М. А. Капустин [M. Al. Kapustin] [1, 2]
А. С. Чубарова [A. S. Chubarova] [1]
И. А. Евдокимов [I. Al. Evdokimov] [2]
С. В. Лодыгина [S.V. Lodygina] [2]
А. Д. Лодыгин [A. D. Lodygin] [2]
А. В. Янцевич [Al. V. Yancevich] [3]
В. П. Курченко [Vl. P. Kurchenko] [1, 2]

УДК 615.322

DOI: 10.37493/2307- 910X.2022.3.10

КУРКУМИНОИДЫ: ПОЛУЧЕНИЕ, СВОЙСТВА И ПРИМЕНЕНИЕ СООБЩЕНИЕ 2. АНТИОКСИДАНТНАЯ И АНТИМУТАГЕННАЯ АКТИВНОСТЬ КУРКУМИНОИДОВ.

CURCUMINOIDS: PRODUCTION, PROPERTIES AND APPLICATION REPORT 2. ANTIOXIDANT AND ANTIMUTAGENIC ACTIVITY OF CURCUMINOIDS.

[1] Белорусский государственный университет (Belorussian State University)
[2] Северо-Кавказский федеральный университет (North Caucasus Federal University)
[3] Научно-практический центр гигиены (Scientific and Practical Center for Hygiene)
e-mail: hramcov2018@inbox.ru

Аннотация

Показано, что антиоксидантная активность в ряду куркумин, бис-деметоксикуркумин, деметоксикуркумин снижается. Определена величина TEAC для куркумина, бис-деметоксикуркумина, деметоксикуркумина, которая составляет 0,41, 0,32 и 0,21 соответственно. Суммарный препарат куркуминоидов обладает антимутагенной активностью при концентрации 8,3 мг/л в тест системе штамма S. typhimurium TA100 и S. typhimurium TA98.

Ключевые слова: куркуминоиды, куркумин, деметоксикуркумин, бис-деметоксиксикуркумин, антиоксидант, антимутаген, АБТС-радикал, тролокс.

Abstract

As a result of studies, it has been shown that the antioxidant activity in the series curcumin, bis-demethoxycurcumin, demethoxycurcumin decreases. The TEAC value was determined for curcumin, bis-demethoxycurcumin, demethoxycurcumin, which is 0.41, 0.32 and 0.21, respectively. The total preparation of curcuminoids has antimutagenic activity at a concentration of 8.3 mg / l in the test system of S. typhimurium TA100 and S. typhimurium TA98 strains.

Keywords: curcuminoids, curcumin, demethoxycurcumin, bis-demethoxycurcumin, antioxidant, antimutagen, ABTS radical, trolox.

Introduction.

Turmeric Rhizome *Curcuma longa* L. _ serve as a source of highly active compounds that are widely used in the food industry [1, 2]. Chemical analysis of the composition of turmeric rhizome extracts showed that the plant material contains carbohydrates (69.4%), water (13.1%), proteins (6.3%), fats (5.1%) and minerals (3.5%). %), essential oil (5.8%), and curcumin (3–6%) [3]

The active components of turmeric extracts are curcuminoids [4]. Curcuminoids are a mixture of curcumin (K) and two of its derivatives, demethoxycurcumin (DMC) and bis-demethoxycurcumin (BDMC) [5]. The ratio of curcuminoids in the composition of curcumin is 52–63% for K, 19–27% for DMC, and 18–28% for BDMC. Due to the presence in their structure of two benzenemethoxy rings connected by an unsaturated chain, these compounds exhibit keto-enol tautomerism. Aromatic groups in the structure of molecules provide the hydrophobicity of curcuminoids, and the presence of an isoprenoid linker causes flexibility, tautomeric transitions of

the structure, and also affects their hydrophobicity and polarity [5]. Due to the peculiarities of the chemical structure, curcuminos are poorly soluble in water at acidic and neutral pH values, but soluble in methanol, ethanol, dimethyl sulfoxide and acetone.

Curcuminoids and their derivatives have a wide spectrum of biological activity, including antioxidant, anti-inflammatory, antitumor, bactericidal, neuro-, cardio- and radioprotective [6, 7].

A number of studies have shown that the administration of curcuminoids to laboratory animals at a dose of 300 mg/kg has a neuroprotective activity under conditions of hypoxia of the nervous tissue and significantly reduces the percentage of neuron and neuroglia death, and reduces the risk of cerebral infarction [8]. The introduction of the drug at a dosage of 5–100 mg/kg led to a decrease in the symptoms of ketamine-induced syndrome in laboratory animals [9], the preservation of the functional activity of GABAergic receptors and the normalization of GABA metabolism in the nervous tissue, reducing the toxic effects caused by the administration of streptozotocin to rats [10]. The introduction of the curcuminoids drug led to inhibition of peroxidation reactions of microglia cell membranes and a decrease in the production of nitrogen monoxide. Moreover, the inhibitory activity decreased in the series demethoxycurcumin, bis-demethoxycurcumin, and curcumin [11].

The study of the antioxidant effect of the total preparation of curcuminoids and its individual components showed the presence of pronounced activity in various test systems. Thus, the administration of curcuminoids to laboratory rats at a dosage of 50–250 mg/kg led to the induction of synthesis and an increase in the activity of enzymes of the antioxidant system: serum and erythrocyte glutathione peroxidase, superoxide dismutase, and catalase [12, 13]. In the urine of the examined animals, a decrease in the level of biomarkers of oxidative stress, allantoin, m-tyrosine, 3-nitrotyrosine, and 8-hydroxy-2-deoxyguanosine, was observed [14]. Similar studies were obtained in the study of the oxidative status of the tissues of the heart, kidneys, and liver of laboratory animals [13]. In the phosphomolybdenum and DPPH model systems, the studied preparations showed pronounced antioxidant activity [15, 16].

Curcumin preparations showed pronounced anticancer and antiproliferative activity against a number of cell lines: MCF-7 human breast tumor cells [17], K 562 human leukemia cells [18], HeLa cells [19], H22 mouse hepatoma cells [20] , HT1080 human fibrosarcoma cells [21], rectal cancer cells [22, 23], A549 human lung adenocarcinoma cells and A549 cisplatin-resistant cells [24], HMEC1 dermal capillary endothelial cells [25].

On a model object, a histidine auxotrophic mutant strain of Salmonella typhimurium TA97, the presence of mutagenic activity of curcuminoids was shown when exposed to the cultivation medium at concentrations of 10–50%, which is expressed in an increase in the amount of revertants [26].

The cardioprotective activity of curcuminoids has been shown when the drug is administered to laboratory animals at a dosage of 75 mg/kg. Oral administration of curcuminoids led to significant improvements in the physiological and functional parameters of the heart, a decrease in necrotic zones, and a decrease in the level of serum markers in an experiment on an induced myocardial infarction model [27].

Along with antioxidant activity, the presence of radioprotective activity was shown for the curcuminoids preparation. Oral administration of curcuminoids at a dose of 50 mg/kg to laboratory rats caused a significant decrease in the number of necrotizing cells and a significant decrease in the number of chromosomal mutations [28, 29].

