ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Effect of different doses of melanin in the blood protein changes in rats under alkaline esophageal burns.

Chornenka NM*, Raetska Ya. B, Savchuk OM, Kompanets IV, Beregova TV, Ostapchenko LI.

Taras Shevchenko National University of Kyiv, ESC "The Institute of biology", Ukraine.
2/12 Academician Glushkov Avenue, Kyiv 03022, Ukraine.

ABSTRACT

The studied effect of different doses of melanin in the blood protein changes in rats under alkaline esophageal burns first and second degree. It shows the positive effect of melanin in doses of 0.5 and 1 mg / kg on indicators of endogenous intoxication and distribution of protein fractions. The melanin demonstrates anti-toxic activity and is a promising tool for the prevention and treatment of burn effects.
Keywords: alkali burn of esophagus, peptide pool, melanin.

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Today, corrosive substances commonly used in daily life and even warning signs and bright markings do not prevent accidents that occur during ingestion of these substances to children worldwide. Although the mortality rate is not high, burn the esophagus leads to disability of the child [1]. Burn disease causes dysfunction of all tissues and organs [2]. Is well known that about 40% of ingesting damaging agent accounts for lesions of the esophagus [3,4]. The major strategies of the treatment of burns is inhibiting inflammation, bacterial colonization and prevent further esophagostenosis [5]. There are different methods for the treatment of esophageal burns consequences, but none of the treatment strategies has generally recognized. This problem leads to increased researches of new therapeutic drugs to prevent the complications after esophageal burns. Some practical and theoretical interest is the study of protein fractions in blood after burns and using medical therapy, can open new perspectives for the treatment of ambustial complications.

The aim of this study was determine the content changes of protein fractions in serum upon the simulation of alkaline esophageal burns of the 1st and 2nd grade, when using the drug melanin in different dosages.

MATERIALS AND METHODS

In the experiment followed the general ethical principles of experiments of animals, approved the first National Congress on Bioethics Ukraine and other international agreements and the national legislation in this area. We used nonlinear immature white rats (1 month) weighing 90-110g (according to 1-4 age children). The animals were experimentally simulated with the alkali esophageal burn (ABE) with 10% (grade 1) and 20% (grade 2) solvent of NaOH [6]. The animals were kept on a standard vivarium diet. The animals were divided into 9 groups: 1st- intact rats, 2nd and 3rd group ABE of 1st and 2nd grade saline was injected in the appropriate dose and time, 4th 5th and 6th group ABE of 1st grade , which was injected with melanin start from 2nd day of the experiment at a dose of 0,1mg/kg, 0,5mg/kg and 1mg/kg respectively for 14 days, 7th , 8th and 9th group ABE of 2nd grade , which was injected with melanin start from 2nd day of the experiment at a dose of 0,1mg/kg, 0,5mg/kg and 1mg/kg respectively for 14 days. In our investigate we used the melanin that produced yeast-like fungi *Nadsoniella nigra* strain X1 which obtained from cliffs Halindez island. The material selected for the research at 7th , 15th and 21st day, according to the stage of burn disease [7]. The method of removing animals from the experiment was cervical dislocation. Biochemical parameters were measured in serum, which receiving of blood centrifugation at 2000g × 40 min. Indexes of total protein were determined by biochemical analyzer Humalyser 3000 using respective sets. Level of peptides pool were measured by method Gabrielian with modifications [8]. Number of short-chain oligopeptides pool was estimated by the level of protein in the supernatant using the method of Bredford. Separation of protein fractions serum rats were determined by method Lemmli with modifications with sodium dodecyl sulfate (SDS) [9]. Polyacrylamide gels (PAGE) were 10%. After the electrophoresis gels were kept in solution of Coumassie R. For estimate the results of electrophoresis used the program Totallab 2.01. Total protein was measured by the method of Bradford [10]. The statistical analysis of the obtained results was performed using the methods of variation statistics using the computer program Excel. To determine the reliability of the differences between the two samples we used the Student test (t). Whereby differences $P < 0.05$ were deemed reliable.

