

дили острый эмоционально-болевого стресс. За 60 минут до стрессирования крысы получали per os: II группа – воду, III группа – диазепам в дозе 1,25 мг/кг массы тела; IV группа – препарат биотрит в дозе 50 мг/кг.

Препарат растительного происхождения биотрит в условиях действия острого ЭБС проявил защитное нормализующее влияние в отношении тест-органов, слизистой оболочки желудка, а также состояния периферической крови крыс.

რეზიუმე

მცენარეული წარმოშობის პრეპარატის დამცველობითი თვისებები მწვავე ემოციურ-ტოკიკილითი სტრესის დროს ვირთაგვებში

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უკრაინის სამედიცინო მეცნიერებათა ეროვნული აკადემიის სტომატოლოგიისა და ება-სახის ქირურგიის ინსტიტუტი, ???????

კვლევის მიზანს შეადგენდა მცენარეული წარმოშობის პრეპარატის ბიოტრიტის და დიაზეპამის დამცველობითი თვისებების შესწავლა ემოციურ-ტოკიკილითი სტრესის პირობებში ვირთაგვებში.

ექსპერიმენტი ჩატარდა 5 თვის ასაკის 24 მამრ ვირთაგვებზე. ცხოველები (თითოეულ ჯგუფში – 6) იმყოფებოდნენ ვივარიუმის სტანდარტულ რაციონზე: I ჯგუფი – ინტაქტური, II, III და IV ჯგუფის ცხოველებში 3 საათის განმავლობაში ავითარებდნენ ემო-

ციურ-ტოკიკილით სტრესს. სტრესამდე 60 წუთით ადრე ცხოველები per os იღებდნენ: II ჯგუფის ცხოველები – წყალს, III ჯგუფის – დიაზეპამს, დოზით 1,25 მგ/კგ, IV ჯგუფის – პრეპარატ ბიოტრიტს, დოზით 50 მგ/კგ. ჩატარებული კვლევებით გამოვლინდა პრეპარატ ბიოტრიტის მნიშვნელოვანი ადაპტაციური თვისებები, ამასთან, მათი გამოხატვის ხარისხი უფრო მაღალი იყო, ვიდრე დიაზეპამის სტრეს-პროტექციული ეფექტები.

THE INFLUENCE OF SODIUM SALTS OF CARBOXYMETHYLATES OF OXYETHYLATED ISONONYLPHENOLS ON THE NEUTRALIZING FUNCTION OF THE LIVER IN A SUBACUTE TOXICOLOGICAL EXPERIMENT

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At present, the problem of environmental pollution is urgent and its solution is of global significance. The anthropogenic activity of the man at the modern stage of development of science and engineering has resulted in the appearance of chemical toxic substances in the biosphere. Most xenobiotics are able to form delayed effects of their (mutagenic, gonadotrophic, embryotrophic, teratogenic) influence on the organism of homoithers [7,8,10]. Chemical contaminants take a leading place among unfavourable environmental and industrial factors. Their long-term influence develops ecology-dependent pathology. The scale-up of organic synthesis chemistry results in the placement of its basic enterprises in densely populated areas, development and production of a wide spectrum of new chemicals, thereby endangering the health of people. In full measure it applies to the production of both surface-active substances (SAS) and synthetic detergents. In the opinion of many authors [4 6], a significant number of chemical compounds can modulate radiomimetic effects and are membranotropic, they develop free-radical pathology in the organism, inhibit humoral and cellular immunity. The unstudied SAS, widely used in different sectors of the national economy, include sodium salts of carboxymethylates of oxyethylated isononylphenols of such brands as AFS 9-4 KM, AFS 9-6 KM, AFS 9-10 KM. The interest to this group of detergents is caused by a large turnout, a wide range of the production output and absence of any prognostic assessment of a potential danger for homoithers and human beings.

The purpose of the present work was to study the effects produced by a group of derivatives of oxyethylated nonylphenols - sodium salts of carboxymethylates of oxyethylated isononylphenols of such brands as AFS 9-4 KM, AFS 9-6 KM, AFS 9-10 KM on the state of the microsomal monooxygenase system (MMS) of hepatocyte detoxification and on the conjugation reaction in conditions of a subacute experiment and to reveal a potential danger for homoithers and human beings.