The antifungal and antiviral activities of the curcuminoids preparation have been shown against strains of the pathogenic fungus Candida albicans [30] and influenza virus [31].

A number of authors have shown that curcuminoids have a pronounced anti-inflammatory effect. Experiments on cell lines and when administered to laboratory animals showed a decrease in the activity of calmodulin-dependent protein kinase II and, as a result, inhibition of NO synthase activity [32]. Along with a decrease in the immunoreactive status of the organism and activation of

enzymatic systems of xenobiotic metabolism, there was a decrease in the migration of neutrophils from the bloodstream to tissues and an increase in the barrier function of the endothelium [33].

In recent years, intensive studies have been carried out on the bioavailability, safety and efficacy of curcuminoids, which are used in complex therapy or as an independent drug in the treatment of various diseases. Due to the pronounced biological activity and low toxicity of curcuminoids, they can be used as part of functional foods [34–36].

The aim of the work was to study the antioxidant and gene-protective properties of curcuminoids.

Materials and methods.

The object of the study were curcuminoids: curcumin, demethoxycurcumin, bisdemethoxycurcumin, obtained from the rhizome of turmeric (*Curcuma longa* L.).

Determination of antioxidant activity.

The antiradical activity of curcuminoids was evaluated in the model system for the reduction of the radical cation ABTS˙+ [37, 38]. The generation of radical cations ABTS˙+ was carried out in the presence of ammonium persulfate. Trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid), a water-soluble analog of vitamin E, was used as a standard antioxidant. under the action of the test compound) and calculated by the formula:

$$\% \text{ inhibition} = 100*(1-A2/A1),$$

where A1 is the optical density of the ABTS˙+ solution at a wavelength of 734 nm without adding the test sample; A2 is the optical density of the ABTS˙+ solution 6 min after the addition of the test sample.

The results were plotted as percent inhibition versus test substance concentration. To calculate the IC50 and TEAC values, a calibration curve was constructed for Trolox as a standard antioxidant. According to the calibration curve, a linear regression equation of the form y=ax+b was calculated, which was used for further calculations.

Determination of antimutagenic activity

The antimutagenic effect of purified curcuminoids was studied in a series of in vitro experiments using one of the variants of the Ames bacterial test, the FAT plate test (High Throughput Fluctuation Ames Test) [39, 40]. Histidine auxotrophic strains of *Salmonella typhimurium* TA100 and TA98 were used as test objects . 2-nitrofluorene was used as a standard mutogen causing frameshift mutations in the *S. typhimurium* TA98 strain. Sodium azide was used for base pair substitution mutations in the *S. typhimurium* TA100 strain. These substances caused a reverse mutation in test strains, as a result of which they acquired the ability to develop in an environment deficient in histidine and return to prototrophy. An increase in the number of revertants in this test indicates that the test compound induces gene mutations. When standard mutagens and curcuminoids under study are introduced into the incubation medium of *Salmonella typhimurium strains* , a decrease in the amount of revertants indicates that the tested compounds have antimutagenic activity [41, 42]. For analysis, the total preparation of curcuminoids was dissolved in 96% ethanol. Studies were carried out at 2 concentrations of the total preparation of curcuminoids, the final concentration of which in the test systems was 1.7 and 8.3 mg/l. To exclude the influence of the solvent, 96% ethanol was used as a negative control. To prevent contamination of the culture medium by microorganisms, the initial solutions were filtered through a sterile filter tank with a pore size of 0.2 μm.

Results and Discussion

Traditionally, turmeric is used as an active component in the composition of herbal remedies, in everyday nutrition as an independent seasoning (turmeric) or as part of spices [1, 2]. As a result of clinical trials, curcumin was recognized as safe and classified as a hazard class 5 (is not hazardous). According to the decision of the US Food and Drug Administration (FDA US), turmeric is included in the group of "generally recognized as safe" compounds [1]. Curcumin has a

wide spectrum of biological activity, which makes it possible to use it in functional foods. In this regard, it is important to determine its antioxidant and gene protective properties.

Antioxidant activity of curcuminoids. Studies have been carried out on the antioxidant activity of the total preparation of curcuminoids and individual compounds included in its composition: curcumin, demethoxycurcumin and bisdemethoxycurcumin. The antioxidant activity of curcuminoids was studied in the model system for the reduction of the radical cation $ABTS^{\cdot+}$. Trolox was used as a standard antioxidant. Antioxidant activity was expressed as a percentage decrease in the concentration of the radical cation $ABTS^{\cdot+}$ in the reaction system as a result of its reduction by the molecules of the test compound.

Based on the obtained results, graphs of the dependence of the percentage of inhibition of the $ABTS^{\cdot+}$ radical on the concentration of Trolox and the curcuminoids preparation were plotted (Figure 1).

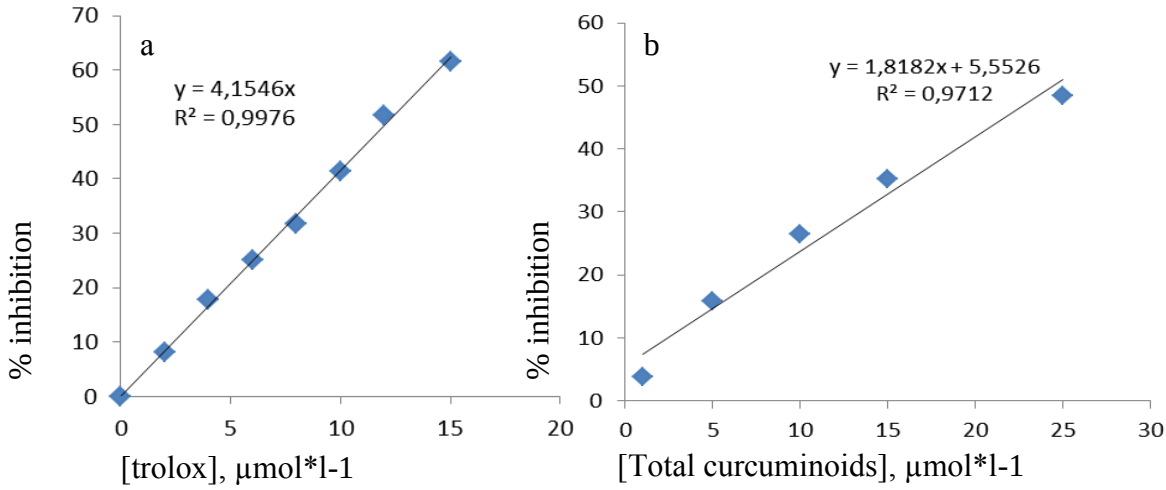


Figure 1. Dependence of the inhibition of the radical cation $ABTS^{\cdot+}$ on the concentration of trolox (a) and curcuminoids preparation (b)

For the resulting plots, linear regression equations were calculated and used for further calculations of Trolox equivalent (TEAS) and IC_{50}.

For Trolox, the $IC_{50\ value}$ was 12.04 µmol/L, and for the total preparation of curcuminoids it was 24.45 µmol/L. The TEAC value of the total preparation of curcuminoids, calculated as the ratio of the tangents of the slope of the curves presented in Figures 1a and 1b, was 0.44. This indicates that the studied preparation of curcuminoids has a 2.3 times lower antioxidant activity compared to Trolox.