RESULTS

To date, most of the authors describe the peptides pool (PP) and short-chain oligopeptide pool (OP) as a universal marker of endogenous intoxication [11-14] PP and SOP are belonging nonspecific toxins are formed by proteolytic cleavage of plasma proteins, biogenic amines, prostaglandins and several other compounds. [14,15]. Previously already studied the concentration of PP and OP in serum of rats after experimental alkali burns of esophagus ABE 1st and 2nd grade [16], so the next step was determine the PP and OP under conditions of administration of melanin in different doses (Table 1,2).

Found that the highest level of PP and OP in serum under conditions ABE 1st and 2nd grade was on day 7 of the experiment, for the peptides pool was exceeded by 36% and 42%, for short-chain oligopeptide pool on 17.6% and 82% respectively, for ABE 1st and 2nd grade, compared with the control. With the administration of the drug melanin, we saw decrease meaning in ABE 1st and 2nd grade with most significant, on 7th days for PP

on 18% and 19% for OP on 32% and 33% respectively compared to the ABE 1st and 2nd grade. It was also studied the concentration of total protein in serum under conditions of ABE 1st and 2nd grade and under conditions of administered drug (Table 1, 2). The total protein level in serum of rats after experimental ABE grade 1st and 2nd a significant reduction in all days of the experiment [16] when administered melanin at ABE 1st and 2nd grade most effective was a dose of 1 mg / kg, increased the concentration of total protein on 7th days by 9% and 54.1% compared to esophageal burn 1st and 2nd degrees, respectively.

Electrophoretic analysis of serum protein composition in experimental animals and in control of the studied samples showed the presence of protein fractions from 15 to 168 kDa (Table 3, 4). Previously, was studied quantitative changes in protein fractions under conditions of esophageal burn, 1st and 2nd grade [16], the next stage was comparison the content of protein fractions under conditions of administration melanin.

Were obtained the protein fractions with molecular weight 168 kDa and 150kDa these protein stripes correspond to IgG fraction, and in view of obtained data on fluctuations of their levels, of some interest are analysis of their levels and a more detailed study. With the introduction melanin, in all different doses throughout the experiment, on 7th , 15th and 21st days (168kDa at doses of 0.5mg/kg to 51.8%, 76.7% and 61.4%, for ABE 1st grade, 150kDa 86%, 87.2% and 83.8% for ABE 2nd grade), which may indicate the influence of melanin on the mechanisms of inflammation.

Protein faction m.m. 130kDa reduced under condition of introduction of melanin throughout all days of the experiment (dose of 0.5 mg / kg to 91.8%, 86.3% and 11.4%, respectively 7th,15th and 21st days of ABE 1st grade and 85%, 93.7% and 65.6% respectively 7th, 15th and 21st days of ABE 2nd grade).

Analysis of electrophoretograms showed decreased levels of protein fraction m.m. in consequence of melanin, these fraction can match, C-reactive protein, which is one of the major proteins in the acute phase of inflammation, the application of melanin in all doses at ABE 1st grade decreased throughout the experiment compared with the performance without melanin(the dose of 0.5 mg/kg by 85%, 14.8% and 26.5%), with ABE 2nd grade the concentration of the fraction increased with all doses of melanin, on the 7th day of the experiment and fell to 15th and 21st days (dose 1 mg/kg 77.7% and 52.6%).

We have shown decreased levels of the fraction m.m. 67kDa that can match albumin faction, after simulation of chemical burns grade 1 and 2 in all days of the experiment [16], the administration of melanin was observed with increase in concentration of this index on all days of experiment in ABE 1st (dose of 0.5 mg/kg to 74.4%, 46.3%and 232,2%) and ABE 2nd (dose 0.5 mg/kg 113%, 64,7% and 37.4%), which indicated a positive influence of melanin on protein synthesis, after simulation of chemical burn of the esophagus.