Material and methods. Sodium salts of carboxymethylates of oxyethylated isononylphenols of such brands as AFS 9-4 KM, AFS 9-6 KM, AFS 9-10 KM are anion-active SAS with scheduled physical-chemical properties; they are well soluble in water and organic solvents. On the basis of acute toxicity parameters they belong to moderately toxic (danger class 3) compounds, which have pronounced cumulative properties. Half-lethal doses (LD_{50}) were determined at the levels of 6.1, 2.2 and 3.2 g/kg of the animal weight, cumulation coefficients being on the levels of 3.16, 2.2 and 2.39, respectively, for AFS 9-4 KM, AFS 9-6 KM, AFS 9-10 KM. The experimental part of the research was performed on white rats of WAG population; every day before feeding they received orally, through a metal probe, aqueous solutions of xenobiotics with 1/10, 1/100 and 1/1000 of LD_{50} . The duration of subacute influence was 45 days. The experiments on white rats were performed in compliance with the international prin-

ciples of the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes (Strasbourg, 1986). The programme of the research stipulated study of the influence of sodium salts of carboxymethylates of oxyethylated isononylphenols on two microsomal electron transport systems: NADPH, which is bound with cytochrome P450 as the end acceptor, and NADN, which is bound with cytochrome b_5 as the electron acceptor. The study involved such parameters of microsomal oxidation as respiratory activity, content of cytochromes P450 and b_5 , activity of reductases. The microsomal oxidation system activity can be most fully and objectively assessed by the rate of metabolism of xenobiotics, which reflects the activity of both initial (NADPH, NADN reductases) and terminal (cytochromes P450, b_5) sites. As a substrate of the microsomal P450-dependent system we used p-nitroanisole; this is a xenobiotic, which is subjected to oxidative methylation with formation of p-nitrophenol, the latter having a characteristic absorption spectrum in alkaline media. In this work, the following parameters of microsomal oxidation were used: activity of 0-demethylase, N-demethylase, NADPH-cytochrome c reductase, NADN-cytochrome c reductase, endogenous respiration rate of microsomes, NADPH oxidation rate, NADPH oxidation rate in the presence of EDTA, lipid peroxidation (LPO) rate, and content of cytochromes P450 and b_5 [3, 6, 8]. The content of ketone bodies in blood was determined after precipitation of proteins with zinc sulphate and barium hydroxide. The essence of this method consists in displacing acetone from blood filtrate with sulphuric acid and binding acetone with salicylic aldehyde [1]. Nonesterified free fatty acids were detected by extraction of fatty acid salts in blood plasma with organic solvents followed by determination of the content of copper [2]. Glycogen in the liver was detected by the Seifter method after hydrolysis of a weighed portion of the liver in 30% solution of potassium hydroxide, ethanol precipitation of glycogen and revealing of glucose content by the anthrone method [9]. The activity of UDP-glucuronyltransferase in the microsomal fraction of the liver was assessed by the paranitrophenol conjugation rate [13, 14], that of N-acetyltransferase in the postmitochondrial fraction by the conjugation rate of para-aminobenzoic acid (PABA), whose quantity was measured by the diazo compound reaction with N-naphthylethylenediamine. The activity of glutathione S-transferase was assessed by the formation of glutathione conjugates with 1-chloro-2,4-dinitrobenzene ($\lambda_{\text{abs}} = 340 \text{ nm}$) [11]. The total content of CoA (CoA-SH and acetyl-CoA) was determined by the PABA acetylation method [5]. The content of reduced and oxidized glutathione was determined with help of the glutathione transferase reaction [12], cysteines were determined by the reaction with ninhydrin in a trichloroacetic filtrate [15]. Group differences were statistically assessed by the parametric Student's t-test.

Results and their discussion. Results of the study on the influence of xenobiotics on the detoxification system revealed in the MMS of hepatocytes an increased activity of 0-demethylase, N-demethylase, NADPH-cytochrome c reductase, NADN-cytochrome c reductase, higher values of LPO rate and content of cytochromes P450 and b_5 in the groups of animals, which were subjected to intoxication with sodium salts of carboxymethylates of oxyethylated isononylphenols at doses of 1/10 and 1/100 of LD_{50} . The dose of 1/1000 of LD_{50} was not effective. The analysis showed that sodium salts of carboxymethylates of oxyethylated isononylphenols of such