The antioxidant activity of individual curcuminoids was studied using a series of standard solutions with different concentrations of curcumin, demethoxycurcumin, and bisdemethoxycurcumin in 96% ethanol. To calculate the IC_{50} and TEAC values, the corresponding graphs were constructed and linear regression equations were calculated for curcumin (Figure 2a), demethoxycurcumin (Figure 2b) and bisdemethoxycurcumin (Figure 2c).

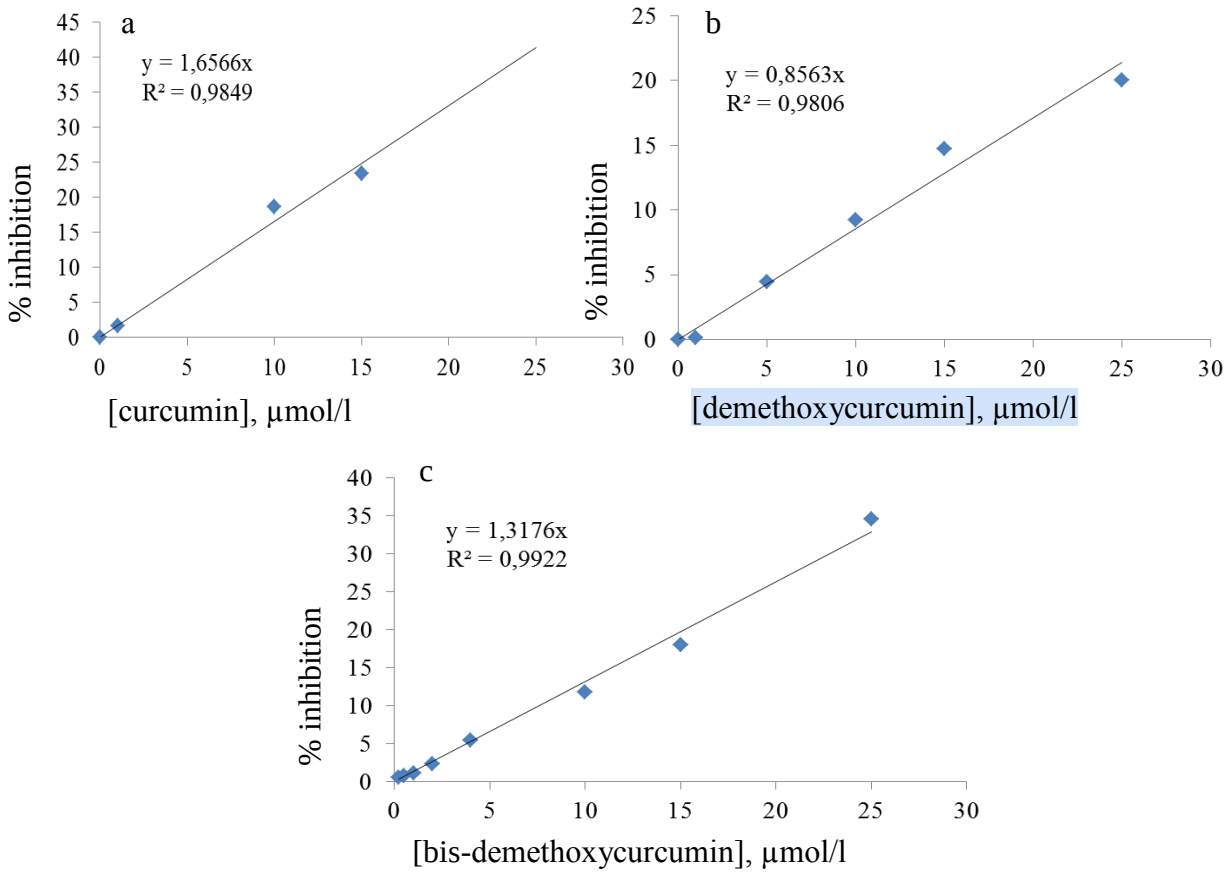
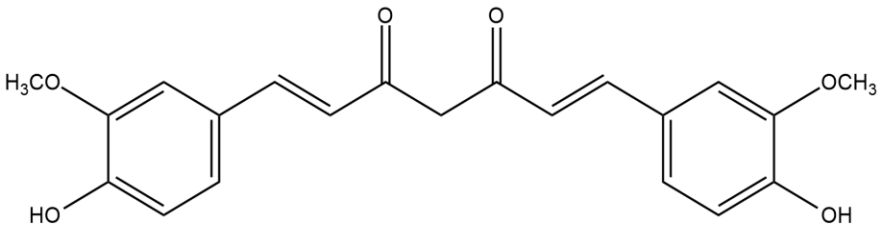


Figure 2. Dependence of ABTS˙+ inhibition on the concentration of curcumin (a), demethoxycurcumin (b) and bis-demethoxycurcumin (c)

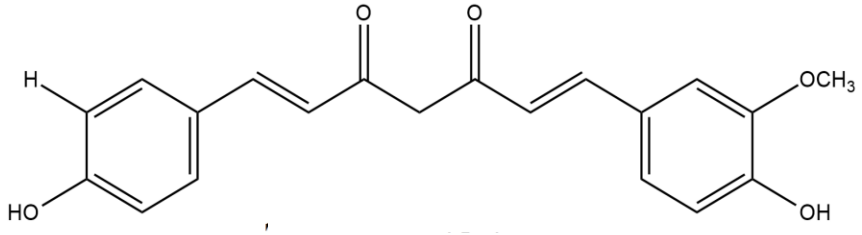
The antioxidant activity of individual curcuminoids with respect to the ABTS $^{+\bullet}$ radicals formed in the aqueous phase depends on the amount of methoxy and OH groups in the aromatic rings of their structure (Figure 3). The efficiency of reduction of ABTS $^{+\bullet}$ radicals is also associated with the presence of a –C=C –bond conjugated to the aromatic ring.

For Trolox, the $IC_{50\ value}$ was 12.04 µmol/L (3.13 a), and for curcumin, demethoxycurcumin, and bisdemethoxycurcumin, it was 30.19 µmol/L, 58.41 µmol/L, and 37.97 µmol/L, respectively. The calculated TEAC values for these compounds were 0.41, 0.21 and 0.32, respectively. The data obtained indicate that in the series curcumin, bisdemethoxycurcumin, demethoxycurcumin, the anti-radical activity is reduced compared to trolox by 2.4, 3.1, and 4.7 times, respectively [43]. The curcuminoids preparation exhibits antioxidant activity mainly due to curcumin and bis-demethoxycurcumin, and to a lesser extent, demethoxycurcumin.

