to cells, cellular structures, and organ dysfunction⁷³. The widespread use of radiation in diagnostics, treatment, industry and energy, the risk of accidental exposure as a result of man-made accidents at nuclear facilities requires protection from human exposure⁸.

Exogenous factors, including radiation, affect humans and animals not in isolation, but in combination with each other. Due to the increase of technogenic factors in the environment, the assessment of their toxicity, carcinogenicity and mutagenicity, as well as protection from their effects is relevant. This applies in particular to ionizing radiation and, in this case, hexavalent chromium (CrVI). Eco pathogenic risk in Western Kazakhstan is associated with the presence of a chromium-biogeochemical province. There is a regional feature of ensuring radiation safety (the exposure dose rate and the average annual effective dose of external radiation to the population are higher than the average national indicators)^{30,42}.

Environmental contamination with hexavalent chromium is a serious threat to human health and is increasing due to the wide spectrum of industrial chromium around the world³. One of the most widely used chromium compounds is potassium dichromate ($K_2Cr_2O_7$), a hexavalent form of chromium (Cr^{+6})^{59,41,78}. Cr(VI) can enter the cell via sulfate-phosphate anion channels using non-specific anion transporters^{62,74}. When the valence is reduced by cellular enzyme or non-enzyme reducing agents, Cr (III) is formed^{60,83,48}, which is accompanied by the generation of reactive oxygen species (ROS).

The interaction of reactive oxygen species (ROS) with chromium reduction intermediates (Cr VI) can cause oxidative stress. Induction will occur I cascade cellular events: apoptosis, inflammation, gene toxicity and carcinogenicity^{20,77,79,5,59,1,16,72,12,7,70}.

Thus, the effects of gamma radiation and Cr (CrVI) are based on the generation of reactive

oxygen species, which lead to oxidative stress and biological damage. Free radical scavengers can work as effective radio, and chemo protectors against oxidative damage. The search for protective agents that counteract oxidative damage is a necessity. It will have a huge application in radiation therapy for prophylactic purposes, in various biogeochemical processes, where the population is exposed to combined or combined effects of exogenous factors of various nature. The search and identification of protective agents, including radio-protectors, for use in prevention is one of the priority areas of research. Radio-protective agents minimize or prevent damage from exposure to toxic exogenous factors or gamma radiation in the population.

Recently, much attention has been paid to the role of natural antioxidants in protecting cells from damage caused by chromium and / or radiation^{1,2,6}. And coming from the main mechanism of free radical generation, their anti mutagenic, antioxidant, and immunomodulatory properties are important for the appearance of a protective effect. Natural protectors that meet the requirements of non-toxicity with the absence of side effects^{5,1} and provide minimal radiation damage to normal tissues are promising in this direction.

Numerous reports have focused on the antioxidant effects of Burdock (*Actium landplane L*). It has been consumed as a nutritious and healthy food, as well as a medicine, in Asia, Europe, and the United States for approximately 3,000 years⁶. The main active compounds of burdock roots are phenolic compounds such as lignin's, coffee and chromogenic acids, quartzite and lutein, inulin, essential amino acids, asparagine and arginine, minerals, vitamins and fibers^{6,56,1,5,4}. Traditionally, burdock root is used to treat a number of diseases, such as skin diseases, kidney and liver diseases, cancer, diabetes, rheumatic diseases, gout, hypertension, arteriosclerosis, and other inflammatory disorders^{6,2,58,76,1,76,15,23}. *Arctium Lappa LL*. exhibits hepatic-protective^{5,22}, antibacterial and antiviral properties^{18,7,6,7,66,8,80}, anti-mutagenic⁹, and anti-inflammatory effects^{84,71,64}, which may be related to its free radical scavenging activity^{82,66}. Chemical and biochemical properties are attributed to its components with antioxidant

abilities^{13,5,54,80,1,80} – almost all phenolic substances, flavonoids^{56,50,14}.

The present study is devoted to the evaluation of the protective effect of the herbal medicine “Burdock root oil” on oxidative stress (oxidative damage to the blood, liver and kidneys) induced by isolated and combined exposure to gamma radiation and hexavalent chromium.

MATERIAL AND METHODS

The study was conducted on white male rats weighing 180-220 kg. The animals were kept under standard conditions in the vivarium of the Scientific and Practical Center of the Non-Profit Joint Stock Company “ West Kazakhstan Marat Ospanov Medical University “(Aktobe, Republic of Kazakhstan) on a standard diet with free access to food and water. Experiments all manipulations were carried out in accordance with the European Convention for the Protection of Vertebrates Used for Experimental and Other Purposes (Strasbourg, 1986). The protocol of the experiment was developed with the participation and approval of the regional ethics commission of the university.

10 days after acclimatization, the rats were randomly divided into 5 groups. The first group – the control group, the second and third groups – were subjected to fractional gamma irradiation (0.6 Gr/day, dose rate 1 Gr/min; ⁶⁰CO). The total dose was 3 Gr. Animals of the fourth and fifth groups were exposed to combined radiation g (both groups II and III) and potassium dichromate (Cr⁺⁶).

Cr(VI) was administered intraperitoneal daily at a dose of 2.8 mg/kg of body weight (0.1^{LD50}) for 5 days. Rats of Groups 3 and 5 received Burdock root oil (PK-LK-5-N014181) at a dose of 2.5 ml/kg of body weight intragastrically through a probe for 14 days before g irradiation and combined exposure to the studied agents.

Whole-body gamma irradiation of rats was carried out fractionally (0.6 Gy/day⁵=3 Gy/min) for 5 days on the “Teragam” radiotherapy (Czech Republic, 2008). The distance from the source to the skin is 70 cm.

Dose of herbal medicine “Burdock root oil”, the method of application and duration of treatment are based on literature data^{36,37}. Euthanasia of animals in all groups was performed at the end of the experimental period by instant

decalitation under light ether anesthesia to avoid stress.

The blood was collected in test tubes and centrifuged at 2200g for 10 minutes. Collected serum samples were stored at -20⁰. from before analysis (if necessary at -80⁰C). The liver and kidneys were washed from the blood with a cold phosphate buffer solution (pH=7.4) and the samples were stored at - 80⁰ with the purpose of analysis. During the analysis, they were crushed, homogenized, and centrifuged. The obtained supernatants were used for biochemical analysis.