brands as AFS 9-4 KM, AFS 9-6 KM, AFS 9-10 KM in 1/100 of LD_{50} increased, respectively, the activity of 0-demethylase by 113.4%, 159.7% and 132.8%, the activity of N-demethylase by 54.2%, 108.7% and 95.4%, the activity of NADPH-cytochrome c reductase by 30.3%, 52.6% and 44.5%, the activity of NADN-cytochrome c reductase by 48.3%, 63.05% and 60.1%, the rate of endogenous respiration by 60%, 143% and 124%, the rate of NADPH oxidation by 85.6%, 109.3% and 92.2%, the rate of NADPH oxidation in the presence of EDTA by 92.8%, 153.6% and 144.3%, the rate of POL by 309%, 422% and 373.3%, the content of cytochrome P450 by 65.3%, 154.3% and 126.6%, the content of cytochrome b_5 by 135.2%, 252.2% and 218%. The above data demonstrate that sodium salts of carboxymethylates of oxyethylated isononylphenols are inducers of the hydroxyling MMS of hepatocytes; this system is able to modify xenobiotics and change their biological activity, providing their possible mutagenic and cancerogenic properties [6, 8, 10]. Against this background sodium salts of carboxymethylates of oxyethylated isononylphenols increased the activity of N-acetyltransferase by 62.5%, 143.7% and 103.1%, as well as the total amount of CoA (CoA-SH and acetyl-CoA) by 71.4%, 128.6% and 112%, respectively, in cases of subacute influence of 1/100 of LD_{50} of AFS 9-4 KM, AFS 9-6 KM and AFS 9-10 KM. This fact makes it possible to conclude that sodium salts of carboxymethylates of oxyethylated isononylphenols activate the processes, which are engaged in the formation of acetyl conjugation. Besides, we observed a reduction in the activity of UDP-glucuronyl transferase, glutathione-S-transferase and in the content of reduced glutathione in the liver (Table 1). Thus, sodium salts of carboxymethylates of oxyethylated isononylphenols AFS 9-4 KM, AFS 9-6 KM and AFS 9-10 KM decreased, respectively, the activity of UDP-glucuronyl transferase by 37.4%, 57.6% and 54.9%, the activity of glutathione-S-transferase by 45.5%, 54.3% and 51.2%, the content of reduced glutathione by 27.2%, 57.3% and 36.6% and that of cysteine by 39.3%, 57.1% and 50.0%. Sodium salts of carboxymethylates of oxyethylated isononylphenols in 1/100 of LD_{50} inhibit the mechanisms of formation of glucuronid and glutathione conjugations, which are associated with inhibition of the antioxidant defence system, as it is demonstrated by decreases of cysteine and reduced glutathione and an increase of glutathione disulphide by 74.2%, 151.6% and 116%, respectively, when influenced by AFS 9-4 KM, AFS 9-6 KM and AFS 9-10 KM.

Our results revealed increases in the content of free fatty acids in blood serum and ketone bodies in blood against a background of a decrease of glycogen in the liver (Table 2). Studies detected higher levels of free fatty acids by 83.6%, 135.8% and 117.9%, and ketone bodies by 332.4%, 529.4% and 464.7%; these facts demonstrate an activation of lipolysis and ketogenesis against a background of a lower content of glycogen in the liver by 53.4%, 67% and 61.2%, respectively, during intoxication in a subacute experiment with sodium salts of carboxymethylates of oxyethylated isononylphenols of such brands as AFS 9-4 KM, AFS 9-6 KM and AFS 9-10 KM. These data show that studied compounds in 1/100 of LD_{50} activate catabolic processes of breakdown of glycogen and triacylglycerols, which may be associated with an acid-base imbalance and development of metabolic acidosis, as it was confirmed by a significant increase in the content of ketone bodies in blood by 4.2, 6.3 and 5.6 times, respectively, when influenced by AFS 9-4 KM, AFS 9-6 KM and AFS 9-10 KM.

