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The influence of 1.4-naphtoquinone derivative and of vitamin E on nitroso-oxidative processes in digestive organ mucous membranes under the conditions of cyclooxygenase blockage, and against the background of low intensity X-ray irradiation

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ABSTRACT

In recent years, the influence of chronic low intensity irradiation on the human body has increased. This is mediated not only by the consequences of technogenic catastrophies, but also due to application of radiation therapy of of radiation usage in industry. Hence, we investigated the influence of 1.4-naphtoquinone and vitamin E on the nitroso-oxidative processes in the digestive organ mucous membranes, while affected by low intensity X-ray irradiation alone and in combination with the experimental blockage of COX, in rats. Our results show that X-ray irradiation of a total dose of 20 sGy during twenty days, induced an increase of the oxidative processes, as well as an increase in the activity of iNOS and myeloperoxidase in the mucous membranes of the stomach, small and large intestine. Both the effect of vitamin E and a 1.4-naphtoquinone derivative on the background of low intensity X-ray irradiation, and under the simultaneous effect of X-ray irradiation and COX blockage, brought about a decrease of the level of oxidative processes and of iNOS activity, whereas MPO activity increased. We also noted that the effect of vitamin E on the background of X-ray irradiation more significantly increased both the activity of SOD and catalase, when compared to the induced effect of the 1.4-naphtoquinone derivative. Under the conditions of COX-1/COX-2 blockage (as induced by way of indomethacin administration), against the background of X-ray irradiation, the content of TBA-active products (in the stomach and small intestine mucous membranes), the level of iNOS activity and the sum of nitrites and nitrates, were lower than that of independent effect. Taking into account the prominent antioxidant and anti-inflammatory attributes of 1.4-naphtoquinone-3-[3-(3.5-di-*tret*-butyl-4-hydroxy-phenyl)-1.4-dihydronaphtalene-2-aminoil] butyrate, when compared to the effect of sole administration of vitamin E, both under the conditions of X-ray irradiation alone, and the simultaneous effect of X-ray irradiation and COX blockage, this derivative may be considered suitable as a perspective radiprotectant.

INTRODUCTION

The effect of chronic radiation on the human body has been associated not only with the consequences of the Chernobyl catastrophe and that of technological emergencies at other atomic electrical stations (Fukusima, Japan), but also with the use of radiation in cancer therapy and in industrial practices. It is thus a common risk factor for the development of pathological processes, including cancer [11]. Numerous negative side effects with regard to the digestive organs were noted in radiation therapy. Indeed, irradiation

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is known to induce peptic ulcer disease, bleeding in the small intestine, development of fistulas, and obstructive changes [10,19], and radiation therapy is recognized as causing a variety of negative side actions, among these, radiation enteritis or colitis, in 50-70% of all patients [14,17].

The effect of radiation on the epitheliocytes of the digestive organ mucous membranes, which are extremely sensitive to irradiation, is that of direct cytotoxic effect and of the alteration of the mucous barrier, as well as of the inhibition of the processes of growth and differentiation. These effects are associated with the increase of the level of free radical reactions in the cell, and with the development of nitroso-oxidative stress [2,15,18].

The use of nonsteroidal anti-inflammatory drugs brings about side effects, such as development of the erosive-ulcerative injuries in stomach and small intestine. This is mediated by the blockage of the both forms of cyclooxygenases (COX). Prostaglandins, synthesized through COX-1, play a cytoprotective effect in the mucous membranes by way of regulating blood flow, motility, the secretion of mucous and bicarbonates and their involvement in intercellular integration. Of note: the expression of COX-2 and particular prostaglandins of the E2 group acutely increases under the conditions of stress, inflammation and development of erosive-ulcerative injuries [20].

The search for new compounds which may have cyto- and radioprotective effect on the mucous membrane of the digestive organs, and, in this way, prevent or enhance the healing of the damage or increased cell proliferation, is a priority direction in gastroenterology [1]. Vitamin E is a prominent antioxidant, the role of which is associated with the bounding of lipid radicals and active forms of nitrite-anions [21]. Other compounds that are being treated as potential antioxidants include derivatives of 1.4-naphtoquinone, which may block both COX-2 and 5-LOX, inhibit growth of cancer cells [6,8].

The aim of the study was to evaluate the effect of a derivative of 1.4-naphtoquinone and of vitamin E on nitroso-oxidative processes in the mucous membranes of the digestive organs under the conditions of low intensity X-ray irradiation and of blockage of COX.