Shown faction m.m. 55 kDa, which corresponds prealbumin fraction was decreased compared to control animals [16], provided, introduced of melanin there factions increased within the experiment with ABE 1st (dose of 1 mg / kg of 40%, 47.7% and 203.5%), while ABE 2nd observed increased fractions on 7th day and reduced on the 15th and 21st days of the experiment.

Postalbumin fraction at 40 kDa were decreased at the all days of the experiment, the used of melanin, this index concentration increased at ABE 1st (dose of 1 mg / kg 140.5%, 591.5% and 698%), with ABE 2nd, concentration decreased by 15th days the application all doses of melanin, and the concentration was increased to 7th and 21st days (dose of 0.5 mg / kg to 70.8% and 30%).

Level of postalbumin ~ 25 kDa and 15 kDa fraction was significantly decreased after simulation of alkali burns. Level of 25 kDa was increased at the ABE 1st (dose of 1 mg / kg to 157.5% 157% and 158%) while for the ABE 2nd grade level decreased of 7th and 15th days (dose of 1 mg / kg of 35% and 89%) and increased of 21st day (dose of 1 mg / kg to 198%) at the introduction of melanin in respective doses. The level of fraction 15kDa, was decreased after burn, owing to introduction of melanin was increased at the ABE 1st (dose of 1 mg / kg 7.4%, 10.6% and 205%), the ABE 2nd was increased (dose 0.5 mg / kg to 11.6%, 78.2% and 19%).

ISSN: 0975-8585

Table 1 Level of peptide pool, short-chain oligopeptide pool and total protein in blood serum after ABE grade 1st and after administration of melanin of various doses (M ± m, n = 8)

Index	Control	Burn NaOH 10%											
		7th day				15th day				21st day			
		ABE 1	ABE 1+melanin 0,1mg/1 kg	ABE 1+melanin 0,5mg/1 kg	ABE 1+melanin 1mg/1 kg	ABE 1	ABE 1+melanin 0,1mg/1 kg	ABE 1+melanin 0,5mg/1 kg	ABE 1+melanin 1mg/1 kg	ABE 1	ABE 1+melanin 0,1mg/1 kg	ABE 1+melanin 0,5mg/1 kg	ABE 1+melanin 1mg/1 kg
PP, (mg/ml)	0,42±0,01	0,59±0,01*	0,46±0,02*#	0,51±0,02*#	0,49±0,01*#	0,51±0,02*	0.46±0,01*#	0.44±0,01#	0.46±0,02*#	0,48±0,01*	0.38±0,02*#	0.4±0,02#	0.46±0,02*
SOP, (mg/ml)	0,17±0,01	0,27±0,01*	0,22±0,02*#	0,195±0,01*#	0,185±0,01#	0,1±0,02*	0.16±0,02#	0.15±0,02#	0.21±0,02*#	0,13±0,03*	0.15±0,02	0.14±0,01*	0.18±0,02#
Total protein(mg/dl)	65,01±0,8	62,3±0,8*	63,7±1,5	59,8±1,2*#	63,1±1,4	64,1±0,36	64,2±1,1	47,2±1,5*#	70,1±1,0*#	67,3±1,3*	70,6±0,9*#	73,4±1,2*#	73,1±1,4*#

* – p<0,05 compared with control value; # - p<0,05 compared with AEB value

ISSN: 0975-8585

Table 2 Level of peptide pool, short-chain oligopeptide pool and total protein in blood serum after ABE grade 2nd and after administration of melanin of various doses (M ± m, n = 8)