Table 1. The state of the system of xenobiotic detoxification in the liver in conditions of a subacute experiment under the influence of sodium salts of carboxymethylates of oxyethylated isononylphenols at a dose of 1/100 of LD₅₀

Indices	Group M ± m			
	Control	AFS 9-4 KM	AFS 9-6 KM	AFS 9-10 KM
0-demethylase (nmol of p- nitrophenol/min·mg of protein)	6.70 ± 0.58	14.3 ± 0.9*	17.4 ± 1.8*	15.6 ± 1.4*
NADPH-cytochrome c reductase (nmol of cytochrome c/min·mg of protein)	180.4 ± 17.3	235.2 ± 12.4*	275.3 ± 10.5*	260.8 ± 9.3*
NADN-cytochrome c reductase (nmol of cytochrome c/min·mg of protein)	865.2 ± 57.8	1283.5 ± 18.7*	1410.7 ± 56.3*	1385.6 ± 42.7*
Endogenous respiration rate (nmol of O ₂ /min·mg of protein)	1.50 ± 0.21	2.40 ± 0.17*	3.65 ± 0.34*	3.37 ± 0.28*
NADPH oxidation rate (nmol of O ₂ /min·mg of protein)	3.20 ± 0.34	5.94 ± 0.48*	6.70 ± 0.53*	6.15 ± 0.42*
NADPH oxidation rate in the presence of EDTA (nmol of O ₂ /min·mg of protein)	2.80 ± 0.32	5.40 ± 0.62*	7.10 ± 0.83*	6.84 ± 0.76*
Lipid peroxidation rate (nmol of O ₂ /min·mg of protein)	0.44 ± 0.05	1.80 ± 0.14*	2.30 ± 0.15*	2.10 ± 0.18*
Content of cytochrome P-450 (nmol/mg of protein)	0.865 ± 0.07	1.43 ± 0.04*	2.20 ± 0.16*	1.96 ± 0.13*
Content of cytochrome b ₅ (nmol/mg of protein)	0.582 ± 0.06	1.37 ± 0.05*	2.05 ± 0.07*	1.85 ± 0.06*
N-demethylase (nmol of formaldehyde / min·mg of protein)	3.45 ± 0.18	5.32 ± 0.48*	7.20 ± 0.65*	6.74 ± 0.56*
UDP-glucuronyl transferase (nmol/min·mg of protein)	2.97 ± 0.23	1.86 ± 0.05*	1.26 ± 0.05*	1.34 ± 0.03*
N-acetyltransferase (nmol/mg of protein/60 min)	0.32 ± 0.04	0.52 ± 0.02*	0.78 ± 0.03*	0.65 ± 0.04*
Glutathione-S-transferase (nmol/min·mg of protein)	29.7 ± 2.36	16.2 ± 1.40*	13.6 ± 0.94*	14.8 ± 1.23*
Reduced glutathione (mcmol/g)	6.70 ± 0.43	4.83 ± 0.42*	3.10 ± 0.46*	4.25 ± 0.56*
Glutathione disulphide (mcmol/g)	0.31 ± 0.02	0.54 ± 0.03*	0.78 ± 0.05*	0.67 ± 0.08*
Cysteine (mcmol/g)	0.28 ± 0.012	0.17 ± 0.006*	0.12 ± 0.007*	0.14 ± 0.005*
CoA, total amount (nmol/g)	297.6 ± 14.3	510.5 ± 30.4*	680.3 ± 27.8*	630.4 ± 22.5*

note: * - differences are reliable, p<0.05

Table 2. Effects of sodium salts of carboxymethylates of oxyethylated isononylphenols on the state of carbohydrate and fat metabolism in conditions of a subacute experiment under the influence of 1/100 of LD₅₀

Indices	Group m ± τ			
	Control	AFS 9-4 KM	AFS 9-6 KM	AFS 9-10 KM
Free fatty acids (mmol/l), serum	0.67 ± 0.05	1.23 ± 0.08*	1.58 ± 0.12*	1.46 ± 0.14*
Ketone bodies (mol/l), blood	0.34 ± 0.016	1.47 ± 0.15*	2.14 ± 0.18*	1.92 ± 0.16*
Glycogen (mcmol/g), liver	137.8 ± 9.4	64.22 ± 5.74*	44.5 ± 3.73*	53.6 ± 4.25*

note: * - differences are reliable, p<0.05

Conclusions. Our analysis shows severe disruptions in the neutralizing function of the liver and predominance of catabolic processes over anabolic syntheses in groups of animals, which were subjected to the influence of sodium salts of carboxymethylates of oxyethylated isononylphenols at a dose of 1/100 of LD₅₀.