MATERIALS AND METHODS

Animals. The structure of this study and the experimental procedures performed on the animals were approved by the Ethical Committee of Lviv National Medical University. Moreover, the experimental procedures were carried out in accordance with international guidelines for the use and care of laboratory animals. Male, white rats weighing 200-220 g were used (n=32). They were housed under conditions of controlled temperature (21-22°C) and light cycle (lights on at 08:00 and off at 20:00) and were fed standard rat chow and water *ad libitum*. The rats fasted for 24 hours prior to the experimental procedures.

Low intensity X-ray radiation. The animals met with irradiation for 20 days at a daily dose of 1 sGy, by way of the use of a RUM-17 apparatus (total dose made 20 sGy), using Cu (0.5 mm) and Al (1.0 mm) filters; dose power 0.042 mGy/s; electric potential 110 kV, current intensity 4 mA, skin-focus distance 178 cm [7].

Test drugs. Vitamin E ("Sigma") and derivative of 1.4-naphtoquinone (3-[3-(3.5-di-*tret*-butyl-4-hydroxyphenyl)-1.4-dihydronaphtalene-2-aminoil]butyrate acid, synthesized in the laboratory of the Department of the Technology of Biologically Active Compounds, Pharmacy and Biotechnology of the National University "Lviv Polytechnic"), were introduced per os twice per week in a dose of 30 mg/kg, against the irradiation background. Indomethacin (Sopharma, Bulgaria) was administered once in a dose of 10 mg/kg and also in this dose on the 20th day of irradiation and consecutive introduction of 1.4-naphtoquinone and vitamin E.

Study protocol. The rats were randomly placed within 7 groups (n=8 in each group). Group 1 consisted of rats treated only with a vehicle; the second group included animals which, during 20 days, were solely irradiated at a daily dose of 1 sGy (for a total dose of 20 sGy); the third consisted of animals to which, twice per week per os, the 1.4-naphtoquinone derivative-3-[3-(3.5-di-*tret*-butyl-4-hydroxyphenyl)-1.4-dihydronaphtalenyl] was introduced at a dose of 30 mg/kg, against the irradiation background; the fourth group was of animals, which, twice per week per os, were administered vitamin E (30 mg/kg); the fifth group included animals which on the 20th day, against an X-ray irradiation background, indomethacin (10 mg/kg) was administered; the sixth group was of animals, which on the 20th day, against an X-ray irradiation background, and exposure to the 1.4-naphtoquinone derivative treatment, indomethacin was administered; the seventh group included animals, which on the 20th day, against an X-ray irradiation background and vitamin E introduction, were administered indomethacin.

The rats were anaesthetized with 1 ml of urethane at a dose of 1.1 mg/kg injected intraperitoneally and killed by cervical dislocation. The stomach, small and large intestines were then harvested, opened and washed in isotonic sodium chloride solution. Samples of mucosal membranes of the stomach, small and large intestines were collected and homogenized in saline (1:4), centrifuged at 2,000 *g* and the supernatant was used for measurement of various biochemical parameters (see below).

Biochemical assessment. Lipid peroxidation levels were determined as malonic dialdehyde (MDA) and nitrite-anion concentration, while the activity of superoxide dismutase and catalase in homogenates of mucosal and muscle membranes were measured by the method described in detail previously [15]. NOS activity (iNOS and cNOS) [3] was expressed in nmol NADPH/min·g of protein. Arginase activity was determined by way of method [9] and was expressed in μmol/min·mg of protein, while the activity of myeloperoxidase (MPO) was measured by [4]. Finally, the content of nitrite anion and the amount of nitrates and nitrites was ascertained by way of method [13].

Statistical analyses. The data are expressed as mean ± SEM. Statistical comparisons were performed utilizing Student's *t* test. Comparisons involving more than two groups were performed by a one-way analysis of variance

(ANOVA). Differences with p-value < 0.05 were considered as significant.