Index	Control	Burn NaOH 20%											
		7th day				15th day				21st day			
		ABE 2	ABE 2+melanin 0,1mg/1 kg	ABE 2+melanin 0,5mg/1 kg	ABE 2+melanin 1mg/1 kg	ABE 2	ABE 2+melanin 0,1mg/1 kg	ABE 2+melanin 0,5mg/1 kg	ABE 2+melanin 1mg/1 kg	ABE 2	ABE 2+melanin 0,1mg/1 kg	ABE 2+melanin 0,5mg/1 kg	ABE 2+melanin 1mg/1 kg
PP, (mg/ml)	0,42±0,01	0,6±0,01*	0,51±0,02*#	0,52±0,02*#	0,486±0,01*#	0,49±0,01*	0.53±0,01*#	0.46±0,01*#	0.4±0,02#	0,42±0,01	0.38±0,02*#	0.4±0,02	0.44±0,02
SOP, (mg/ml)	0,17±0,01	0,31±0,03*	0,23±0,02*#	0,2±0,01*#	0,21±0,01#	0,15±0,02*	0.175±0,02	0.165±0,02	0.17±0,02	0,17±0,03*	0.15±0,02	0.17±0,01	0.186±0,02
Total protein(mg/dl)	65,01±0,8	41,2±1*	62,5±0,56*#	60,01±0,96*#	63,5±0,89#	60,5±0,7*	63,5±1,2*#	64±0,45#	61,4±1,5*#	67,3±0,8*	65,5±0,89#	73,8±1,2*#	62,7±0,38*#

* – p<0,05 compared with control value; # - p<0,05 compared with AEB value

ISSN: 0975-8585

Table 3. Relative content of proteins fraction in blood serum after simulation ABE grade 1st and after administration of melanin of various doses (µg /mg protein) M±m, n=3

Proteins fraction m.m. (kDa)	Control	Burn NaOH 10%											
		7th day				15th day				21st day			
		ABE 1	ABE 1+melanin 0,1mg/1 kg	ABE 1+melanin 0,5mg/1 kg	ABE 1+melanin 1mg/1 kg	ABE 1	ABE 1+melanin 0,1mg/1 kg	ABE 1+melanin 0,5mg/1 kg	ABE 1+melanin 1mg/1 kg	ABE 1	ABE 1+melanin 0,1mg/1 kg	ABE 1+melanin 0,5mg/1 kg	ABE 1+melanin 1mg/1 kg
168 (γ- globulin fraction)	86±3,4	136.0±6.5*	82.9±1.5#	65.6±5.5*#	90.2±3.5#	291.0±10.5*	52,1±5.8*#	67,9±4.7*#	62,4±5.1*#	219.3±3.7*	80,3±7.2#	84,6±6.5#	57,6±4.3*#
150(γ- globulin fraction)	156.1±5.2	160.7±1.2*	101,4±6.8*#	90,1±4.4*#	85,8±7.8*#	244.0±13.4*	61,3±6.7*#	67,1±5.9*#	52,3±3.5*#	301.0±12.7*	42,1±3.9*#	60,8±4.5*#	72,4±5.1*#
130	449.2±8.6	931.1±21.5*	71.6±6.9*#	76.1±8.5*#	70.9±5.8*#	417.5±3.9*	45,1±7.8*#	57,3±5.7*#	36,8±3.5*#	62.9±3.1*	50,7±3.7*#	55,7±4.5*	66,6±5.5*
113	60.2±2.1	207.3±8.4*	50.7±3.5*#	31.4±3.1*#	46.7±4.2*#	62.1±1.9	40,1±3.5*#	52,9±5.5*#	73,3±5.4*#	60.5±2.8	44,5±3.9*#	44,5±3.5*#	91,1±5.7*#
103	185.7±3.8	189.5±6.2	68.9±4.7*#	62.6±3.7*#	48,9±3.9*#	127.0±4,3*	59,2±5.1*#	68,2±3.5*#	96,8±4.5*#	190.0±7,8*	58±3.5*#	150,6±5.8*#	156,3±4.8*#
89	126.1±5,1	54.8±0.9*	89.4±4.7*#	76.5±3.9*#	63.5±4.0*#	18.7±0.3*	50,5±2.7*#	73,1±5.2*#	73,8±4.6*#	14.0±0.7*	104,7±5.8*#	114,8±4.8*#	91,5±6.8*#
Albumin fraction – 67	54.7±1.6	48.9±1.8*	94,9±2.5*#	85,3±3.1*#	80,5±3.5*#	41.5±1.4*	71,2 ±3.8*#	60,7±2.5*#	57,7±3.2*#	32.1±0.7*	60,7±2.1*#	106,3±3.5*#	80,7 ±2.6*#
Prealbumin fraction – 55	350.0±18.2	305.4±12.2*	400,8±12.5*#	371,5±9.5#	427,1±11.7*#	231.5±8.4*	315,3±12.1*#	393,2±10.5*#	341,9±9.9#	184.5±6.8*	317,1±8.7*#	420±13.5*#	560±13.9*#
Postalbumin fraction ~ 40	18.7±1.1	27.9±0.5*	44,2±2.5*#	40.5±2.8*#	67,1±3.2*#	8.0±0.2*	70,6±4.5*#	70±4,1*#	55,3±2.5*#	7.8±0.1*	61,2±4.2*#	57,2±3.0*#	62,3±3.7*#
Postalbumin fraction ~25	79.5±1.1	22.1±0.76*	71,8±2.5*#	55.1±2.1*#	56.9±1.9*#	24.5±0.57*	84,1±2.7*#	82,1±3.1#	63±2.5*#	25.5±0.3*	71,2±3.1*#	94±4.1*#	65,8±2.8*#
Postalbumin fraction ~15	74.7±1.2	112.0±3.4*	69,3±2.7*#	67.5±1.5*#	120.3±5.1*	73.9±2.3	94,7±3.8*#	89,7±3.2*#	81,7±2.8*#	26.5±1.8*	107,4±5.0*#	99,1±4.7*#	80,8±4.1*#