1



2



3

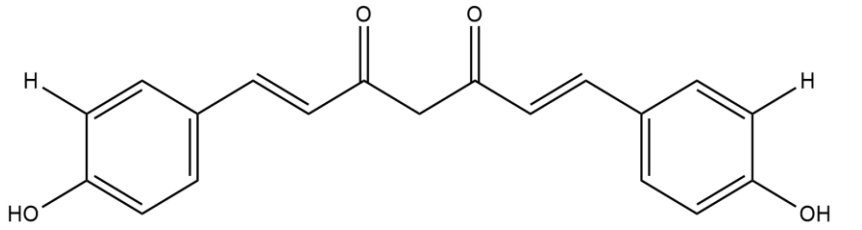


Figure 3. Structural formulas of curcumin (1), demethoxycurcumin (2) and bis-demethoxycurcumin (3)

Thus, the antioxidant activity of curcuminoids, as a rule, is maximal in the presence of a pyrocatechin group, which increases the stability of the phenoxy radical. A significant contribution is made by the presence in the structure of the molecule of two double –C=C –bonds conjugated with aromatic rings. Such a structure ensures the delocalization of the spin density of the phenoxy radical [44]. In the absence of one of these structural fragments, the antioxidant activity of curcuminoids, as a rule, decreases.

Antimutagenic activity of curcuminoids preparation. An analysis of the literature data showed that curcuminoids are characterized by antioxidant and anticarcinogenic activity [41, 42]. To evaluate the antimutagenic activity of the obtained total preparation of curcuminoids, a series of experiments was carried out using the Ames test. Histidine auxotrophic strains of *Salmonella typhimurium* TA100 and TA98 were used as test objects . Due to the difference in genotype, the parallel use of these strains makes it possible to fairly fully assess the nature of the DNA-damaging effect of mutagenic substances - base pair replacement for the *S. typhimurium* TA100 strain or frame shift for *S. typhimurium* TA98 [39, 40].

To assess the antimutagenic effect of curcuminoids, a standard mutagen, 2-nitrofluorene, was introduced into the *S. typhimurium TA 98 test system, which caused the formation of a large amount of prototrophic revertants.* In the presence of antimutagenic activity in curcuminoid compounds, their introduction into the incubation medium caused a decrease in the amount of formed revertants, due to their inhibition of frameshift mutations. caused by 2-nitrofluorene. For the *S. typhimurium* TA100 strain, a standard mutagen, sodium azite, was used. The presence of the antimutagenic effect of the total preparation of curcuminoids was taken into account by reducing the frequency of induction of reverse mutations from histidine auxotrophy to prototrophy.

The final concentration of the total preparation of curcuminoids after adding the working solution to the test system of strains *S. typhimurium* TA98 and *S. typhimurium* TA100 was 1.7 and 8.3 mg/l.

The results of the study of the antimutagenic activity of the total preparation of curcuminoids in the test system with the *S. typhimurium* TA98 strain are shown in Table 1.

Table 1 - The results of the antimutagenic effect of the total preparation of curcuminoids with the mutagenic effect of 2-nitrofluorene in the test system with the *S. typhimurium* TA98 strain

Sample	concentration of curcuminoids, 1.7 mg/l		concentration of curcuminoids, 8.3 mg/l	
	Share of positive wells, %	Share of negative wells, %	Share of positive wells, %	Share of negative wells, %
Standard mutagen (2-nitrofluorene)	14,58	85,42	50,00	50,00
Negative control (96% ethyl alcohol)	8,33	91,67	8,33	91,67
Total preparation of curcuminoids	8,33	91,67	25,00	75,00

When the total preparation of curcuminoids at a final concentration of 1.7 mg/l was introduced into the test system of the *S. typhimurium* TA98 strain containing 2-nitrofluorene in the culture medium, the level of induced mutagenesis did not decrease. An increase in the final concentration of the total preparation of curcuminoids in the cultivation medium of the test object *S. typhimurium* TA98 to 8.3 μg/ml leads to an increase in gene protective activity. There is a decrease in the proportion of positive wells by 42.87% when an alcohol solution of the total preparation of curcuminoids is added.

Table 2 shows the results of a study of the antimutagenic activity of the total preparation of curcuminoids in a test system with the *S. typhimurium* TA100 strain.

Table 2 - The results of the antimutagenic effect of the total preparation of curcuminoids with the mutagenic effect of sodium azide in the test system with the *S. typhimurium* TA100 strain

Sample	concentration of curcuminoids, 1.7 mg/l		concentration of curcuminoids, 8.3 mg/l	
	Share of positive wells, %	Share of negative wells, %	Share of positive wells, %	Share of negative wells, %
Standard mutagen (sodium azide)	83,33	16,67	100	0,00
Negative control (96% ethyl alcohol)	12,50	87.50	16,67	83,33
Total preparation of curcuminoids	75,00	25,00	14,58	85,42

According to the results of the test, the presence of a total preparation of curcuminoids at a concentration of 1.7 mg/l in the cultivation medium of the *S. typhimurium* TA100 strain did not lead to a significant antimutagenic effect. With an increase in the final concentration of the total preparation of curcuminoids in the test system of the *S. typhimurium* TA100 strain to 8.3 mg/l, there is a decrease in the frequency of induced mutations in the *S. typhimurium* TA100 strain by more than 6 times ($p<0.01$) to a level comparable to spontaneous mutagenesis.

The conducted studies allow us to conclude that at low concentrations, the total preparation of curcuminoids does not show a pronounced antimutagenic effect in the considered test systems. With an increase in the final concentration of the total preparation of curcuminoids to 8.3 mg/l, a pronounced antimutagenic effect is observed, preventing 50% of the frameshift mutations for the *S. typhimurium* TA98 strain under the action of 2-nitrofluorene. At this concentration, the curcu-

minoids preparation prevented base pair substitution mutations for the *S. typhimurium* TA100 strain under the action of sodium azide to a spontaneous level.

Conclusion.

A study was made of the antioxidant and gene-protective activity of the total preparation of curcuminoids and individual compounds included in its composition: curcumin, demethoxycurcumin and bisdemethoxycurcumin. The antioxidant activity of curcuminoids was studied in the model system for the reduction of the radical cation $ABTS^{\cdot+}$. For Trolox, the $IC_{50\ value}$ was 12.04 μmol/l, and for the total preparation of curcuminoids - 24.45 μmol/l, and for curcumin, demethoxycurcumin and bisdemethoxycurcumin - 30.19 μmol/l, 58.41 μmol/l and 37. 97 μmol/l, respectively. The calculated TEAC values for these compounds were 0.41, 0.21 and 0.32, respectively.

The TEAC value of the total curcuminoids preparation was 0.44. This indicates that the total preparation of curcuminoids has a 2.3 times lower antioxidant activity compared to Trolox.

The data obtained indicate that in the series curcumin, bisdemethoxycurcumin, demethoxycurcumin, the antiradical activity is reduced compared to trolox by 2.4, 3.1 and 4.7 times, respectively. The antioxidant activity of individual curcuminoids depends on the number of methoxy and OH groups in the aromatic rings of their structure, as well as on the presence of a –C=C –bond conjugated with the aromatic ring.