RESULTS AND DISCUSSION

The total X-ray irradiation in the dose of 20 sGy for 20 days, brought about an increase of the lipid peroxidation processes. Herein, TBA-active products content in the stomach mucous membrane (MMS) was enhanced to a degree of 41% ($p < 0.05$), in the mucous membrane of the small intestine (MMSI) – to 16% ($p < 0.05$), in the large intestine mucous membrane (MMLI) – to 20% ($p < 0.05$); simultaneously, in the investigated organs, the increased activity of myeloperoxidase (MPO) was evidenced (to 46%, 42% and 3-fold, relevantly), while the activity of inducible NO-synthase (iNOS) increased (to 101%, 3.6-fold and 94%, relevantly), as did nitrite-anion content (to 41%, 13% and 14%, respectively) when compared to the control animals. However, the activity of cNOS and arginase did not change significantly, while that of catalase activity increased in all organs, and SOD activity significantly increased only in the MMS (table 1 and 2). It should be underlined that the effect of X-ray irradiation is known to induce an increased NO-synthase activity due to the increase of iNOS activity [12].

The blockage of the activity of COX-1/COX-2 with indomethacin against the irradiation background, when compared to indices obtained under the conditions of the independent effect of irradiation, showed an increase of the content of TBA-active products in MMS to a degree of 11% ($p < 0.05$), and in MMLI – to 13% ($p < 0.05$). Herein, the activity of MPO also had a tendency to induce in MMS and MMLI an increase (to 32% and 46%, relevantly), while in MMSI, it increased to a degree of 67% ($p < 0.05$). Moreover, SOD activity decreased in MMS (to 14%, $p < 0.05$),

Table 1. The effect of 1.4-naphtoquinone and vitamin E administration in situations of X-ray irradiation and COX blockage, on the content of TBA-active products and on the activity of SOD, catalase and myeloperoxidase, in the stomach mucous membrane (MMS), the small intestine mucous membrane (MMSI) and the large intestine mucous membrane (MMLI).

Group of animals	Organs of gastrointestinal tract	Malonic dialdehyde μmol/g	Superoxide dismutase μmol NST/min · mg protein	Catalase H_2O_2/min · mg/ protein	MPO U
Vehicle	MMS	209.9±6.36	21.6±2.1	12±2.6	1.36±0.67
	MMSI	212.7±16.8	20.3±4.1	19.05±1.63	1.68±0.62
	MMLI	219.1±19.02	18.6±1.5	19.7±2.0	0.96±0.29
X-ray radiation + vehicle	MMS	256.9±14.9*	34.7±1.83*	17.1±4.17	3.18±0.96*
	MMSI	246.8±10.6*	22.4±1.88	26.4±4.6*	3.87±0.99*
	MMLI	264±12.1*	20.8±1.6	24.6±3.33*	2.6±0.78*
X-ray radiation + indomethacin	MMS	284.2±13.7#	29.7±1.4	24.6±1.35#	4.2±0.22
	MMSI	257.8±6.2	29.2±0.49#	27±4.1	6.47±0.48#
	MMLI	298.6±10.8#	25.7±1.31	29.7±0.72	3.8±0.29
Indomethacin + vehicle	MMS	321.2±13.9#^	30.0±3.6#	17.4±2.57^	3.8±0.8*
	MMSI	301.8±19.3#^	30.2±2.4#	22.8±2.99	2.86±0.36^
	MMLI	306.8 ±12.7#	29.6±1.31#	21.6±3.7^	2.8±0.38*^
X-ray radiation + derivative of 1.4-naphtoquinones	MMS	247.8±27.5	28.6±1.84#	25.4±1.38#	4.83±1.43#
	MMSI	234.8±13.0	30.9±1.77#	24.4±4.66	7.32±0.81#
	MMLI	252.8±12.6	18.1±1.22#	32.6±2.63#	3.28±0.68
X-ray radiation + vitamin E	MMS	231.6±19.7	27.6±2.8#	26.05±1.02#	5.03±1.28#
	MMSI	224.8±9.4#	29.2±2.86#	32.9±3.43#	6.75±1.42#
	MMLI	256.7±12.3	17.3±1.92#	33±2.65#	4.08±0.32
X-ray radiation + derivative 1.4-naphtoquinones + indomethacin	MMS	243±11.6^	27.3±2.94	25.1±1.88	4.5±1.2
	MMSI	228.1±12.9^	27.2±3.15	32.7±4.2	5.9±1.0
	MMLI	269.3±7.3^	20.3±2.12	28.9±3.1	3.19±0.19
X-ray radiation + vitamin E + indomethacin	MMS	243.9±16.9^	28±2.53	27.1±1.11	5.05±0.36
	MMSI	228.9±16.8^	26.1±1.38	33.4±2.0	6.36±0.45
	MMLI	266.8±12.1^	18.7±1.7^	28.6±2.82	3.7±0.78