Biochemical analysis

Lipid peroxidation. Determination of diene conjugates (DC) was carried out by a generally accepted method⁵⁵ modified¹⁹ by the ultraviolet spectrum of the first oxidation products of polyunsaturated lipids with an absorption maximum at 233 nm; the molar extinction coefficient is $2.2 \times 10^5 \text{ l} \cdot \text{cm}^{-1}$. The content of DC was expressed in units of optical density (ODU/ml). The content of malonic dialdehyde (MDA) was determined using thiobarbituric acid (TBA) according to a modified method². The principle of the method: at high temperatures in an acidic medium, MDA reacts with 2-TBA to form a colored trimethine complex with an absorption maximum at 532 nm. The MDA level was expressed in imol/L.

Antioxidant blood defense system

The content of sulfhydryl (SH) groups in blood plasma was determined by the method¹⁷. The amount of thionitrophenyl anion formed in the sample is directly proportional to the amount of SH-groups that reacted with 5,5- dithiobis. After 40 minutes, the optical density of the sample was measured spectrophotometrically at 412 nm. The number of SH groups was expressed in imol/L. The serum glutathione (GSH) level was determined according to the method¹⁷ modified in²⁹.

Catalase activity (CAT) was measured by the method³⁰. The reaction was started by the addition of 2.0 ml of hydrogen peroxide to 10 il of the hemolysate and, after 10 minutes, was stopped by the addition of 1.0 ml of 4% ammonium molybdate. The absorbance of the sample was measured at 410 nm. The enzyme activity was expressed in units of activity per mg protein (U min/mg protein). One unit of catalase activity was defined as the activity to decompose 1 imol of hydrogen peroxide per minute (60s).

Superoxide dismutase (SOD) activity in erythrocytes was determined by the method⁴. As a unit of SOD activity, we took the amount of enzyme necessary to inhibit the decrease in nitroblue tetrazolium (NBT) by 50%, and the activity was expressed as U/mgPt.

The activity of glutathione peroxidase (GPx) was determined by the method³⁹ by the oxidation of NADPH•H₂ in the conjugated glutathione reductase reduction reaction on a spectrophotometer at 340 nm. Results are expressed as nmol oxidized NADPH min/mg protein or U min/mg protein. Protein content was determined by the method of Lowry *et al.*⁴⁰.

Statistical analysis

Statistical data processing was performed using the Statistic methods 10 software package from StatSoft, IncUSA. The null hypothesis that there are no differences between the observed distribution was tested using Shapiro's W-test, Wilkie. Differences between the samples were evaluated: in the case of a normal distribution of paired variables using the Student's t-test and in the case of a set of independent variables. Arithmetic mean values of quantitative indicators presented in the text as $M \pm \bar{\alpha}$ are calculated, where M is the average value and $\bar{\alpha}$ is the standard deviation. In all statistical analysis procedures, the significance level was assumed to be $p < 0.05$.

RESULTS AND DISCUSSIONS

The results presented in Table 1 showed that fractional (0.6 Gy day⁻¹ for 5 days) g-total body irradiation of rats (I group) resulted in a significant decrease in the content of sulfhydryl groups (SH) in plasma up to 287 nmol/l, the activity of glutathione peroxidase in erythrocytes to 12 Umin/mgPt on the background of a reliable increase in activity in red blood cells superoxide dismutase (SOD) and 3.6 U/mgPt, catalase (CAT) up to 87 Umin/mgPt and in the blood plasma of the biochemical marker MDA up to 2.52 nmol/ml, as well as DC up to 2.08 con. units, compared with the control data.

In the group of animals who fractional irradiation was administered herbal remedies "Burdock root oil" the amount of MDA and DC in the blood plasma is reduced to 1.61 nmol/l and 1.45 con. units, SOD activity, CAT in erythrocytes, respectively, to 2.33 U/mgPt, 61 Umin/mg Pt at

the background of the increase of the content of SH-groups in the plasma to 327 nmol/l compared with rats subjected to irradiation. This indicates an inhibition of LPO in the blood during the preventive administration of Burdock root oil.

With the combined effects of g radiation and K₂Cr₂O₇ is a sharp activation of POL processes: levels of MDA and DC in the plasma increased to 5.9 nmol/l and 5.2 con. units in the background of a significant reduction in plasma SH-groups of up to 190 nmol/l; in the red blood cells dramatically reduced the activity of COD to 2.20 U/mgPt, CAT to 45.5 Umin/mgPt and GPx up to 10.0 Umin/mgPt compared to the data of the control group and the second groups (g- irradiation). Thus, in terms of the combined effects of fractional g irradiation and Cr(VI) status of lipid peroxidation and antacid protection in the blood system is exacerbated by the largely - content of MDA and DC in the plasma increases, respectively, 2.34 and 2.5 times the background of falling of activity in erythrocyte enzymes SOD 39%, CAT 48%, GPX 33% and decrease in the concentration of SH-groups in plasma 34% in comparison with the figures of animals subjected to isolated fractional gamma irradiation.

Plication phytomedicine "Burdock root oil" inhibited free radical oxidation: the number of MDA and DC in the blood plasma decreased to 3.3 nmol/l and 2.6 con. units. decreases 1.79 times and 2 times increased the level of SH-groups in the plasma of the blood by 30%, increase the activity of antioxidant enzymes in red blood cells of SOD by 27.3% (to 2.8 U/mgPt), CAT 25.3% (up to 57 Umin/mgPt) and GPx by 33% (to 13.3 Umin/mgPt) are compared with those of rats subjected to the combined action of gamma irradiation and dichromate (IV group).

Table 2 shows the effective effect of Burdock root oil on the indicators of LPO and AOP in liver tissues in rats with isolated (g- irradiation) and combined exposure to gamma radiation and potassium dichromate. Fractional exposure g-irradiation resulted in a significant decrease in CAT activity and $\delta\delta\delta\delta\delta$ GSH levels by 22% and 37%, respectively, an increase in SOD activity by 2 times, and an increase in MDA levels by 20% compared to the control group. Prophylactic administration of the phyto-preparation for 14 days caused a significant decrease in SOD activity

in liver tissues SOD by 59%, and the amount of MDA by 15%, while increasing CAT activity by 14% and GSH concentration by 23% compared to the data II of group II (g- irradiation).