* – p<0,05 compared with control value; # - p<0,05 compared with AEB value

ISSN: 0975-8585

Table 4. Relative content of proteins fraction in blood serum after simulation ABE grade 2nd and after administration of melanin of various doses (μg /mg protein) M±m, n=3

Proteins fraction m.m. (kDa)	Control	Burn NaOH 20%											
		7th day				15th day				21st day			
		ABE 2	ABE 2+melanin 0,1mg/1 kg	ABE 2+melanin 0,5mg/1 kg	ABE 2+melanin 1mg/1 kg	ABE 2	ABE 2+melanin 0,1mg/1 kg	ABE 2+melanin 0,5mg/1 kg	ABE 2+melanin 1mg/1 kg	ABE 2	ABE 2+melanin 0,1mg/1 kg	ABE 2+melanin 0,5mg/1 kg	ABE 2+melanin 1mg/1 kg
168 (γ-globulin fraction)	86,8 ± 2,5	143,0±00,9*	77,1±2,8*#	87,4±1,8#	74,2±2,1*#	190,2±0,2*	68,7±1,9*#	96,9±2,5*#	69±1,5*#	183,8±5,2*	77,9±1,8*#	67,4±2,3*#	55,1±2,8*#
150 (γ-globulin fraction)	156,7±3,7	219.9±11,4*	52,3±1,7*#	30,8±0,8*#	39,2±2,3*#	275,0±10,2*	36,1±1,1*#	35,2±1,3*#	41,9±1,5*#	320,7±19,6*	56,8±2,2*#	52,1±1,7*#	56,1±2,1*#
130	449,2±28,9	326,4±9,2	60,1±2,9*#	49,7±1,8*#	47,1±2,8*#	231,6±8,12*	22,2±2,15*#	14,6±0,8*#	142,4±1,5*#	73,2±7,4*	34±1,2*#	25,2±0,9*#	26±0,8*#
113	60,8±2,8	9,5±0,8	45,8±2,2*#	35,8±1,75*#	43,3±2,05*#	62,4±2,8*	13,7±0,8*#	11,4±1,04*#	13,9±1,2*#	30,6±1,4*	26,1±1,5*#	28,6±1,8*	14,5±2,8*#
103	185,2±11,7	21,8±2,6*	33,7±2,7*#	49,9±3,1*#	25,4±1,6*	33,7±1,7*	42±2,2*#	30,2±2,9*	23,8±1,56*#	13,6±0,07*	67,8±3,2*#	51,6±2,9*#	30,1±1,45*#
89	126,0±9,1	6,2±0,2*	28,8±1,9*#	27,9±2,2*#	60,6±3,5*#	9,8±0,4*	8,7±0,8*	6,8±1,1*#	3,9±0,4*#	5,02±0,1*	6,1±0,3*#	30,4±1,8*#	50,2±2,7*#
Albumin fraction –67	325,3±16,7	149,3±2,9*	281,2±4,8*#	317,9±6,1#	349,7±7,2*#	173,0±16,9*	360,8±3,9*#	284,9±3,1*#	128,7±4,8*#	234,0±9,9*	319,1±4,9#	321,4±7,8#	311,8±6,9#
Prealbumin fraction – 55	221,0±9,7	57,4±1,8*	60,8±2,8*	65,7±3,1*#	54,1±2,5*	136,1±6,8*	38±1,3*#	34,9±1,2*#	47,9±2,7*#	128,2±4,2*	46,2±2,9*#	50,6±3,4*#	63,4±2,2*#
Postalbumin fraction ~ 40	145,0±0,9	40,0±0,6*	58,2±1,8*#	68,3±2,1*#	54,8±2,5*#	139,0±3,2*	33,1±1,5*#	22,8±2,2*#	20,1±1,8*#	40,0±0,8*	73,5±3,8*#	52±1,1*#	50,1±1,3*#
Postalbumin fraction ~25	79,8±3,1	77,0±2,6*	42,2±2,05*#	50,2±3,8*#	50,1±2,1*#	48±0,8*	18,4±1,3*#	28,5±2,07*#	5,3±0,08*#	18,0±0,05*	54,6±2,1*#	45,8±1,9*#	53,7±0,8*#
Postalbumin fraction ~15	74,5±1,9	68,3±1 *	67,1±0,8*	76,2±2,08#	81,4±1,8*#	20,2±0,1 *	68,1±2,8*#	36±1,7*#	38,4±2,7*#	69,81±0,9 *	116,1±1,8*#	83,1±1,1*#	45,5±1,8*#

* – p<0,05 compared with control value; # - p<0,05 compared with AEB value

DISCUSSION

In many diseases in serum ratio may vary protein fractions, although the overall protein content can remain normal. Represents a practical and theoretical study of possible interest ratio changes protein fractions in experimental animals after alkaline esophageal burns of the 1st and 2nd grade and in condition of administration of melanin. In esophageal burn, is observed deepening of destructive processes that can appear in the enhancing of endogenous intoxication, characterized by peptides pool