Results are expressed as the mean±SEM for 8 rats per each group; * p - < 0,05 versus the indices in control animals; # p - < 0,05 versus the indices in X-ray radiation + Vehicle; ^ - p - < 0,05 versus the indices in X-ray radiation + indomethacin

Table 2. The effect of 1.4-naphtoquinone and vitamin E administration, in situations of X-ray irradiation and COX blockage, on the activity of isoforms of NO-synthase and arginase, as well as the nitrite-anion content and sum of nitrates and nitrites, in the stomach mucous membrane (MMS), small intestine mucous membrane (MMSI) and the large intestine mucous membrane (MMLI).

Group of animals	Parts of digestive system	iNOS nmol NADPH/ min·g/ protein	cNOS nmol NADPH/ min·g/protein	Arginase μmol/min · mg/ protein	Nitrite anion μmol/l	Sum of nitrites and nitrates μmol/l
Vehicle	MMS	124.7±27.1	536±62.5	0.24±0.02	0,53±0.05	3.27±0.39
	MMSI	55.4±15.7	661.4±29.7	0.27±0.02	0.63±0.04	2.89±0.28
	MMLI	63.1±26.7	602±102.1	0.24±0.02	0,62±0.04	2.92±0.18
X-ray radiation	MMS	251.1±28.7*	624.5±48.1	0.19±0.01	0.75±0.03*	2.95±0.37
	MMSI	200.3±39.9*	610.2±57.5	0.22±0.02	0.72±0.05*	2.89±0.34
	MMLI	119.2±13.1	649.9±47.5	0.26±0.03	0.71±0.05*	3.24±0.47
X-ray radiation + indomethacin	MMS	178.4±13.1	379.7±35.9#	0.18±0.02	0,67±0.01	2.64±0.32
	MMSI	145.1±8.9	367.9±12.0#	0.25±0.04	0,78±0.04	1.56±0.2
	MMLI	105.1±9.5#	426.7±44.7#	0.26±0.02	0,74±0.02	3.11±0.4
Indomethacin	MMS	517.1±29.8+	366.1±32.4*	0.18±0.01	0,84±0.04*	4.42±0.45*
	MMSI	235.4±32.3+	404.5±36.6*	0.19±0.02	0,89±0.05*	5.38±0.38*
	MMLI	265.2±35.0*	352.2±42.1*	0.19±0.03	0,83±0.06*	5.21±0.28*
X-ray radiation + derivative of 1.4 -naphtoquinones	MMS	129.7±11.7#	553.9±47.2	0.21±0.02	0.67±0.03	2.33±0.31
	MMSI	45.2±21.4#	555.4±53.1	0.28±0.04	0.68±0.04	1.45±0.42
	MMLI	87±15.7#	693.2±37.7	0.28±0.03	0.7±0.04	3.12±0.29
X-ray radiation + vitamin E	MMS	152.7±53.1#	453.6±58.6	0.23±0.02	0.63±0.03#	2.26±0.28
	MMSI	65.2±18.8#	456.4±42.3	0.25±0.03	0.6±0.03#	1.79±0.18
	MMLI	72.5±14.1#	616.5±134.1	0.26±0.02	0.65±0.04	3.41±0.18
X-ray radiation + derivative of 1.4- naphtoquinones + indomethacin	MMS	144.8±7.38^	464.4±21	0.21±0.02	0.64±0.03	2.56±0.31
	MMSI	97.1±13.8^	619.3±21.5^	0.29±0.03	0.61±0.04^	1.45±0.42
	MMLI	93.3±11.5	590.0±45.5^	0.27±0.02	0.66±0.04	2.23±0.39
X-ray radiation + vitamin E + indomethacin	MMS	131.5±12.0^	490.5±24^	0.23±0.03	0.63±0.03	2.45±0.19
	MMSI	79.1±14.1^	615.9±49.5^	0.22±0.04	0.65±0.07	3.19±0.29
	MMLI	91.9±7.1	596.1±26.5^	0.28±0.03	0.69±0.07	2.13±0.19