Results of our researches showed that during their subacute influence in a toxicological experiment on white rats sodium salts of carboxymethylates of oxyethylated isononylphenols AFS 9-4 KM, AFS 9-6 KM and AFS 9-10 KM stimulated the hydroxyling MMS of hepatocytes and inhibited reactions of the formation of gluc-

uronid and glutathione conjugations against a background of more active processes of the formation of acetyl conjugation, higher levels in the content of CoA-SH, acetyl-CoA and ketone bodies.

These violations are believed to be caused by structural and functional disorders inside hepatocytes, such as impairments of plasma membrane and proteins of cytoskeleton, mitochondria dysfunctions as well as activation of catabolic enzymes and misbalance of ionic homeostasis.

The effect of xenobiotics at a dose of 1/100 of LD₅₀ was accompanied by an increased disintegration of triacylglyc-

erols and glycogen and inhibition of the antioxidant defence system, which was accompanied by decreases of reduced glutathione, cysteine and glutathione-S-transferase. These results suggest the misbalance between prooxidant and antioxidant systems towards prevalence of prooxidants and activation of processes with the involvement of free radicals which probably leads to the oxidative stress. Eventually, the harmful effect of xenobiotics might result in mutation of cells genome, progression of malignization, cellular necrosis and overgrowth of connective tissue. Therefore, compensation of oxidative stress, which is accepted as an important reason of pathology caused by environmental factors in persons who was dealing with manufacture chemicals for a long time, is of great practical importance. Obtained results are highly relevant to be taken in account in laboratory tests as early diagnostic criteria indicating misbalance of oxidative homeostasis of an organism in conditions of sodium salts of carboxymethylates of oxyethylated isononylphenols effecting.

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SUMMARY

THE INFLUENCE OF SODIUM SALTS OF CARBOXYMETHYLATES OF OXYETHYLATED ISONONYLPHENOLS ON THE NEUTRALIZING FUNCTION OF THE LIVER IN A SUBACUTE TOXICOLOGICAL EXPERIMENT

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The study was conducted as a part of research work “Biochemical mechanisms of the development of dismetabolic processes under the influence of chemical environmental factors”. The purpose of the present work was to study the effects produced by sodium salts of carboxymethylates of oxyethylated isononylphenols on the state of the microsomal monooxygenase system of hepatocyte detoxification and on the conjugation reaction in conditions of a subacute experiment and to reveal a potential danger for homoithers and human beings. The object of the study were the white rats of WAG population.

The effects produced by sodium salts of carboxymethylates of oxyethylated isononylphenols of such brands as AFS 9-4 KM, AFS 9-6 KM, AFS 9-10 KM on the state of the microsomal monooxygenase system of hepatocyte detoxification and on the conjugation reaction in conditions of a subacute experiment were studied.

It was set that studied compounds during their subacute influence in a toxicological experiment stimulated the hydroxyling microsomal monooxygenase system of hepatocytes and inhibited reactions of the formation of glucuronid and glutathione conjugations against a background of more active processes of the formation of acetyl conjugation, higher levels in the content of CoA-SH, acetyl-CoA and ketone bodies.

Keywords: sodium salts of carboxymethylates of oxyethylated isononylphenols, microsomal monooxygenase system, isononylphenols, liver.

РЕЗЮМЕ

ВЛИЯНИЕ НАТРИЕВЫХ СОЛЕЙ КАРБОКСИМЕТИЛАТОВ ОКСИЭТИЛИРОВАННЫХ ИЗОНИЛФЕНОЛОВ НА ОБЕЗВРЕЖИВАЮЩУЮ ФУНКЦИЮ ПЕЧЕНИ В ПОДОСТРОМ ТОКСИКОЛОГИЧЕСКОМ ЭКСПЕРИМЕНТЕ

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Целью исследования явилось изучение влияния натриевых солей карбоксиметилатов оксиэтилированных изонилфенолов на состояние микросомальной монооксигеназной системы детоксикации гепатоцитов и реакции конъюгации в условиях подострого эксперимента и определение потенциальной опасности для теплокровных животных и человека.

Объектом исследования были белые крысы популяции WAG. Изучено влияние натриевых солей карбоксиметилатов оксиэтилированных изонилфенолов марок АФС9-4 КМ, АФС9-6 КМ, АФС9-10 КМ на состояние микросомальной монооксигеназной системы детоксикации гепатоцитов и реакции конъюгации в условиях подострого эксперимента.