and short-chain oligopeptide pool (OP). This is the substance of protein nature with a molecular weight of 300-5000 Da, in connection with what are often referred to as the molecules of peptides pool and short-chain oligopeptide pool [15]. Peptides pool became known as important factors of universal intoxication. Accumulation of peptides pool is not only a marker of endogenous intoxication, but also an aggravating factor for the pathological process - getting the role of secondary toxins, they cause the disorder of blood-brain barrier, the microvasculature, violate the transport of amino acids. Play an important role in determining of the course of many biochemical processes in the bodies of burnt patients and in forming of toxemic disorders specific of burn disease [12, 13]. By used electrophoresis can identify the ratio of proteins by their molecular weight and charge. The presence of different protein fractions have different electrophoretic mobility may be a marker of different pathological processes related to metabolic mechanisms on systemic and cellular level. By normal functional proteins contained in serum include albumin and globulin proteins. Albumin – a homogeneous molecular fraction mass (MM) 60-70 kDa. They are well retaining water, which accounted for 80% colloidal osmotic pressure of blood. Serum globulins are a group of proteins lesser degree of dispersion and of varying molecular weight, so MM α1-, α2- and β-globulin ranges from 100 to 450 kDa. The increase of α-globulins in blood observed in inflammatory processes, stress. Increase of γ-globulin observed with increasing immune processes. Reducing γ-globulin observed in conditions associated with exhaustion, depression of the immune system [17]. The burning injury regeneration increases the protein, carbohydrates and nucleic acids metabolism level locally as well as in the whole body. Serum albumin is the most plentiful plasma protein. In humans, albumin is the most abundant plasma protein, accounting for 55–60% of the measured serum protein. Unlike other plasma proteins which tend to have single, specific functions, albumin has been assigned numerous physiological roles. It is the principal agent responsible for the osmotic pressure of blood, for transport of fatty acids, and for the sequestration and transportation of bilirubin [18]. There are different methods for the treatment of esophageal burns consequences, but none of the treatment strategies has generally recognized. To date, there are widespread uses of substances of natural origin to facilitate the flow of burn disease and post complications. Among them, special attention is paid to phenolic compounds, polyphenol compounds [19] belonging to the pigment melanin.Melanin has the following properties fotoprotective, radioprotective [20] and anti-tumor [21,22] immunomodulatory[23], hepatoprotective, antitoxic and antioxidants [24, 25, 26].