With the combined effects of fractional g-irradiation and K₂Cr₂O₇ in liver tissues, the number of MDA increased by 229% compared to the control and 2.74 compared with animals subjected to isolated action of g radiation on the background of a decrease in the activity of SOD, respectively, 37% and 69%, CAT – 51% and 37% and the level of GSH– 37.5% and 14.3%. Preventive administration of Burdock root oil (2 weeks) leads to a significant decrease in the amount

of MDA in liver tissues by 26% and an increase in SOD activity by 19%, CAT by 19.2% and the GSH level by 20% in comparison with the data of irradiated animals (IV-group IV). However, compared to the control group, the amount of MDA remains increased by 2.44 times, the activity of SOD, CAT and GSH level-reduced by 2.5%, 41.6% and 25%, respectively.

Data from Table 3 show that fractional gamma irradiation leads to a significant increase in MDA in the renal tissue by 66% and a significant decrease in SOD activity by 55%, CAT by 35% and GSH content by 25% compared to the control group. Preventive administration of “Burdock

Table 1. Effect of the herbal medicine “Burdock root oil”à on lipid peroxidation and antioxidant protectiony in rat blood

	Control	γ (IRR)	Phyto-drug (PhD)+γ	K ₂ Cr ₂ O ₇ +γ	PhD+K ₂ Cr ₂ O ₇ +γ
MDA	1.42±0.191	2.52±0.32 ^x	1.61±0.221 ^{x+}	5.9±0.75 ^{x₀}	3.3±0.365 ^{x₊₊}
DK	1.3±0.125	2.08±0.223 ^x	1.45±0.136 ^{x₋}	5.2±0.665 ^{x₀}	2.6±0.37 ^{x₊₊}
SH-group	372±47.43	287±40.939 ^x	327±42.123 ^{x+}	190±24.231 ^{x₀}	247±34.766 ^{x₊₊}
COD	2.7±0.408	3.6±0.662 ^x	2.33±0.338 ^{x+}	2.2±0.38 ^{x₀}	2.8±0.345 ^{0₊₊}
KAT	69±7.874	87±17.062 ^x	61±7.304 ^{x+}	45.5±5.679 ^{x₀}	57±9.44 ^{x₊₊}
GP _x	15±3.651	12.0±2.518	14.2±3.826	10.0±2.23 ^x	13.3±2.826 ^{x₊₊}

Note: x - p <0.05 in comparison with the data of the control group; 0 - p<0.05 - compared with the data of irradiated animals. Each value represents the mean ± standard deviation (M ± σ) of 10 animals.

Table 2. Protective effect of Burdock root oil on the level of lipid peroxidation product and antioxidant protection in liver tissues in rats under the action of gamma irradiation and potassium dichromate

	Control	γ (IRR)	Phyto-drug (PhD)+γ	K ₂ Cr ₂ O ₇ +γ	PhD+K ₂ Cr ₂ O ₇ +γ
MDA	258±47.352	310±38.047 ^x	265±33.192 ₊	850±136.105 ^{x₀}	630±107.314 ^{x₊₊}
COD	350±66.416	702±135.884 ^x	285±37.94 ^{x₊}	221±28.887 ^{x₀}	263±50.592 ^{x₊₊}
KAT	9.25±0.789	7.2±1.074 ^x	8.2±1.023 ^{x₊}	4.53±0.505 ^{x₀}	5.40±0.577 ^{x₊₊}
GSH	48±0.949	35±0.886 ^x	43±1.577 ^{x₊}	30±0.664 ^{x₀}	36±1.651 ^{x₊₊}

Note: the designation is the same as in Table 1

Table 3. Effect of “Burdock root oil” on the level of MDA, GSH, activity of antioxidant enzymes in the kidneys of rats exposed to gamma radiation and potassium dichromate

	Control	γ (IRR)	Phyto-drug (PhD)+γ	K ₂ Cr ₂ O ₇ +γ	PhD+K ₂ Cr ₂ O ₇ +γ
MDA	61±9.498	101±22.559 ^x	71±15.874 ₊	180±37.96 ^{x₀}	113±25.304 ^{x₊₊}
COD	250±66.409	113±28.39 ^x	205±57.03 ^{0₊}	80±18.94 ^{x₀}	150±41.204 ^{x₊₊}
KAT	9.6±0.657	6.2±0.945 ^x	8.70±0.66 ^{x₊}	4.30±0.37 ^{x₀}	6.2±0.634 ^{x₊₊}
GSH	30±3.797	22.5±4.109	33±3.475 ₊	15.0±1.908 ^{x₀}	23±2.84 ^{x₀₀}

Note: the designation is the same as in Table 1

root oil” causes a decrease in the level of MDA by 30% against the background of an increase in the activity of SOD by 81%, CAT by 40% and the concentration of GSH by 47% in the renal tissue of rats in comparison with the indicators of animals of the irradiated group (2nd).

Under conditions of combined action of fractional g radiation and $K_2Cr_2O_7$, the state of POL-AOS in the renal tissue is even more aggravated than under isolated fractional g radiation. Thus, in comparison with the data of irradiated animals, the amount of MDA increases by 1.78 times, the activity of SOD decreases by 29%, CAT-by 31%, and the level of GSH- by 33%. Two-week administration of “Burdock root oil” before combined exposure-g-irradiation and $K_2Cr_2O_7$ causes a significant decrease in the level of MDA by 33% and an increase in the activity of SOD, KAT and GSH content by 87.5%, 44%, and 53%, respectively, compared to group IV- (combined exposure). However, all the studied data significantly differ from the nesting rats of the control group: The amount of MDA was increased by 1.85 times, the activity of COD, CAT, and GSH levels were reduced by 40, 35, and 23%, respectively.

Protection of organs and systems of the body as a whole, against oxidative damage induced by ionizing effects and/or combined effects of g-irradiation and exogenous factors such as physical and chemical origin, in particular metals variable valence (Fe, Cr), the determination of the protective means (including radio protectors) for use with the purpose of prevention /correction (treatment) i.e. protection of workers (personnel) of the relevant industries, personnel, involved in radiation therapy, patients who undergo radiotherapy and biochemical population of the provinces the use of modernity and priorities not only clinical work is meant and but also in medicine.