To assess the antimutagenic activity of the total preparation of curcuminoids, the Ames test was used on histidine-auxotrophic strains of *Salmonella typhimurium* TA100 and TA98. Studies have shown that at a concentration of curcuminoids of 1.7 mg/l, the antimutagenic effect on both strains is not manifested. At a concentration of the total preparation of curcuminoids of 8.3 mg/l, a pronounced antimutagenic effect is observed, preventing 50% of the frameshift mutations caused by the action of 2-nitrofluorene for *S. typhimurium* TA98. At this concentration, the curcuminoids preparation prevented base pair substitution mutations for the *S. typhimurium* TA100 strain under the action of sodium azide to a spontaneous level.

Thus, the conducted studies showed that the total preparation of curcuminoids and individual compounds curcumin, demethoxycurcumin and bis-demethoxycurcumin, due to their antioxidant and gene-protective properties, can be recommended for use in the food industry to create functional foods.

ЛИТЕРАТУРА | REFERENCES

1. Gupta, S. Curcumin, a Component of Turmeric: From Farm to Pharmacy / S. Gupta, G.Kismali, B. B. Aggarwal // BioFactors. – 2013. – Vol. 39, № 1. – P. 2–13.

2. Prasad, S. Curcumin, a component of golden spice: From bedside to bench and back / S. Prasad [et al.] // Biotechnology Advances. – 2014. – Vol. 32, № 6. – P. 1053–1064.

3. Bagchi, A. Extraction of curcumin / A. Bagchi [et al.] // IOSR J. Environ. Sci. Toxicol. Food Technol. – 2012. – Vol. 1. – P. 1–16.

4. Wiggers, H.J. Curcumin, a multitarget phytochemical: challenges and perspectives / H.J. Wiggers [et al.] // Studies in Natural Products Chemistry. – 2017. –Vol. 53. – P. 243–276.

5. Siviero, A. Curcumin, a golden spice with a low Bioavailability / A. Siviero, E. Gallo, V. Maggini // J. Herb. Med. – 2015. – Vol. 5. – P. 57–70.

6. Kathryn, M. Nelson. The Essential Medicinal Chemistry of Curcumin / M. Nelson Kathryn [et al.] // J. Med. Chem. – 2017. – Vol. 60, № 5. – P. 1620–1637.

7. Amalraj, A. Biological activities of curcuminoids, other biomolecules from turmeric and their derivatives – A review / A. Amalraj, A. Pius, S. Gopi // J. of Tradit. and Complem. Medicine. – 2017. – Vol 7, № 2. – P. 205–233.

8. Dohare, P. Dose dependence and therapeutic window for the neuroprotective effects of curcumin in thromboembolic model of rat / P. Dohare, P. Garga, V. Jain, C. Natha, M. Ray // Behav. Brain Res. – 2008. – Vol. 193. – P. 289–297.

9. Gazal, M. Neuroprotective and antioxidant effects of curcumin in a ketamine-induced model of mania in rats / M. Gazal, M.R. Valente, B.A. Acosta // Eur. J Pharmacol. – 2014. –Vol. 724. – P. 132–139.

10. Jayanarayanan, S. NMDA and AMPA receptor mediated excitotoxicity in cerebral cortex of streptozotocin induced diabetic rat: ameliorating effects of curcumin / S. Jayanarayanan [et al.] // Chem. Biol. Interact. – 2013. – Vol. 201. – P. 39–48.

11. Zhang, L.J. Comparison of inhibitory potency of three different curcuminoid pigments on nitric oxide and tumor necrosis factor production of rat primary microglia induced by lipopolysaccharide / L.J. Zhang, C.F. Wu, X.L. Meng // Neurosci. Lett. – 2008. – Vol. 447. – P. 48–53.

12. Kalpravidh, R.W. Improvement in oxidative stress and antioxidant parameters in b-thalassemia/Hb E patients treated with curcuminoids / R.W. Kalpravidh, N. Siritanaratkul, P. Insain // Clin. Biochem. – 2010. – Vol. 43. – P. 424–429.

13. Naik, S.R. Protective effect of curcumin on experimentally induced inflammation, hepatotoxicity and cardiotoxicity in rats: evidence of its antioxidant property / S.R. Naik, V.N. Thakare, S.R. Patil // Exp. Toxicol. Pathol. – 2011. – Vol. 63. – P. 419–431.

14. Dall'Acqua, S. New findings on the in vivo antioxidant activity of Curcuma longa extract by an integrated 1H NMR and HPLCeMS metabolomic approach / S. Dall'Acqua, M. Stocchero, I. Boschiero // Fitoterapia. – 2016. – Vol. 109. – P. 125–131.

15. Jayaprakasha, G.K. Antioxidant activities of curcumin, demethoxycurcumin and bisdemethoxycurcumin / G.K. Jayaprakasha, L.J. Rao, K.K. Sakariah // Food Chem. – 2006. – Vol. 98. – P. 720–724.

16. Galano, A. Role of the reacting free radicals on the antioxidant mechanism of curcumin / A. Galano [et al.] // J. Chem. Phys. – 2009. – Vol. 363. – P. 13–23.

17. Simon, A. Inhibitory effect of curcuminoids on MCF-7 cell proliferation and structure-activity relationships / A. Simon [et al.] // Cancer Lett. – 1998. – Vol. 129. – P. 111–116.

18. Semsri, S. Inhibitory mechanism of pure curcumin on Wilms' tumor 1 (WT1) gene expression through the PKCa signaling pathway in leukemic K562 cells / A. Simon [et al.] // FEBS Lett. – 2011. – Vol. 585. – P. 2235–2242.

19. Jiang, J. Identification of antitumor constituents in curcuminoids from Curcuma longa L. based on the composition-activity relationship / J. Jiang [et al.] // J. Pharm. Biomed. Anal. – 2012. – Vol. 70. – P. 664–670.

20. Man, S. Turmeric enhancing anti-tumor effect of Rhizoma paridis saponins by influencing their metabolic profiling in tumors of H22 hepatocarcinoma mice / S. Man, H. Chai, P. Qiu // Pathol. Res. Pract. – 2015. – Vol. 211. – P. 948–954.

21. Yodkeeree, S. Curcumin, demethoxycurcumin and bisdemethoxycurcumi differentially inhibit cancer cell invasion through the down-regulation of MMPs and uPA / S. Yodkeeree, W. Chaiwangyen, S. Garbisa // J. Nutr. Biochem. – 2009. – Vol. 20. – P. 87–95.

22. Basile, V. Curcumin derivatives: molecular basis of their anti-cancer activity / V. Basile [et al.] // Biochem. Pharmacol. – 2009. – Vol. 78. – P. 1305–1315.

23. Yue, G.G. Turmeric ethanolic extract possesses stronger inhibitory activities on colon tumour growth than curcumin – the importance of turmerones / G.G.Yue, L. Jiang, H. Kwok // J. Funct. Foods. – 2016. – Vol. 22. – P. 565–577.

24. Ye, M. Curcumin reverses cisplatin resistance and promotes human lung adenocarcinoma A549/DDP cell apoptosis through HIF-1a and caspase-3 mechanisms / M. Ye, Y. Zhao, Y. Li // Phytomedicine. – 2012. – Vol. 19. – P. 779–787.