Antioxidants are considered as potential protectors in protecting against the development of oxidative stress. Relevant there are non-toxic natural antioxidants as cytoprotectors [27]. The melanin demonstrates anti-toxic activity and is a promising tool for the prevention and treatment of burn effects. Earlier we showed the effectiveness of this drug in the correction of disorders in the endogenous intoxication system in cases of simulation of alkali burns in the esophagus of the 2nd degree at immature rats was [28].

CONCLUTION

We have investigated changes in the content of protein fractions in serum, under conditions esophageal burns, first and second degree, with used drug of melanin, in different doses, the most effective dose of melanin was found 0.5 mg/kg and 1 mg / kg. In summary, after the burn was destruction and cleavaged of proteins tissue and serum, resulting in a peptides pool and short-chain oligopeptide pool. These substances characterized of development of endogenous intoxication. Represents interest of theoretical and practical study of peptide pool and test these molecules in the formation of autoantibodies.

REFERENCES

[1] Efficacy of keratinocyte growth factor (palifermin) for the treatment of caustic esophageal burns Exp Ther Med. 2014 Oct; 8(4): 1087–1091

[2] Jeschke MG, Herndon DN. Burns in children: standard and new treatments. 2014 Mar 29;383(9923):1168-78

[3] Tiryaki T, Livanelioğlu Z, Atayurt H. Early bougienage for relief of stricture formation following caustic esophageal burns. Pediatr Surg Int. 2005;21:78–80.
[4] Han Y, Cheng QS, Li XF, Wang XP. Surgical management of esophageal strictures after caustic burns: a 30 years of experience. World J Gastroenterol. 2004;10:2846–2849.
[5] Cakmak M, Nayci A, Renda N, Erekul S, Gökçora H, Yücesan S. The effect of corticosteroids and pentoxifiline in caustic esophageal burns. Int Surg. 1997;82:371–375).
[6] Raetska Ya.B., Ishchuk.T.V., Dzhus O.I., Savchuk O.M., Ostapchenko L.I. Experimental modeling of 1st and 2nd degrees alkali esophageal burn in immature rats. Biological system, 116-120., 2013.
[7] Fistal E.Y., Koziniec G.G., Samojlenko G.E. et al. (2005). Combustiology. Donetsk.
[8] Gabrielyan N.I., L.E.R., Dmitriev A.A. (1985). Screening method of middle molecules in biological fluids. In Medicine methodical recommendations Medicine, Moscow.
[9] Laemmli, U.K. (1970). Cleavage of structural proteins during the assembly of the head of bacteriophage T4. Nature 227, 680-685.
[10] Bradford, M.M. (1976). A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. Anal Biochem 72, 248.
[11] Chmielewski, M., Cohen, G., Wiecek, A., and Jesus Carrero, J. (2014). The peptidic middle molecules: is molecular weight doing the trick? Semin Nephrol 34, 118-134.
[12] Karyakin, B.S.V. (2004). The middle mass molecule as an integral indicator of metabolic disorders. Clinical Laboratory Services, 3-8.
[13] Krotenko N.M., B.A.S., Yepanchintseva Ye.M., Ivanova S.A (2012). Parameters oxidative stress and endogenous intoxication of peripheral blood in patients with exogenous organic disorders in dynamic of the pharmacotherapy. Bulletin of Siberian Medicine, 179-185.