In the present study, fractional g-irradiation, as well as combined exposure g-radiation and potassium dichromate (CrVI), led to a significant increase in MDA and DC in blood plasma, the amount of malondialdehyde in liver and kidney tissues – a marker of the intensity of lipid peroxidation, which determines the degree of oxidative stress in cells of organs and systems (blood). It should be noted that in terms of the combined effects of potassium dichromate and

fractional g-irradiation MDA level in plasma, the liver and kidney increased 4.15 times, 3.3 times and 2.95 times respectively in comparison with control and 2.34 times 2.74 times and 1.78 times (respectively) in comparison with the data of the isolated effects of radiation, i.e. under the influence of Cr(VI) increases oxidative damage. Under these conditions, a significant contribution to the implementation of oxidative stress mechanisms, and processes triggered by the action of supraphysiolytic Cr(VI) concentrations is likely. Once inside the cell, Cr(VI) is restored to Cr(III), which is accompanied by the generation of reactive oxygen species and induces damage to cellular structures-blood, liver, and kidney cells^{2,9,32}. Under the influence of radiation, free radical oxidation is also activated, the activity of rapidly renewing tissues – the hematopoietic system, the gastrointestinal tract-is disrupted, and the production of antioxidant factors by these organs is suppressed^{22,27,2-6}. The combination of mechanisms (factors) of combined effects determines the severity and degree of oxidative damage to organs and systems. These results are consistent with the results studied by a number of scientists^{61,43,33}. For preventive use “Burdock root oil” in these circumstances, the impact of physically and/or physico-chemical factors of environment’s level of marker decreased/or normalized, i.e. the introduction of herbal remedies prior to irradiation and also before the combined effects of gradiation and hexavalent chromium protected from animals induced oxidative stress, indicating its radical cleansing activity and/or the mechanism of destruction of the chains.

In the present study, in addition to the level of MDA (DC), the intensity of oxidative stress is characterized by a significant decrease in the activity of antioxidant enzymes (reducing the activity of SOD in the liver) and GSH in the liver and kidney tissues of irradiated rats, which corresponds to the previous results^{68,69}. We assume that the increase in MDA is moreover, low levels of antioxidants may be associated with radiolysis of water caused by ionizing radiation and generation of reactive metabolites, which ultimately causes oxidative damage to cells, there is an imbalance of prooxidants /antioxidants, causing dysfunction of several organs⁴⁵. Oxidative damage to cellular structures leads to changes in the permeability

of cells and tissues and subsequently leads to the release of intracellular antioxidants into the blood circulation (the activity of SOD and CAT enzymes increases compensatory, the activity of GPx in red blood cells does not change, and the activity of liver SOD increases almost 2 times and their use for compensation or neutralization, overproduction of free radicals caused by radiation. Under conditions of combined exposure g radiation and potassium dichromate, the increase in the level of MDA in tissues in the blood, liver and kidneys by 2.34 times, 2.74 and 1.78 times (respectively) in comparison with the indicators of animals exposed g radiation reflects peroxidation of the membranes of blood, liver and kidney cells. Consequently, purification from excessive ROMS production requires an increasing number of antioxidant molecules (GSH, SOD, CAT, GPx), and the present study showed a significant decrease in the activity of SOD and CAT enzymes in liver, kidney, and blood tissues (GPx) and the level of GSH in all the tissues studied. A number of authors⁴⁻⁹ explain the decrease in antioxidant enzymes as a consequence of the destruction of chemical bonds by irradiation energy. In addition, decreases in the activity of SOD, CAT, and GPx in blood, liver, and kidney cells may result from the release of SOD, CAT, and GPx after damage to cell membranes due to lipid peroxidation⁶⁻⁷, denaturation, or partial inactivation (of antioxidant enzymes) due to RHMS due to water radiolysis. Under conditions of combined action, although Cr(VI) and its compounds do not directly generate free radicals, however, when Cr(VI) is reduced to Cr(III), as well as by radicals such as superoxidation, peroxidenitrite, nitric oxide, and hydroxyl appear, which cause damage characteristic of oxidative stress⁶⁵, activate LPO, and lead to destabilization and disintegration of cell membranes^{75,34}. In our previous studies, we showed, that potassium dichromate enhances lipid peroxidation in tissues (increases the level of DC, hydroperoxidation, and MDA) and reduces the activity of antioxidant enzymes in red blood cells, reproductive organs, liver, kidney, and lung tissues, and the level of GSH in all the studied tissues developed^{25,29,28}, and the use of phyto oils, including, phyto-medicine "Burdock root oil" in terms of chromium-induced oxidative damage in kidney, lung and reproductive system showed a positive effect: inhibited lipid peroxidation

increased and antioxidant protection in armed force sex the examined tissues and organs^{35,38,31,32,33}. At the same time, it should be emphasized that 10 days after the change of phytopreparations (corrective mode of use), the indicator of balance of peroxidation homeostasis showed a predominance of antioxidants over prooxidants in kidney tissues in animals³⁹. When studying the effect of burdock root oil extract in experimental cytophosphate hepatitis, it was established that the phytopreparation has antioxidant properties: when administered prophylactically, it prevents disturbances in the processes of peroxidation and the antioxidant system of the animal body⁸⁵. In the present study, it was shown that the administration of the herbal preparation "Burdock root oil" to rats both under fractional g-irradiation and under combined exposure to radiation and potassium dichromate Cr(VI) protected liver, kidney, and blood tissues from oxidative damage. This was established due to the ability of Burdock root oil to significantly inhibit LPO (decrease in MDA) and increase the content of antioxidants (GSH, SOD, CAT, GPx) in all the studied tissues (liver, kidneys, and blood). An increase in the power of both the enzymatic and non-enzymatic links of the antioxidant system in the liver, kidney, and blood tissues may be a partial hepatoprotective and hemotropic (protecting the hematological parameters of the hematopoietic system as a whole) effect of the herbal "Burdock root oil". Our results show that burdock root oil extract reduces oxidative stress caused by fractional g-irradiation, as well as fractional g-irradiation and bichromate of potassium, i.e. it exhibits antioxidant activity, removing free radicals and restoring the imbalance of pro-oxidant / antioxidant homeostasis when used prophylactically. Probably, the antioxidant activity of the drug is associated with the content of the complex of biologically active substances, including inulin, carotenoids, protein, ascorbic acid, flavonoids and phenolic compounds, which possesses anti-inflammatory. Antimutagenic, antioxidant, anti-carcinogenic action^{58,50,44,24,1,19} and maybe photo-protectors the effect of phyto-preparation "Burdock root oil" can be explained by its activity, clean up free radicals (antioxidant effect), which eliminates the harmful effects g-radiation and combined effects g-radiation and Cr(VI) on all the studied tissues.