25. Yue, G.G.L. Evaluation of in vitro anti-proliferative and immunomodulatory activities of compounds isolated from Curcuma longa / G.G.L Yue, B.C.L Chan, P. Hon // Food Chem Toxicol. – 2010. – Vol. 48. – P. 2011–2020.

26. Vieira, I.L. In vitro muta-genicity and blood compatibility of paclitaxel and curcumin in poly (DL-lactidecoglicolide) films / I.L. Vieira [et al.] // Toxicol. In Vitro. – 2013. – Vol. 27. – P. 198–203.

27. Hong, D. Altered profiles of gene expression in curcumin-treated rats with experimentally induced myocardial infarction / D. Hong [et al.] // Pharmacol. Res. – 2010. – Vol. 61. – P. 142–148.

28. Lopez-Jornet, P. Radioprotective effects of lycopene and curcumin during local irradiation of parotid glands in Sprague Dawley rats / P. Lopez-Jornet [et al.] // Br. J. Oral Maxillofac Surg. – 2016. – Vol. 54. – P. 275–279.

29. Sebastia, N. Curcumin and trans-resveratrol exert cell cycle-dependent radioprotective or radiosensitizing effects as elucidated by the PCC and G2-assay / N. Sebastia, A. Montoro, D. Hervas // Mutat. Res. – 2014. – Vol. 766–767. – P. 49–55.

30. Zhang, D. Effects of two curcuminoids on Candida albicans / D. Zhang [et al.] // Chin Herb Med. – 2012. – Vol. 4. – P. 205–212.

31. Chen, D. Curcumin inhibits influenza virus infection and haemagglutination activity / D. Chen, J. Shien, L. Tiley // Food Chem. – 2010. – Vol.119. – P. 1346–1351.

32. Kim, A.N. Up-regulation of heme oxygenase-1 expression through CaMKII-ERK1/2-Nrf2 signaling mediates the anti-inflammatory effect of bisdemethoxycurcumin in LPS-stimulated macrophages / A.N. Kim, W. Jeon, J.J. Lee // Free Radic Biol Med. – 2010. – Vol. 49. – P. 323–331.

33. Cooney, J.M. A combined omics approach to evaluate the effects of dietary curcumin on colon inflammation in the Mdr1aA/A mouse model of inflammatory bowel disease / J.M. Cooney, M.P.G. Barnett, Y.E.M. Dommels // J Nutr Biochem. – 2016. – Vol. 27. – P. 181–192.

34. Kaur, I.P. Antimutagenicity of curcumin and related compounds against

genotoxic heterocyclic amines from cooked food: the structural requirement / I.P. Kaur [et al.] //

Food Chem. – 2008. – Vol. 111. – P. 573–579.

35. Fu, S. Bioaccessibility of curcuminoids in buttermilk in simulated gastrointestinal digestion models / S. Fu [et al.] // Food Chem. – 2015. – Vol. 179. – P. 52–59.

36.Laokuldilok, N. Optimisation of microencapsulation of turmeric extract for masking flavor / N. Laokuldilok, P. Thakeow, P. Kopermsub // Food Chem. – 2016. – Vol. 194. – P. 695–704.

37. Re, R. Antioxidant activity applying an improved ABTS radical cation decolorization assay / R. Re [et al.] // Free Radical Biology and Medicine. – 1999. – Vol. 26, № 9/10. – P. 1231–1237.

38. Ильясов, И.Р. Применение радикал-катионов ABTS˙+ в оценке антирадикальной активности флаволноидов / И.Р. Ильясов [и др.] // Фармация. – 2008. – № 6. – С. 15–18.

39. Hajime, S. Improvement and Evaluation of High Throughput Fluctuation Ames Test Using 384-well Plate with Salmonella typhimurium TA100 and TA98 / S. Hajime [et al.] // Genes and Environment. – 2009. – Vol. 31, № 2. – P. 47–55.

40. Maron, D. Revised methods for the Salmonella mutagenicity test / D. Maron, B. Ames // Mut. Res. –1983. – Vol.113. – P. 173–215.

41. Kanai, M. Dose-escalation and pharmacokinetic study of nanoparticle curcumin, a potential anticancer agent with improved bioavailability, in healthy human volunteers / Kanai M. [et al.] // Cancer Chemother Pharmacol. – 2012. – Vol. 69, № 1. – P. 65–70.

42. Hewlings, S.J. Curcumin. A Review of Its' Effects on Human Health / Susan J. Hewlings, Douglas S. Kalman // Foods. – 2017. – Vol. 6, № 92. – P. 1–11.

43. Капустин М.А. Антирадикальная активность куркумина, деметоксикуркумина и бисдеметоксикуркумина, выделенных из корневища Curcuma longa L. / М.А. Капустин, А.С. Чубарова // Биологическая осень 2017: к Году науки в Беларуси: тезисы докладов Международной конференции молодых ученых, Минск, 9 ноября 2017 г. / БГУ, Биологический факультет, Совет молодых ученых; редкол.: В.В. Лысак (гл. ред.) [и др.]. – Минск: БГУ, 2017. – С. 22–23.

44. Rice-Evans, C.A. Structure-antioxidant activity relationships of flavonoids and phenolic acids / C.A. Rice-Evans, N.J. Miller, G. Paganga // Free Radic. Biol. Med. – 1996. – Vol. 20, № 7. – P. 933–956.

REFERENCES

1. Gupta, S. Curcumin, a Component of Turmeric: From Farm to Pharmacy / S. Gupta, G.Kismali, B. B. Aggarwal // BioFactors. – 2013. – Vol. 39, № 1. – P. 2–13.

2. Prasad, S. Curcumin, a component of golden spice: From bedside to bench and back / S. Prasad [et al.] // Biotechnology Advances. – 2014. – Vol. 32, № 6. – P. 1053–1064.

3. Bagchi, A. Extraction of curcumin / A. Bagchi [et al.] // IOSR J. Environ. Sci. Toxicol. Food Technol. – 2012. – Vol. 1. – P. 1–16.

4. Wiggers, H.J. Curcumin, a multitarget phytochemical: challenges and perspectives / H.J. Wiggers [et al.] // Studies in Natural Products Chemistry. – 2017. –Vol. 53. – P. 243–276.

5. Siviero, A. Curcumin, a golden spice with a low Bioavailability / A. Siviero, E. Gallo, V. Maggini // J. Herb. Med. – 2015. – Vol. 5. – P. 57–70.

6. Kathryn, M. Nelson. The Essential Medicinal Chemistry of Curcumin / M. Nelson Kathryn [et al.] // J. Med. Chem. – 2017. – Vol. 60, № 5. – P. 1620–1637.

7. Amalraj, A. Biological activities of curcuminoids, other biomolecules from turmeric and their derivatives – A review / A. Amalraj, A. Pius, S. Gopi // J. of Tradit. and Complem. Medicine. – 2017. – Vol 7, № 2. – P. 205–233.

8. Dohare, P. Dose dependence and therapeutic window for the neuroprotective effects of curcumin in thromboembolic model of rat / P. Dohare, P. Garga, V. Jain, C. Natha, M. Ray // Behav. Brain Res. – 2008. – Vol. 193. – P. 289–297.