[14] Nikolskaya V. A., Memetova Z.N. (2013). Level of middle mass molecules in serum and mouth liquid in pregnant women in a state of hyperinsulinism and gestational diabetes mellitus. Scientific Notes of-Taurida National V.I. Vernadsky University eries “Biology and Chemistry” 26, 132-137.
[15] Bondarenko V.V, Netyuhaylo L.G, Avetikov D.S., Average mass molecules in the tissues of the salivary glands in experimental burn disease // Taurian Medical and Biology -2012- Journal Volume: 15 Number: 3-1 p: 49-50
[16] Ishchuk, T., Raetska, Y., Savchuk, O., & Ostapchenko, L. (2015). Changes blood protein composition under experimental chemical burns of esophageal development in rats. Biomedical Research And Therapy, 2(3):241-249.
[17] E. Klimova*, O. Zvyagintseva**, A. Malyshev**Change of blood serum protein fraction ratio at experimental animals of different age after immunization by cytotoxic serum of patient with autoimmune disease – myasthenia
[18] Norbury, W.B., Herndon, D.N., Branski, L.K., Chinkes, D.L., and Jeschke, M.G. (2008). Urinary cortisol and catecholamine excretion after burn injury in children. The Journal of clinical endocrinology and metabolism 93, 1270-1275.
[19] B Srikanta, M Siddaraju, S Dharmesh A novel phenol-bound pectic polysaccharide from Decalepis hamiltonii with multi-step ulcer preventive activity. World journal of gastroenterology 13 (39), 5196-5207
[20] Sobko V.M. , Martynyuk V.S., Gudkova D.O. Protectsve effect of melanine on the h2o2-indused injury and programmed cell death of rat’s thymocytes upon influence electromagnetic field with frequency of 8 Hz Phisics of alive T. 18, 2010. P. 65-70
[21] Kripke ML. Skin cancer, photoimmunology, and urocanic acid //Photodermatology. – 1984. – Vol.1. – P.161–163.
[22] Mackintosh JA. The antimicrobial properties of melanocytes, melanosomes and melanin and the evolution of black skin // J Theor Biol. – 2001. – Vol.211. – P.101–113.
[23] Lin JY, Fisher DE. Melanocyte biology and skin pigmentation // Nature. – 2007. – Vol.445. – P.843–850.
[24] Brenner M. Hearling V.G. The protective role of melanin against UV damage in human skin // Photochem Photobiol.– 2008. – Vol. 84(3). – P. 539-549.
[25] Goding CR. Melanocytes: the new Black// Int J Biochem Cell Biol. – 2007. – Vol.39. – P.275–279.
[26] Holleran WM, Uchida Y, Halkier-Sorensen L, Haratake A. Structural and biochemical basis for the UVB-induced alterations in epidermal barrier function// Photodermatol Photoimmunol Photomed. – 1997. – Vol.13. – P.117–128.

[27] Chaturvedi A1, Kumar MM, Bhawani G, Chaturvedi H, Kumar M, Goel RK. Effect of ethanolic extract of Eugenia jambolana seeds on gastric ulceration and secretion in rats. Indian J Physiol Pharmacol. 2007 Apr-Jun;51(2):131-40.

[28] Chornenka NM, Raetska YA. B, Savchuk OM, Torgalo EO, Beregova TV, and Ostapchenko LI. Correction Parameters of Endogenous Intoxication in Experimental Burn Disease at the Stage of Toxemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences September – October 2016 RJPBCS 7(5) Page No. 1042