CONCLUSIONS

Our results show, that the phytopreparation “Burdock root oil” can weaken damage to the liver, kidney and blood cells, caused by fractional g-irradiation and/or a combination of the influence of the tails operating gamma radiation and $K_2Cr_2O_7$, through mechanisms check out about bar the AFC, removal of free radicals, thus modulating the oxidation of lipids and proteins, increasing the activity of antioxidant enzymes, whether content restored glutation of the endogenous antioxidant and thereby improve the (reducing or eliminating the imbalance) of the endogenous antioxidant status. The results of this study open up new prospects for the therapeutic use of phytopreparation “Burdock root oil” in softening and oxidative damage caused by g-radiation and / or combine exposure to g-radiation and chromium compounds (Cr(VI). Further studies in the human population support our observations of the antioxidant potential (cleaning/neutralization and disposal) from free radicals) phytopreparations “Burdock root oil”.

ACKNOWLEDGEMENT

I express my gratitude to the staff of the clinical laboratory and vivarium (Sahanova S.K.), the staff of the radiation therapy department (Baizakov B.T.), and the university administration (Musin N.M.).

Conflict of interest

No conflicts of interest.

Funding source

The funds were allocated by the university free of charge within the framework of a research grant. Grant number 02-04-2018.

REFERENCES

- Alhusaini A., Fadda L., Hasan I.H., Ali H.M., Orabi N.F., Badr A.M., Zakaria E., Alenazi A.M., Mahmoud A.M. Arctium lappa root extract prevents Lead – induced liver injury by attenuating oxidative stress and inflammation, and activating Akt/GSK - 3 β signaling. *Antioxidants (Basel)*. **8**: 582 (2019).
- Alipoor B., Norouzabad L.M., Abed R., Oskouei M.A.E., Sadat B.E., Jafarabadi M.A. Effect of Arctium lappa L. (burdock) root tea on clinical signs and symptoms in patients with knee osteoarthritis. *Curr. Topics Nutraceutical Res.* **12**(4): 149-154 (2014).
- Banu S.K. 2013. Heavy metals and ovary. In: Hoyer P.B. (Ed), *Ovarian Toxicology*, second ed. CRC Press/Taylor & Francis Group. Boca Raton. FL. 193-229 (2013).
- Beauchamp Ch. and Fridovich I. Superoxide dismutase: improved assays and an assay applicable to acrylamide gels. *Anal. Biochem.* **44**: 276-287 (1971).
- Cerveira J.F., Sanchez – Arago M., Urbano A.M., Cuezva J.M. Short-term exposure of nontumorigenic human bronchial epithelial cells to carcinogenic chromium (VI) compromises their respiratory capacity and alters their bioenergetic signature. *FEBS Open Bio.*; **4**:594-601 (2014).
- Chan Y.S., Cheng L.N., Wu J.H., Chan E., Kwan Y.W., Lee S.M.Y., Leung G.P.-H., Yu P.H.-F., Chan S.W. A review of the pharmacological effects of Arctium lappa (burdock). *Inflammopharmacology*; **19**(5): 245-254 (2011).
- Chiang L.C., Chiang W., Chang M.Y., Ng LT, Lin C.C. Antiviral activity of plantago major extracts and related compounds in vitro. *Antiviral Res.*; **55**(1): 53-62 (2002).
- Damodara Gowda K.M., Shetty J., Krichna A.P., Kumari S.N., Sanjeev G., Naveen P. Protective effect of Nardostachys Jatamansi root extract against radiation induced damage on liver and kidney functions in albino Wistar rats. *J.Pharma. Res.* **4**: 2462-2465 (2011).
- Draper H.H., Hadley M. Malondialdehyde determination as index of lipid peroxidation. *Methods in Enzymology*. **186**: 421-431 (1990).
- Ellman G.L., 1959. Tissue sulphhydryl groups. *Arch Biochem Biophys*. **82**(1): 70-77 (1959).
- Elshazly M.O., Ashraf M.M., Merhan E.A., Abdel-Mawla E., Abd El-Rahman S.S. The mitigative effect of Raphanus sativus oil on chromium – induced geno- and hepatotoxicity in male rats. *Journal of Advanced Research*. **7**(3): 413-421 (2016).
- Fang Z, Zhao M, Zhen H., Chen L., Shi P, Huang Z. Genotoxicity of tri – and hexavalent chromium compounds in vivo and their modes of action on DNA damage in vitro. *PLoS ONE*, **9**(8): e103194 (2014).
- Ferracane R., Graziani G., Gallo M., Fogliano V., Ritieni A. Metabolic profile of the bioactive compounds of burdock (Arctium lappa) seeds, roots and leaves. *J Pharm Biomed Anal.* **51**(2): 399-404 (2010).
- Fierascu R.C., Georgiev M.I., Fierascu I.,