9. Gazal, M. Neuroprotective and antioxidant effects of curcumin in a ketamine-induced model of mania in rats / M. Gazal, M.R. Valente, B.A. Acosta // Eur. J Pharmacol. – 2014. –Vol. 724. – P. 132–139.

10. Jayanarayanan, S. NMDA and AMPA receptor mediated excitotoxicity in cerebral cortex of streptozotocin induced diabetic rat: ameliorating effects of curcumin / S. Jayanarayanan [et al.] // Chem. Biol. Interact. – 2013. – Vol. 201. – P. 39–48.

11. Zhang, L.J. Comparison of inhibitory potency of three different curcuminoid pigments on nitric oxide and tumor necrosis factor production of rat primary microglia induced by lipopolysaccharide / L.J. Zhang, C.F. Wu, X.L. Meng // Neurosci. Lett. – 2008. – Vol. 447. – P. 48–53.

12. Kalpravidh, R.W. Improvement in oxidative stress and antioxidant parameters in b-thalassemia/Hb E patients treated with curcuminoids / R.W. Kalpravidh, N. Siritanaratkul, P. Insain // Clin. Biochem. – 2010. – Vol. 43. – P. 424–429.

13. Naik, S.R. Protective effect of curcumin on experimentally induced inflammation, hepatotoxicity and cardiotoxicity in rats: evidence of its antioxidant property / S.R. Naik, V.N. Thakare, S.R. Patil // Exp. Toxicol. Pathol. – 2011. – Vol. 63. – P. 419–431.

14. Dall'Acqua, S. New findings on the in vivo antioxidant activity of Curcuma longa extract by an integrated 1H NMR and HPLCeMS metabolomic approach / S. Dall'Acqua, M. Stocchero, I. Boschiero // Fitoterapia. – 2016. – Vol. 109. – P. 125–131.

15. Jayaprakasha, G.K. Antioxidant activities of curcumin, demethoxycurcumin and bisdemethoxycurcumin / G.K. Jayaprakasha, L.J. Rao, K.K. Sakariah // Food Chem. – 2006. – Vol. 98. – P. 720–724.

16. Galano, A. Role of the reacting free radicals on the antioxidant mechanism of curcumin / A. Galano [et al.] // J. Chem. Phys. – 2009. – Vol. 363. – P. 13–23.

17. Simon, A. Inhibitory effect of curcuminoids on MCF-7 cell proliferation and structure-activity relationships / A. Simon [et al.] // Cancer Lett. – 1998. – Vol. 129. – P. 111–116.

18. Semsri, S. Inhibitory mechanism of pure curcumin on Wilms' tumor 1 (WT1) gene expression through the PKCa signaling pathway in leukemic K562 cells / A. Simon [et al.] // FEBS Lett. – 2011. – Vol. 585. – P. 2235–2242.

19. Jiang, J. Identification of antitumor constituents in curcuminoids from Curcuma longa L. based on the composition-activity relationship / J. Jiang [et al.] // J. Pharm. Biomed. Anal. – 2012. – Vol. 70. – P. 664–670.

20. Man, S. Turmeric enhancing anti-tumor effect of Rhizoma paridis saponins by influencing their metabolic profiling in tumors of H22 hepatocarcinoma mice / S. Man, H. Chai, P. Qiu // Pathol. Res. Pract. – 2015. – Vol. 211. – P. 948–954.

21. Yodkeeree, S. Curcumin, demethoxycurcumin and bisdemethoxycurcumi differentially inhibit cancer cell invasion through the down-regulation of MMPs and uPA / S. Yodkeeree, W. Chaiwangyen, S. Garbisa // J. Nutr. Biochem. – 2009. – Vol. 20. – P. 87–95.

22. Basile, V. Curcumin derivatives: molecular basis of their anti-cancer activity / V. Basile [et al.] // Biochem. Pharmacol. – 2009. – Vol. 78. – P. 1305–1315.

23. Yue, G.G. Turmeric ethanolic extract possesses stronger inhibitory activities on colon tumour growth than curcumin – the importance of turmerones / G.G.Yue, L. Jiang, H. Kwok // J. Funct. Foods. – 2016. – Vol. 22. – P. 565–577.

24. Ye, M. Curcumin reverses cisplatin resistance and promotes human lung adenocarcinoma A549/DDP cell apoptosis through HIF-1a and caspase-3 mechanisms / M. Ye, Y. Zhao, Y. Li // Phytomedicine. – 2012. – Vol. 19. – P. 779–787.

25. Yue, G.G.L. Evaluation of in vitro anti-proliferative and immunomodulatory activities of compounds isolated from Curcuma longa / G.G.L Yue, B.C.L Chan, P. Hon // Food Chem Toxicol. – 2010. – Vol. 48. – P. 2011–2020.

26. Vieira, I.L. In vitro muta-genicity and blood compatibility of paclitaxel and curcumin in poly (DL-lactidecoglicolide) films / I.L. Vieira [et al.] // Toxicol. In Vitro. – 2013. – Vol. 27. – P. 198–203.

27. Hong, D. Altered profiles of gene expression in curcumin-treated rats with experimentally induced myocardial infarction / D. Hong [et al.] // Pharmacol. Res. – 2010. – Vol. 61. – P. 142–148.

28. Lopez-Jornet, P. Radioprotective effects of lycopene and curcumin during local irradiation of parotid glands in Sprague Dawley rats / P. Lopez-Jornet [et al.] // Br. J. Oral Maxillofac Surg. – 2016. – Vol. 54. – P. 275–279.

29. Sebastia, N. Curcumin and trans-resveratrol exert cell cycle-dependent radioprotective or radiosensitizing effects as elucidated by the PCC and G2-assay / N. Sebastia, A. Montoro, D. Hervas // Mutat. Res. – 2014. – Vol. 766–767. – P. 49–55.

30. Zhang, D. Effects of two curcuminoids on Candida albicans / D. Zhang [et al.] // Chin Herb Med. – 2012. – Vol. 4. – P. 205–212.

31. Chen, D. Curcumin inhibits influenza virus infection and haemagglutination activity / D. Chen, J. Shien, L. Tiley // Food Chem. – 2010. – Vol.119. – P. 1346–1351.

32. Kim, A.N. Up-regulation of heme oxygenase-1 expression through CaMKII-ERK1/2-Nrf2 signaling mediates the anti-inflammatory effect of bisdemethoxycurcumin in LPS-stimulated macrophages / A.N. Kim, W. Jeon, J.J. Lee // Free Radic Biol Med. – 2010. – Vol. 49. – P. 323–331.

33. Cooney, J.M. A combined omics approach to evaluate the effects of dietary curcumin on colon inflammation in the Mdr1aA/A mouse model of inflammatory bowel disease / J.M. Cooney, M.P.G. Barnett, Y.E.M. Dommels // J Nutr Biochem. – 2016. – Vol. 27. – P. 181–192.

34. Kaur, I.P. Antimutagenicity of curcumin and related compounds against genotoxic heterocyclic amines from cooked food: the structural requirement / I.P. Kaur // Food Chem. – 2008. – Vol. 111. – P. 573–579.