Установлено, что изучаемые вещества при подостром воздействии в токсикологическом эксперименте стимулируют гидроксиллирующую микросомальную монооксигеназную систему гепатоцитов печени, ингибируют реакции образования глюкуронидной и глутатионовой конъюгации на фоне усиления процессов образования ацетильной конъюгации, повышения уровней содержания КоА-SH, ацетил – КоА, кетонных тел.

Исследование проведено в рамках научно-исследовательской работы Харьковского национального медицинского университета «Биохимические механизмы развития дисметаболических процессов в условиях влияния химических факторов окружающей среды».

რეზიუმე

ოქსიეთილირებულ იზონილფენოლთა კარბოქსიმეთილატ ნატრიუმის მარილების ზეგავლენა ღვიძლის გაუვნებლობის ფუნქციაზე ქვემწვავე ტოქსიკოლოგიური ექსპერიმენტის დროს

დ. მარაკუშინი, ი. კარმაზინა, ი. ისაევა, ნ. გლობა

ხარკოვის ეროვნული სამედიცინო უნივერსიტეტი, უკრაინა

კვლევის მიზანს წარმოადგენდა ოქსიეთილირებული იზონილფენოლთა კარბოქსიმეთილატ ნატრიუმის მარილების ზეგავლენის შესწავლა ჰეპატოციტების დეტოქსიკაციის მიკროსომალური მონოოქსიგენაზური სისტემის მდგომარეობაზე და კონიუგაციის რეაქციებზე ქვემწვავე ექსპერიმენტის პირობებში, პოტენციური საფრთხის განსაზღვრით თბილსისხლიანი ცხოველები-სა და ადამიანებისთვის.

კვლევის ობიექტი იყო WAG პოპულაციის თეთრი ვირთაგვები. შესწავლილია ოქსიეთილირებული იზონილფენოლთა კარბოქსიმეთილატ ნატრიუმის მარილების АФС9-4 КМ, АФС9-6 КМ, АФС9-10 КМ მარკების ზეგავლენა ჰეპატოციტების დეტოქსიკაციის მიკროსომალური მონოოქსიგენაზური სისტემის მდგომარეობაზე და კონიუგაციის რეაქციებზე ქვემწვავე ექსპერიმენტის პირობებში.

დადგენილია, რომ შესასწავლი ნივთიერებები, ტოქსიკოლოგიური ექსპერიმენტის პირობებში ქვემწვავე ზემოქმედების დროს იწვევენ ღვიძლის ჰეპატოციტების ჰიდროქსილირებულ მიკროსომალურ მონოოქსიგენაზურ სისტემის სტიმულაციას და გლუკურონიდური და გლუტათიონური კონიუგაციის რეაქციების ინგიბირებას აცეტილირებული კონიუგაციის წარმოქმნის პროცესების გაძლიერების, კეტონის სხეულებში КоА-SH, КоА – აცეტილის შემცველობის დონის ამაღლების ფონზე.

კვლევა ჩატარდა ხარკოვის ეროვნული სამედიცინო უნივერსიტეტის სამეცნიერო-კვლევითი სამუშაოს «დისმეტაბოლური პროცესების განვითარების ბიოქიმიური მექანიზმები გარემოს ქიმიური ფაქტორების ზეგავლენის პირობებში» ფარგლებში.

THE INFLUENCE OF MONOSODIUM GLUTAMATE ADMINISTRATION ON GENERATION OF REACTIVE OXYGEN SPECIES AND APOPTOSIS OF BLOOD LEUKOCYTES IN RATS

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The use of food additives in food manufacturing has been a public health issue for many years. Currently, more than 3000 food additives have been approved by The Food and Drug Administration of the United States and estimates has shown that each person may consume 3.6 to 4.5 kg of food additives per year on average, but these values may be even greater [5,8,10]. The business of food additives is thriving and may reach \$45 billion by 2020. Perhaps the most significant trend driving growth in additives is a general increase in processed foods consumption across the world [18].

One of the most common food additives in Ukraine and in Europe is monosodium glutamate (MSG, C₅H₈NO₄NaH₂O). Encoded E621, it is a food additive from a group of flavor enhancers, used in a wide range of foods, such as soups, sauces, mixed condiments, chips, meat products, and puddings. Despite its widespread use and generally considered safety, there are reports which indicate that MSG is toxic to humans and laboratory animals especially at high doses [21].

Total intake of glutamate from food in European countries is generally stable and ranged from 5 to 12 g/day. A maximum intake of