Results are expressed as the mean±SEM for 8 rats per each group; * p - < 0,05 versus the indices in control animals; # p - < 0,05 versus the indices in X-ray radiation + vehicle; ^ - p - < 0,05 versus the indices in X-ray radiation + indomethacin

and increased in MMSI (to 30%, $p < 0.05$), whereas catalase activity changed significantly only in MMS (to 44%, $p < 0.05$), when compared to indices generated under the conditions of independent effect of irradiation. Thus, the data obtained by way of blockage of COX against a background of low intensity irradiation is indicative of the intensification of the lipid peroxidation processes. This notion is concluded by way of seeing the increased TBA-active products content and the activity of MPO. It should be noted that the activity of antioxidant enzymes under conditions of COX blockage against a low intensity X-ray irradiation background had organospecific change characteristics.

The blockage of COX against the background of low intensity X-ray irradiation induced a decrease of iNOS activity and a decrease of cNOS activity in the investigated organs. However, nitrite-anion content and arginase activity did not change significantly, when compared to the independent effect of irradiation.

The isolated effect of the COX-1/COX-2 inhibitor, indomethacin, brought about macroscopic destructive changes in MMS, whereas visible changes in MMSI and MMLI were not noted. In contrast to the effect of indomethacin against the irradiation background, its independent effect resulted in an increase of TBA-active products, of iNOS activity and in the sum of nitrates and nitrites, whereas the activity of catalase and MPO were seen to have been lowered in the digestive organ mucous membranes. Thus, blockage of COX-1/COX-2 against the background of low intensity X-ray irradiation engendered functioning changes in the NO-synthase system, and affected the activity of MPO and catalase, when compared to the effect of indomethacin without irradiation.

The mechanism of indomethacin induced destructive lesions in the mucous membrane of digestive organs is well known. It is associated with the simultaneous blockage of COX-1 and COX-2 and a decreased production of cytoprotective prostaglandins [5]. In our work, the introduction of indomethacin against the background of X-ray irradiation, on the 20th day, resulted in changes in the nitroso-oxidative processes. These we found to be associated with the decrease of TBA-active products (in MMS and MMSI), with the decrease of iNOS activity, and with the decrease in the the sum of nitrites and nitrates, when compared to its independent effect. These brought about effects may be associated with the decreased activity of the enzymes participating in the production of radicals and NOS due to the decrease of their expression or through post-translational changes.

The 1.4-naphtoquinone derivative, when within the background of irradiation, generated a decrease in the activity of iNOS to a level of 48% ($p < 0.05$) in MMS, 77 % ($p < 0.05$) in MMSI and 25 % ($p < 0.05$) in MMLI. Furthermore, it induced a decrease of TBA-active products, and an increase of MPO activity in the investigated organs. Of note, in such a situation, catalase activity in MMS increased to a level of 49%, while in MMSI, it did not change significantly, and in MMLI, it increased to 33%. SOD activity in MMS and MMLI also decreased, whereas in MMSI, it increased to a level of 38%. Our data indicate that the derivative of 1.4-naphtoquinone has an antioxidant effect. At that, it should be noted that this compound exerted a more prominent effect towards the inhibition of iNOS activity, and, upon its administration, that MPO increased in MMS and MMSI. Furthermore, the antioxidant effect of the derivative of 1.4-naphtoquinone is also associated with increased catalase activity.

In evaluating the effect of vitamin E administration against a background of X-ray irradiation, on the digestive organ mucous membranes, we noted peculiarities of its action towards the nitroso-oxidative processes. In addition, we saw a decrease of TBA-active products. Herein, the level of iNOS activity in MMS decreased to a level of 27% ($p < 0.05$), in MMSI, to 32% ($p < 0.05$), in MMLI, to 39% ($p < 0.05$). Simultaneously, the nitrite-anion content decreased, when compared to indices generated under the conditions of X-ray irradiation alone. It must also be underlined that we saw a multidirectionality of change in the SOD and catalase activity. Herein, SOD activity decreased to 20% in MMS, and to 17% in MMLI, whereas catalase activity increased in all the investigated organs: in MMS, to a level of 52% ($p < 0.05$), in MMSI, to 25% ($p < 0.05$), in MMLI, to 34% ($p < 0.05$). What is more, vitamin E administration induced an increase of the activity of MPO: in MMS, to a level of 58% ($p < 0.05$), in MMSI, to 74% ($p < 0.05$), in MMLI, to 57% ($p < 0.05$). Thus, vitamin E administered against a background of X-ray irradiation decreased the level of nitroso-oxidative activity, although MPO activity increased.

