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Increasing antioxidant protection during mebendazole and AKβ vitamin complex treatment of experimental trichinellosis in rats

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Summary

To enhance the effect of treatment method of Trichinellosis with mebendazole, lipid peroxidation processes (LPP) in blood of Wistar rats experimentally infected with *Trichinella spiralis* were investigated. In accordance with health condition of infected rats treated with mebendazole and combination of mebendazole and AKβ vitamin complex, dynamics of the main values of the LPP (such as: activity of superoxide dismutase (SOD) and catalase (CAT) in erythrocytes and malonic dialdehyde (MDA) concentration in blood serum) were analyzed. It was concluded that mebendazole amplifies the LPP in rat's blood. Additional administrations of the AKβ vitamin complex allow improvement of LPP parameters, raising compensatory-adaptive reactions of the host organism and reducing the rate of the experimental animal's mortality.

Keywords: AKβ vitamin complex; catalase; lipid peroxidation process; malonic dialdehyde; mebendazole; superoxide dismutase; *Trichinella spiralis*

List of abbreviations: LPP - lipid peroxidation processes; (SOD) superoxide dismutase; CAT - atalase; MDA - malonic dialdehyde; AK - AKβ vitamin complex; DNA - deoxyribonucleic acid; RBC - red blood cells, HB - hemoglobin; p.i. - post infection

Introduction

The free-radical process of lipid peroxidation (LPP) is considered physiological because it is typical for physiological cell metabolism (Vladimirov & Archakov, 1972; Dianzani, 1992; Harman, 1992). The activation of free radical chain reactions and excessive accumulation of secondary products of lipid peroxidation - as a ketones and malonic dialdehyde (MDA) - bring about, however, heavy consequences known as peroxide stress. It is manifested by inhibition of glycolysis, destruction of coenzyme A, cytochrome P450 inactivation, protein and DNA biosynthesis alteration; disorder of the cell membrane and the membrane enzyme inactivation have been observed (Vladimirov & Archakov, 1972; Halliwell, 1991).

The free radical oxidation processes are regulated by non-enzymatic bioantioxidants (vitamin E, vitamin A, vitamin C, ubiquinone, glutathion and others) and antioxidant enzymatic systems. The main constituents of enzymatic component of antioxidant defense system of the organism are superoxide dismutase (SOD) and catalase (CAT) which participate in neutralization of free radicals and peroxides surplus (Vladimirov & Archakov, 1972).

Under chronic influence of damaging agents, such as radiation, ksenobiotics and so on, the free radical reactions are activated, which leads to oppression of organism defense or development of antioxidant insufficiency. At the same time this conduces to immunodysfunctions and to damage of the immunocompetent cells; and it is one of the main reasons for the decline of non-specific resistance of organism (Smirnov & Suskova, 1989; Bagley, 2000).

Intensification of free radical oxidation processes is presently considered one of the significant mechanisms in the development of more than fifty human diseases of various etiologies (Halliwell, 1991). At the same time, the study of literature shows that this aspect is the least studied part of pathogenesis of helminthiasis, and Trichinellosis especially.

Trichinellosis is not only a serious medical problem, but also a cause of economic damage. This is conditioned by the general existence of natural sources of infection, which cause a significant level of human and animal morbidity (Hurníková *et al.*, 2005; Pozio & Zarlenga, 2005; Chistenko &Vedenko, 2006; Pozio, 2007).

Anthelmintics (mebendazole, thiabendazole) are used in complex with corticosteroids in Trichinellosis treatment, which can often lead to severe complications (Ozereckovskaya, 1985; Kociecka, 1996). Furthermore,

regarding our observation results and facts noted in other sources: Mebendazole treatment, used for experimental Trichinellosis, leads to deaths of majority of experimental animals. Immune system dysfunction and toxic manifestation, which arise during Trichinellosis and in the background of its specific therapy, can be in many cases conditioned by the intensification of the LPP processes (Bekish *et al.*, 1980a; Tolstoy *et al.*, 2000; Kolodziej-Sobocinska *et al.*, 2006; Tolstoj *et al.*, 2007;). The question of decreasing anthelmintics toxicity without diminishing their therapeutic effect remains open today.

Natural oxidants and special vitamins have been recently used extensively for improving metabolic processes and for increasing general non-specific resistance of an organism. A new vitamin complex AKβ (Rutkovskaya & Morozkina, 2006) comprising of vitamins E, A, C and β-caroten deserves our attention. In practice, Trichinellosis treatment with AKβ may seem to be very interesting not only due to its cytoprotective and anti-stress effect, but also because during Trichinellosis a deficit of exactly those vitamins is present (Bekish, 1978; Figallová, Prokopic, 1987; Senutaite, 1990). We do not have any information about the use of AKβ during Trichinellosis.

As follows from the above-described, the purpose of the present study is to investigate the evolution of the main characteristics of lipid peroxidation processes (LPP) in rats infected with *Trichinella spiralis* without treatment and also with mebendazole and AKβ vitamin complex treatment.