- Ungureanu C., Avramescu S.M., Ortan A., Georgescu M.L., Sutan A.N., Zanfirescu A., Dinu-Pirvu C.E., Velescu B.S., Anuta V. Mitodepressive, antioxidant, antifungal and anti – inflammatory effects of wild – growing Romanian native *Arctium lappa* L. (Asteraceae) and *Veronica persica* Poiret (Plantaginaceae). *Food and Chemical Toxicology*, **111**: 44-52 (2018).
15. Gao Q., Yang M., Zuo Z. Overview of the anti-inflammatory effects, pharmacokinetic properties and clinical efficacies of arctigenin and arctiin from *Arctium lappa* L. *Acta Pharmacol Sin.* **39**(5): 787-801 (2018).
 16. Garcia-Nino W.R., Tapia E., Zazueta C., Zatarain-Barron Z.L., Hernandez-Pando R., Vega-Garcia C.C., Pedraza-Chaverri J. Curcumin pretreatment prevents potassium dichromate-induced hepatotoxicity, oxidative stress, decreased respiratory complex I activity, and membrane permeability transition pore opening. *Evid Based Complement Alternat Med.* 1-19 (2013). 2013: 424692
 17. Gavrilova V.V., Mishkorudnya M.I. Spectrophotometric determination of lipid hydroperoxides in blood plasma. *Laboratory work*, **3**: 33-36 (1983).
 18. Gentil M., Pereira J.V., Sousa Y.T., Pietro R., Neto M.D., Vansan L.P., França S.C. In vitro evaluation of the antibacterial activity of *Arctium lappa* as a phytotherapeutic agent used in intracanal dressings. *Phytotherapy research.* **20**(3): 184-186 (2006).
 19. Giorgio C.Di., Boyer L., Meo M.D., Laurant C., Elias R., Olliver E. In vitro and in VIVO antimutagenic effects of DIG, a herbal preparation of *Berbens Vulgaris*, *Taraxacum officinale* and *Arctium lappa*, against mytomycin C. *J Nat Med*; **69**(3): 267-77 (2015).
 20. Goulart M., Batoreu M.C., Rodrigues A.S., Laires A., Rueff J. Lipoperoxidation products and thiol antioxidants in chromium exposed workers. *Mutagenesis.* **20**(5): 311-315 (2005).
 21. Guan J., Stewart J., Ware J.H., Zhou Z., Donahue J.J., Kennedy A.R. Effects of dietary supplements on the space radiation-induced reduction in total antioxidant status in CBA mice. *Radiat Res.* **165**(4):373-378 (2006).
 22. Gulic Ye.S., Kostesha N. Ya., Barilo G. A. Influence of khitabis and its components on the structural and functional state of the small intestine and hematopoiesis in irradiated rats. Bulletin of Tomsk State University. *Biology.* **3**(19): 146-159 (2012).
 23. Guna G. Therapeutic value of *Arctium lappa* linn. – a review. *Asian J. Pharmaceutical Clin. Res.* **12**:539(2019).
 24. Gurunanselage Don R.A., Yap M.K., *Arctium Lappa* L. root extract induces cell death via mitochondrial – mediated caspase – dependent apoptosis in Jurkat human leukemic T cells. *Biomed Pharmacother.* **110**: 918-929 (2019).
 25. Iztleuov M., Arstan M., Galymzhan Y, Timur J, Yerbolat I, Almasbek Y. Impact of chromium and boron compounds on the reproductive function in rats. *Toxicology and Industrial Health.* **34**(6): 365-374 (2018).
 26. Iztleuov M., Iztleuov Y., Yelubayeva A. Aleuova Z., Turganbayeva Z., Madikhan Z., Sakypova D., Zhumasheva A., Iztleuova G. Effect of “Nettle Oil” on Oxidative Damage to the Heart and Lungs Induced by Radiation. **13**(3): 1495-1504 (2020).
 27. Iztleuov M., Teleuov M., Iztleuov Y., Saparbaev S., Yelubayeva A., Yemzharova G., Sambayeva S., Turganbayeva A., Umirzakova Z. Influence of the Herbal Preparation “Licorice Oil” on the State of Hematopoiesis in Rats Under Ionizing Irradiation *Biomedical & Pharmacology Journal.* **14**(2): 869–879 (2021).
 28. Iztleuov M., Umirzakova Z., Iztleuov E., Sambayeva S., Iztleuova G., Yesmukhanova D., Akhmetova A., Medeuova R., Kolishbaeva I. The Effect of Chromium and Boron on the Lipid Peroxidation and Antioxidant Status (In Experiment). *Journal of Environmental Management and Tourism.* **8**(3): 529-536 (2017).
 29. Iztleuov M.K. Homeostasis and chromium pathology. – Aktobe. 2003. p. 213
 30. Iztleuov M.K., Iztleuov Y.M. Ecology and health. *Medical Journal of Western Kazakhstan.* **2**(10): 8-16 (2006).
 31. Iztleuov M. K., Iztleuova G.M., Iztleuov Y.M. Effect of burdock root oil extract on the combination of the peroxide homeostasis system under the influence of lame compounds on health and disease. **5**: 143-146 (2008).
 32. Iztleuov M. K., Iztleuova G.M., Iztleuov Y.M., Irgalieva G. G. Effect of tri-hexavalent chromium on the state of lipid peroxidation and kidney function in rats in a full-scale experiment. *Medical Journal Astana.* **5**(57): 124 (2009).
 33. Iztleuov M. K., Kibatayev K. M., Abilov T. S., Iztleuov E. M., Madihan J. S. Genotoxicity and oxidative stress induced by combined exposure to hexavalent chromium and gamma radiation. *Medicine and Healthcare: proceedings of the IV International Scientific Conference. conf. (city of Kazan, May M42 2016) - Kazan: “Young Scientist”, 2016. From 27-29.*
 34. Iztleuov M. K., Abilov T.S., Iztleuov Y.M. Evaluation of induced mutagenesis under the