35. Fu, S. Bioaccessibility of curcuminoids in buttermilk in simulated gastrointestinal digestion models / S. Fu [et al.] // Food Chem. – 2015. – Vol. 179. – P. 52–59.

36.Laokuldilok, N. Optimisation of microencapsulation of turmeric extract for masking flavor / N. Laokuldilok, P. Thakeow, P. Kopermsub // Food Chem. – 2016. – Vol. 194. – P. 695–704.

37. Re, R. Antioxidant activity applying an improved ABTS radical cation decolorization assay / R. Re [et al.] // Free Radical Biology and Medicine. – 1999. – Vol. 26, № 9/10. – P. 1231–1237.

38. Ilyasov, I.R. The use of ABTS˙+ radical cations in assessing the antiradical activity of flavolnoids / I.R. Ilyasov [et al.] // Pharmacy – 2008, – № 6. – P. 15–18.

39. Hajime, S. Improvement and Evaluation of High Throughput Fluctuation Ames Test Using 384-well Plate with Salmonella typhimurium TA100 and TA98 / S. Hajime [et al.] // Genes and Environment. – 2009. – Vol. 31, № 2. – P. 47–55.

40. Maron, D. Revised methods for the Salmonella mutagenicity test / D. Maron, B. Ames // Mut. Res. –1983. – Vol.113. – P. 173–215.

41. Kanai, M. Dose-escalation and pharmacokinetic study of nanoparticle curcumin, a potential anticancer agent with improved bioavailability, in healthy human volunteers / Kanai M. [et al.] // Cancer Chemother Pharmacol. – 2012. – Vol. 69, № 1. – P. 65–70.

42. Hewlings, S.J. Curcumin. A Review of Its' Effects on Human Health / Susan J. Hewlings, Douglas S. Kalman // Foods. – 2017. – Vol. 6, № 92. – P. 1–11.

43. Kapustin M.A. Antiradical activity of curcumin, demethoxycurcumin and bisdemethoxycurcumin isolated from the rhizome of Curcuma longa L. / M.A. Kapustin, A.S. Chubarova // Biological Autumn 2017: Towards the Year of Science in Belarus: abstracts of the International Conference of Young Scientists, Minsk, November 9, 2017 / BSU, Faculty of Biology, Council of Young Scientists; editorial board: V.V. Lysak (chief editor) [et al.]. - Minsk: BSU, 2017. –P. 22–23.

44. Rice-Evans, C.A. Structure-antioxidant activity relationships of flavonoids and phenolic acids / C.A. Rice-Evans, N.J. Miller, G. Paganga // Free Radic. Biol. Med. – 1996. – Vol. 20, № 7. – P. 933–956.

ОБ АВТОРАХ / ABOUT THE AUTHORS

Капустин Максим Александрович, магистр биологических наук, науч. сотр. НИЛ прикладных проблем биологии биологического факультета БГУ, г. Минск; тел.: +375 29 7720526, E-mail: maximkapustin84@gmail.com

Kapustin M.A., Master in Biological Sciences, researcher of the Laboratory of Applied Biology, Biology Faculty, Belarusian State University, Biology Faculty, Minsk,; Phone: +375297720526

Чубарова Анна Сергеевна канд. биол. наук, доцент, ст. науч. сотр. НИЛ прикладных проблем биологии биологического факультета БГУ, г. Минск; тел.: +375 29 5576722, E-mail: chubarova.hanna@gmail.com

Chubarova A.S., PhD in Biological Sciences, Associate Professor, senior researcher of the Laboratory of Applied Biology, Biology Faculty, Belarusian State University, Biology Faculty, Minsk,; Phone: +375295576722, E-mail: chubarova.hanna@gmail.com

Евдокимов Иван Алексеевич, док. техн. наук, профессор, зав. базовой кафедрой Технологии молока и молочных продуктов Института живых систем СКФУ, г. Ставрополь; тел.: +79624030847, E-mail: **ievdokimov@ncfu.ru**

Evdokimov I.A., Doctor in Technical Science, Professor, Head of the Department of milk and dairy products technology, Institute of Living Systems NCFU, Stavropol; Phone: +79624030847,E-mail: **ievdokimov@ncfu.ru**

Лодыгин Алексей Дмитриевич, док. техн. наук, профессор, заведующий кафедрой прикладной биотехнологии Института живых систем СКФУ, зам. директора Института живых систем СКФУ по научной работе, г. Ставрополь; тел.: +8652330318, E-mail: allodygin@yandex.ru

Lodygin A.D., Doctor in Technical Science, Professor, Head of the Department of applied biotechnology, Institute of Living Systems NCFU, Stavropol; Phone: +8652330318, E-mail: allodygin@yandex.ru

Лодыгина Светлана Валентиновна, канд. техн. наук, доцент кафедры прикладной биотехнологии Института живых систем СКФУ, г. Ставрополь; тел.: +8652330318, E-mail: svetvallod@mail.ru

Lodygina S.V. PhD in Technical Sciences, Associate Professor of the Department of applied biotechnology, Institute of Living Systems NCFU, Stavropol; Phone: +8652330318, , E-mail: svetvallod@mail.ru

Дудчик Наталья Владимировна, док. биол. наук, доцент, зав. лаб. микробиологии государственного предприятия «Научно-практический центр гигиены», тел.: +375172841370, E-mail: micro_sanitary@rspch.by

Dudchik N.V. Doctor of Biological Sciences, Associate Professor, Head of lab. of microbiology of the State Enterprise "Scientific and Practical Center for Hygiene". Phone: +375 17 284-13-70,E-mail: rspch@ rspch.by.

Цыганков Василий Георгиевич канд. мед. наук., доцент, вед. науч. сотр. лаб. комплексных проблем гигиены пищевых продуктов государственного предприятия «Научно-практический центр гигиены», тел.: +375293733551, E-mai l: vgz@tut.by.

Cigankov V.G. PhD in Medical Sciences, Associate Professor, leading researcher of laboratory of complex problems of food hygiene of the state enterprise "Scientific and Practical Center for Hygiene". Phone: + 375293733551, E-mail: vgz@tut.by.

Бондарук Алла Михайловна канд. мед. наук., зав. лаб. комплексных проблем гигиены пищевых продуктов государственного предприятия «Научно-практический центр гигиены», тел.: + 375 17 284-13-84, E-mail: pitanie_b@rspch.by.

Bondaruk A.M. PhD in Medical Sciences, Head of laboratory of complex problems of food hygiene of the state enterprise "Scientific and Practical Center for Hygiene". Phone: + 375 17 284-13-84, E-mail: pitanie_b@rspch.by.

Курченко Владимир Петрович, канд. биол. наук, доцент, зав. НИЛ прикладных проблем биологии биологического факультета БГУ, г. Минск; тел.: +375 29 6630347, E-mail: kurchenko@tut.by

Kurchenko V.P., PhD, Associate Professor, Head of the Laboratory of Applied Biology, Biology Faculty, Belarusian State University, Biology Faculty, Minsk,; Phone: +375 29 6630347, E-mail: kurchenko@tut.by.

Дата поступления в редакцию: 07.08.2022
После рецензирования:22.08.2022
Дата принятия к публикации:03.09.2022