For the deeper analysis of the character of effect of the 1.4-naphtoquinone derivative and of vitamin E administration, we also conducted our experiments under the conditions of simultaneous X-ray irradiation and COX blockage. Herein, the introduction of the derivative of 1.4-naphtoquinone against a background of X-ray irradiation and of COX blockage, resulted in the decrease of TBA-active products: in MMS, to a level of 14% ($p < 0.05$), in MMSI, to 12% ($p < 0.05$), in MMLI, to 10% ($p < 0.05$). It also resulted in changes in iNOS activity: in MMS, to a level of 19% ($p < 0.05$), in MMSI, to 33% ($p < 0.05$), in MMLI, to 11% ($p > 0.05$). In addition, it brought about an increase of cNOS activity, as well as of catalase and MPO activity. Thus, the antioxidant and anti-inflammatory effect of the derivative of 1.4-naphtoquinone, when administered against a background of simultaneous X-ray irradiation and COX blockage, results in the decrease of TBA-active products, a loss of iNOS activity, and an increase of cNOS activity.

In our work, the administration of vitamin E, under the conditions of simultaneous X-ray irradiation and COX blockage resulted in the decrease of TBA-active products: in MMS, to a level of 14% ($p < 0.05$), in MMSI, to 11% ($p < 0.05$), in MMLI, to 11% ($p < 0.05$). Plus, iNOS activity was modified: in MMS, to a level of 26% ($p < 0.05$), in MMSI, to 45% ($p < 0.05$), in MMLI, to 12% ($p > 0.05$). What is more, SOD activity decreased - predominantly in MMSI and MMLI.The effects of 1.4-naphtoquinone derivative and vitamin E administration against X-ray irradiation alone, and simultaneous X-ray irradiation and COX blockage, when compared, evidences unidirectionality in their antioxidant and anti-inflammatory effects upon the mucous membranes of the digestive organs. Both vitamin E and the 1.4-naphtoquinone derivative, when in the situation of

X-ray irradiation alone, brought about a decrease of TBA-active products, whereas in a situation of simultaneous X-ray irradiation and COX blockage, their effects upon TBA-active products content was null. However, Vitamin E, when administer under irradiation alone, significantly increased SOD and catalase activity, when compared to the results of the administration of 1.4 naphtoquinone. Herein, the effect of 1.4-naphtoquinone derivative and vitamin E administration upon the changes of iNOS activity was unidirectional in both situations of X-ray irradiation alone, and in situations of simultaneous irradiation and COX blockage. Of note, MPO activity, both under the effect of 1.4-naphoquinone derivative and vitamin E administration, within the situation of X-ray irradiation, increased most significantly in MMSI. This reveals its higher sensitivity to the action of the investigated compounds.

Hence, we can state that the 1.4-naphtoquinone derivative (1.4-naphtoquinone (3-[3-(3.5-di-*tret*-butyl-4-hydroxyphenyl)-1.4-dihydronaphtalene-2-aminoil] butyrate) has prominent antioxidant, anti-inflammatory and radioprotective effects both under the conditions of X-ray irradiation and simultaneous X-ray irradiation and COX blockage. Thus, it can be considered to have potential as a perspective pharmacologic remedy of radioprotective action.

CONCLUSION

X-ray irradiation totalling a dose of 20 sGy brought about an increase in oxidative processes and in the activity of iNOS and MPO in MMS, MMSI and MMLI. Both the effect of vitamin E and 1.4 naphtoquinone derivative introduction upon the background of low intensity X-ray irradiation alone and under conditions of simultaneous X-ray irradiation and COX blockage resulted in the decrease of oxidative processes and iNOS activity, whereas MPO activity increased. Vitamin E administration, when in a situation of X-ray irradiation alone, more significantly increased SOD and catalase activity, when compared to the effect of 1.4-naphtoquinone introduction. Moreover, the content level of TBA-active products (in MMS and MMSI), the degree of iNOS activity and the sum of nitrites and nitrates levels upon blockage of COX-1/COX-2, by way of indomethacin administration, when in a simultaneous situation of X-ray irradiation, were lower than that under the conditions of their independent effect. Taking into account the significant antioxidant and anti-inflammatory effects of the derivative of 1.4-naphtoquinone (3-[3-(3.5-di-*tret*-butyl-4-hydroxyphenyl)-1.4-dihydronaphtalene-2-aminoil]butyrate) upon comparison to the effect of vitamin E administration, both under the conditions of X-ray irradiation and the simultaneous effect of X-ray irradiation and COX blockage, this derivative may be considered as a perspective radioprotectant.