- influence of chromium, boron and its correction. *2*(16): 62-65 (2015)
35. Iztleuov M. K., Andldiarova N.T., Zinalieva.N., Iztleuov E. M. Violation of peroxide homeostasis of the lungs in chromium-induced intoxication and ways of their correction. *Pharmaceutical Bulletin. 7-8*: 33-34 (2008).
 36. Iztleuov Y.M. Gonadotropic activity of phytomasels under the influence of chromium compounds. *Pharmacy Kazakhstan. 6*: 31-33 (2007).
 37. Iztleuov Y.M., Iztleuov M. K. Corrective effect of phytopreparations and biothiol on the reproductive system combinations in chromium-induced microelementosis. Proceedings of the II International Conference of Young Scientists "Young Science: the Eurasian Aspect". Almaty., 73-76 (2007).
 38. Iztleuov Y.M., Iztleuov M. K., Kydyrbayeva E. A. Prenatal effects of potassium dichromate exposure and their correction in rat offspring. Medicine and Healthcare: materials IV International Scientific Conference (Moscow Kazan, May M422016) - Kazan: "Young Scientist"; p. 23-26 (2016).
 39. Iztleuova G.M. Pharmacological effect of burdock, nettle and lipoic acid oil extracts in toxic chromium kidney damage in the experiment. *Science and healthcare. 3*: 161-162 (2010).
 40. Jollow D.J., Mitchell J.R., Zampaglione N., Gillette. J.R. Bromobenzene – induced liver necrosis. Protective role of glutathione and evidence for 3,4 – bromobenzene oxide as the hepatotoxic metabolite. *Pharmacology: 4*(3): 151-169 (1974).
 41. Khan F.H., Ambreen K., Fatima G., Kumar S. Assessment of health risks with reference to oxidative stress and DNA damage in chromium exposed population. *Sci Total Environ. 430*: 68-74 (2012).
 42. Kibatayev K.M., Mutigulina G. A., ÄëààìB. K. Elaman, Mamayrbaev A. A., Madihan J. S., Mankuov V. G. External radiation doses of the population of Aktobe region from natural sources of ionizing radiation. *Medical Journal of Western Kazakhstan. 3*(47): 12-14 (2015).
 43. Kim H.G., Jany S.S., Lee J.S., Kim H.S., Son C.G. Panax ginseng Meyer prevents radiation – induced liver injury via modulation of oxidative stress and apoptosis. *J Ginseng Res. 41*: 159-168 (2017).
 44. Kim Y.K., Koppula S., Shim D.W., In E.J., Kwak S.B. Kim M.K., Yu S.H., Lee K.H., Kang T.B. Inhibitory effect and mechanism of *Arctium lappa* extract on NLRP3 inflammasome activation. *Evid Based Complement Alternat Med.* 2018: 6346734
 45. Kodama R., Kato M., Furuta S., Veno S., Zhang Y., Matsuno K., Yabe-Nishimura C., Tanaka E., Kamata. ROS generating oxidases Nox1 and Nox4 contribute to oncogenic Ras induced premature senescence. *Genes. Cells. 18*: 32-341 (2012).
 46. Kohen R, Nyska A. Oxidation of biological systems: oxidative stress phenomena, antioxidants, redox reactions, and methods for their quantification. *Toxicol. Pathol. 30*(6): 620-650 (2002).
 47. Koroluk M.A., Ivanova L.I., Maiorova I.G., Tokarev V.E., 1988. A Method of determining catalase activity. *Lab Delo. 1*: 16-19 (1988).
 48. Kortenkamp A., Casadevall M., Faux S.P., Jenner A., Shayer R.O., Woodbridge N., O'Brien P. A role for molecular oxygen in the formation of DNA damage during the reduction of the carcinogen chromium (VI) by glutathione. *Arch. Biochem. Biophys. 329*(2): 199-207(1996).
 49. Kregel K.C., Zhang H.J. An integrated view of oxidative stress in aging: basic mechanisms functional effects, and pathological considerations. *Am J Phys. Regul. Integr. Comp. Phys. 292*(1): R18-36 (2007).
 50. Kumar N., Pruthi V. Potential applications of ferulic acid from natural sources. *Biotechnol. Rep. 4*: 86-93 (2014).
 51. Kunti V.S., Stankovi M.B., Vuji Z.B., Brbori J.S., Uskokovi – Markovi S.M. Radioprotectors – the evergreen topic. *Chem. Biodivers. 10*: 1791-803 (2013).
 52. Lin S.C., Lin C.H., Lin C.C., Lin Y.C., Chen C.F., Chen I.C., Wang I.Y. Hepatoprotective effects of *Arctium lappa* Linne on liver injuries induced by chronic ethanol consumption and potentiated by carbon tetrachloride. *J.Biomed.Sci. 9*(5): 401-409 (2002).
 53. Little C., Olinescu R., Reid K.G., P.J. O'Brien, Properties and regulation of glutathione peroxidase. *J. Biol. Chem. 245*(14): 3632-3636 (1970).
 54. Liu J., Cai Y.Z. Wong R.N.S., Lee C.K.F., Tang S.C.W., Sze S.C.W., Tong Y., Zhang Y. Comparative analysis of caffeoylquinic acids and lignans in roots and seeds among various burdock (*Arctium lappa*) genotypes with high antioxidant activity. *J.Agric. Food Chem. 60*(16): 4067-4075 (2012).
 55. Lloyd D.R., Carmichael P.L., Phillips D.H. Comparison of the formation of 8-hydroxy-2'-deoxyguanosine and single- and double-strand breaks in DNA mediated by Fenton reactions. *Chem. Res. Toxicol. 11*(5): 420-427 (1998).
 56. Lou Z., Li C., Kou X., Yu F., Wang H., Smith

- G.M., Zhu S. Antibacterial antibiofilm effect of burdock (*Arctium lappa* L.) leaf fraction and its efficiency in meat preservation. *J Food Prot.* **79**(8): 1404-1409 (2016).
57. Lowry O.H., Rosebrough N.J., Farr A.L., Randal R.J. Protein measurement with the Folin phenol reagent. *J. Biol. Chem.* **193**(1): 265-275 (1951).
58. Maghsoumi – Norouzabad L., Alipoor B., Abed R., Sadat B.E., Mesgari – Abbasi M., Jafarabadi M.A. Effects of *Arctium lappa* L. (Burdock) root tea on inflammatory status and oxidative stress in patients with knee osteoarthritis. *Int J Rheum Dis.* **19**(3): 255-261 (2016).
59. Mahvi A.H. Application of agricultural fibers in pollution removal from aqueous solution. *International Journal of Environmental Science & Technology.* **5**(2): 275-285 (2018).
60. Manning F.C., Blankenship L.J., Wise J.R., Xu J., Bridgewater L.C., Patierno S.R. Induction of internucleosomal DNA fragmentation by carcinogenic chromium: relationship to DNA damage, genotoxicity, and inhibition of macromolecular synthesis. *Environ Health Perspect.* **102** (Suppl 3): 159-167 (1994).
61. Marie M.S., Sayed A.A., Abbas O.A., Saad M. Modulatory effect of *Cicerarctium* Extract against α -irradiation – induced some Biochemical Disorders in Rats. *Research Journal of Pharmaceutical, Biological and Chemical Sciences* **8**(3): 599-606 (2017).
62. O'Brien T.J., Ceryak S., Patierno S.R. Complexities of chromium carcinogenesis: role of cellular response, repair and recovery mechanisms. *Mutat. Res.* **533**(1-2): 3-36 (2003).
63. Placer Z. Lipoperoxidationssysteme im biologischen Material 2. Mitt. Bestimmung der Lipoperoxidation im Säugetierorganismus† *Nahrung*, **12**(6): 679-684 (1968).
64. Pomari E., Stefanon B., Colitti M. Effect of plant extracts on H₂O₂ – induced inflammatory gene expression in macrophages. *J. Inflamm. Res.* **7**: 103-112 (2014).
65. Pritchard K.A., Ackerman A. and B.Kalyanaraman, Chromium VI increases endothelial cell expression of ICAM-1 and decreases nitric oxide activity. *J. Environ. Pathol. Toxicol. Oncol.*, **19**: 251-260 (2000).
66. Rajasekharan S.K., Ramesh S., Satish A.S., Lee J. Antibiofilm and anti – α – lactamase activities of burdock root extract and chlorogenic acid against *klebsiellapneumoniae*. *J. Microbiol. Biotechnol.*; **27**: 542-51 (2017).
67. Saada H.N., Said U.Z., Mahdy A.M. Effectiveness of Aloe vera on the antioxidant status of different tissues in irradiated rats. *Pharmazie.*; **58**: 929-931 (2003).
68. Sayed A.A., Abbas O.A., Saad M.A., Marie M-A.S. *Cicer arietinum* extract ameliorate α -irradiation disorders via modulation of oxidative/ antioxidative pathway. *J Photoch Photobiol B.* **183**: 46-56 (2018).
69. Sayed D.F., Nada A.S., M. Mohamed A.H., Ibrahim M.T. Modulatory effects of *chrysophyllum cainito* L. extract on gamma radiation induced oxidative stress in rats. *Biomedicine & Pharmacotherapy.* **111**: 613-623 (2019).
70. Smoliagin A.I., Mikhailova I. V., Ermolina E. V., Krasikov S. I., Boev V. M. Experimental study of the effect of benzene and chromium on the immune system of the body. *Environmental immunology.* N1: 57-60 (2013).
71. Sohn E.H., Jang S.A., Joo H., Park S., Kang S.E., Lee C.H., Kim S.Y. Anti-allergic and anti-inflammatory effects of butanol extract from *Arctium lappa* L. *Clinical and Molecular Allergy.* **9**: 1-11 (2011).
72. Soudani N., Troudi A., Bouaziz H., Amara I.B., Boudawara T., Zeghal N. Cardioprotective effects of selenium on chromium (VI) – induced toxicity in female rats. *Ecotoxicol Environ Saf.* **74**(3): 513-20 (2011).
73. Spitz D.R., Azzam E.I., Li J.J., Gius D. Metabolic oxidation/reduction reactions and cellular responses to ionizing radiation: a unifying concept in stress response biology. *Cancer Metastasis Rev.* **23**(3-4): 311-322 (2004).
74. Stohs S.J., Bagchi D., Hassoun E., Bagchi M. Oxidative mechanisms in the toxicity of chromium and cadmium ions. *J. Environ. Pathol. Toxicol. Oncol.* **20**(2): 77-88 (2001).
75. Susa N., Veno S., Furukawa Y. and M. Sugiyama, 1996. Protective effect of vitamin E on chromium (VI)-induced cytotoxicity and lipid peroxidation in primary cultures of rat hepatocytes. *Arch. Toxicol.*, **71**: 20-24.
76. Tamayo C., Richardson M.A., Diamond S., Skoda I. The chemistry and biological activity of herbs used in flor-essence herbal tonic and essiac. *Phytother. Res.* **14**(1): 1-14 (2000).
77. Wise S.S., Holmes A.L., Wise Sr J.P. Hexavalent chromium – induced DNA damage and repair mechanisms. *Rev. Environ. Health.* **23**(1): 39-57 (2008).
78. Wu F., Sun H., Kluz T., Clancy H.A., Kiok K., Costa M. Epigallocatechin – 3 – gallate (EGCG) protects against chromate – induced toxicity in vitro. *Toxicol. Appl. Pharmacol.* **258**(2): 166-175 (2012).
79. Xin Wang, Young-OK Son, Qingshan Chang, Lijuan Sun, J. Andrew Hitron, Amit Budhraja, Zhuo Zhang, Zunji KE, Fei Chen, Jia Luo,

- Xianglin Shi. NADPH Oxidase Activation is Required in Reactive Oxygen Species Generation and Cell Transformation Induced by Hexavalent Chromium. *Toxicol.Sci.*, **123**(2): 399-410 (2011).
80. Yang C.S., Landau J.M., Huang M.T., Newmark H.L. Inhibition of carcinogenesis by dietary polyphenolic compounds. *Annu. Rev. Nutr.* **21**: 381-406 (2001).
81. Yen C.H., Chiu H.F., Huang S.Y., Lu Y.Y., Han Y.C., Shen Y.C., Venkatakrishnan, Wang C.K. Beneficial effect of burdock complex on asymptomatic helicobacter pylori – infected subjects: a randomized, double-blind placebo – controlled clinical trial. *Helicobacter*. **23**(3): e12469 (2018).
82. Yi D., Kamei C.L.A., Cools T., Vanderauwera S., Takahashi N., Okushima Y., Eekhout T., Yoshiyama K.O., Larkin J., Daele H.V., Conklin P., Britt A., Umeda M., Veylder L. The Arabidopsis Siamese – Related Cyclin – Dependent Kinase Inhibitors SMR5 and SMR7 Regulate the DNA Damage Checkpoint in Response to Reactive Oxygen Species. *The Plant Cell Online*. **26**(1) 296-309 (2014).
83. Zhang X.H., Znan X., Wang X.C., Jin L.F., Yang Z.P., Jiang C.X., Chen Q., Ren X.B., Cao J.Z., Wang Q., Zhu Y.M. Chronic occupational exposure to hexavalent chromium causes DNA damage in electroplating workers. *BMC. Public. Health*. **11**: art. No 224 (2011).
84. Zhao F., Wang L., Liu K. In vitro anti-inflammatory effects of arctigenin, a lignan from *Arctium lappa* L., through inhibition on iNOS pathway. *Journal of Ethnopharmacology*, **122**(3): 457-462 (2009).
85. Zholmyrzayeva A.S. Hepatotropic activity of burdock root oil extract in experimental cyclophosphamide hepatitis. 14.0025. - pharmacology, clinical pharmacology. Abstract for Candidate of Medical Sciences Republic of Kazakhstan. Aktobe, 2009. 28s.