REFERENCES

1. Akita S. Treatment of Radiation Injury. *Adv. Wound Care (New Rochelle)*., 3, 1, 2014.
2. Anwar M. et al.: Effect of antioxidant supplementation on digestive enzymes in radiation induced intestinal damage in rats. *Int. J. Radiat. Biol*., 89, 1061, 2013.
3. Boyde J. R., Rahmotullah M. Optimization of conditions for the colorimetric determination of citrulline, using diacethyl monoxim. *Anal. Biochem*., 107, 424, 1980.
4. Bradley P.P., Christensen R.D., Rothstein G. Cellular and extracellular myeloperoxidase in pyogenic inflammation. *Blood*., 60, 618, 1982.
5. Brzozowski T. et al.: Role of prostaglandins in gastroprotection and gastric adaptation. *J. Physiol. Pharmacol*., 56, 33, 2005.
6. Charlier C., Michaux C. Dual inhibition of cyclooxygenase-2 (COX-2) and 5-lipoxygenase (5-LOX) as a new strategy to provide safer non – steroidal anti-inflammatory drugs. *Eur. J. Med. Chem*., 38, 645, 2003.
7. Datsyuk L.O. et al.: The effects of admibistration of nonselective inhibitor of NO-synthase under X-ray radiation. *Studia Biologica*, 3, 51, 2009.
8. Figurka O. M. et al.: Synthesis and features of 3-chloro-2-(3,5-di-tert-buthyl-4-hydroxyphenil)-1,4-naphtoquinones. *Annals of National University "Lviv Polytechnic". Chemistry, technology of compounds and their application*, 787, 224, 2014.
9. Geyer J.W., Dabich D.: Rapid method for determination of arginase activity in tissue homogenates. *Anal. Biochem*., 39, 412, 1971.
10. Henni M., Ali D. Radiation induced side effects. *Rev. Prat*., 62, 461, 2012.
11. Hernández L. et al.: Aging and radiation: bad companions. *Aging Cell*., 14, 153, 2015.
12. Huang E.Y. et al.: Aminoguanidine alleviates radiation-induced small-bowel damage through its antioxidant effect. *Int. J. Radiat. Oncol. Biol. Phys*., 74, 237, 2009.
13. Kiselyk I.O. et al.: Peculiarities of the determination of nitrates and nitrites in peripheral blood in patients with viral hepatitis and in syndrome of jaundice of other aethiology. *Laboratorna diagnostuka*, 3, 43, 2001.
14. Liu L.N. et al.: Protective Role of Rheum Tanguticum Polysaccharide 1 in Radiation- induced Intestinal Mucosal Injury. *Iran J. Pharm. Res*., 14, 833, 2015.
15. Pisoschi A.M., Pop A.: The role of antioxidants in the chemistry of oxidative stress: A review. *Eur. J. Med. Chem*., 5, 55, 2015.
16. Sklyarov A.Y., Panasyuk N.B., Fomenko I.S. Role of nitric oxide-synthase and cyclooxygenase/lipooxygenase systems in development of experimental ulcerative colitis. *J. Physiol. Pharmacol*., 65, 62, 2011.
17. Stacey R., Green J.T.: Radiation-induced small bowel disease: latest developments and clinical guidance. *Ther. Adv. Chronic. Dis*., 5, 15, 2014.
18. Szumiel I.: Ionizing radiation-induced oxidative stress, epigenetic changes and genomic instability: the pivotal role of mitochondria. *Int. J. Radiat. Biol*., 91, 1, 2015.
19. Theis V.S. et al.: Chronic radiation enteritis. *Clin Oncol (R. Coll. Radiol)*., 22, 70, 2010.
20. Wallace J.L.: Prostaglandins, NSAIDs, and gastric mucosal protection: why doesn't the stomach digest itself? *Physiol. Rev*., 88, 1547, 2008.
21. Yang C.S. et al.: Inhibition of inflammation and carcinogenesis in the lung and colon by tocopherols. A*nn. N Y Acad. Sci*., 1203, 29, 2010.