Our main objectives were: to determine erythrocyte superoxide dismutase (RBC-SOD) activity and erythrocyte catalase (RBC-CAT) activity; to determine malonic dialdehyde (MDA) level in blood serum, and to analyze treatment effectiveness on the health condition of experimental animals.

Materials and methods

Housing/animal care

For our study, we used 236 males of outbred Wistar rats with an average body weight of

180 g. The rats came from the Belarus State Medical University breeding facility and underwent an acclimatization period of 10 days. During the experiment, the rats were housed in a conventional animal room. The animals (in groups of 2 – 4 per cage) were kept in type K5 clear styrofoam cages. Wood shavings were used for bedding. The room was maintained at 20 ± 2°C and 50 ± 10 % relative humidity with natural lighting. The air was automatically ventilated 10 – 15 times per hour. Pellet rodent food and tap water in drinking bottles were given ad libitum. Cages, bedding, steel wire tops and bottles were changed twice a week.

Assessment of superoxide dismutase activity

Superoxide dismutase activity was detected by the method of Kostiuk *et al.* (1990), which is based on the inhibition of quercetin auto-oxidation. SOD activity was measured in diluted hemolysate (1:1,000) by the spectrophotometer CF-46 (LOMO, St. Petersburg, Russia). Experimental tests contained 0.05 ml of hemolysate; the control tests contained the same volume of distilled water. The percentage of inhibition of quercetin auto-oxidation in the experimental and control samples in 20 min ($T_{SOD\text{-}20}$) was calculated on the basis of the formula:

$A_{SOD} = T_{SOD-20}$ x 1,000 / C_{Hb}

A_{SOD} – *superoxide dismutase activity (units / mg Hb)*

1,000 – *hemolysate diluting*

C_{Hb} – *hemoglobin volume in hemolysate (mg)*

Assessment of catalase activity

Catalase activity was measured in diluted hemolysate (1:1,000) by the spectrophotometer CF-46, λ = 410 nm (LOMO, St. Petersburg, Russia), with the use of 0.03% hydrogen peroxide and 4 % ammonium molybdate (Mamontova *et al.*, 1994). Final activities in erythrocytes were expressed in units per gram of hemoglobin.

Malonic dialdehyde concentration

The concentration of MDA was determined by a spectrophotometric method (spectrophotometer CF-46), using thiobarbituric acid (Gavrilov *et al.*, 1987). It was expressed in nmol/ml.

Study design

After the acclimatization period, the rats were randomly divided into six groups. The first one was the control (C, n = 28) group and included *Trichinella*-free rats. The second group (C + M, n = 30) included *Trichinella*-free rats, which were administered mebendazole. The third group (C + M + AK, n = 30) included *Trichinella*-free rats, which were administered mebendazole and AKβ vitamin complex. The fourth group (T, n = 28) included rats experimentally infected with *T. spiralis* without treatment. The fifth group (T + M, n = 60) included rats experimentally infected with *T. spiralis* with mebendazole treatment. And the sixth group (T + M + AK, n = 60) included rats experimentally infected with *T. spiralis* which were administered Mebendazole and AKβ vitamin complex.

In this study we used the laboratory strain of T. spiralis from "Belarus Medical University" which was obtained from a pig and passed on albino rats. Sixty-day-old larvae of *T. spiralis* were recovered from the infected rats by the acid-pepsin digestion method. Groups T, T + M and T + M + AK were infected with larvae of *T. spiralis* in a dose of 20 larvae/g of body weight of the rat (Bekish *et al.*, 1980b). The average intensity of infection was 3,600 larvae per rat.

Vitamin injections were given on days 14, 16, 18 and 20 post infections. The vitamin C (5 % solution of ascorbic acid) dose was 4 ml/kg of body weight in intramuscular injection. Mixture of vitamins A, E and β-caroten were given subcutaneous in dose: Tocoferoli acetas 0.08 mg/g of body weight, Retinoli acetas 0.001 mg/g of body weight, β-caroten 0.0036 mg/g of body weight.

The mebendazole (Vermox, Gedeon Richter, Hungary) dose was 50 mg/kg of body weight. It was given per os by a single application for 3 days (days 15, 16, and 17 p.i.). The first mebendazole application was given on the next day after the first injection with vitamins. The infected and control rats were killed by administration of an overdose of Thiopental Natricum anaesthetic (Thiopental ICN, ICN Czech Republic a.s., Czech Republic) on day 21, 30, 45 and 60 post-infection and their blood was taken for examination. The experimental group consists of between eight to fifteen rats for one period of the experiment. In the groups
C and C + M + AK the blood examination on day 60 was not implemented. All rats were weighed at the beginning of the experiment and then on day 14, 21, 45 and 60.

Statistics
Statistical analysis was performed using Student's *t* test for unpaired data. A *P* value of less than 0.05 was considered statistically significant.

Results and discussion

During our study we detected the intensification of the lipid peroxidation processes (LPP) and also considerable changes in the enzymatic part of the antioxidant system. Therefore, SOD activity in the erythrocytes of untreated animals during Trichinellosis (group T) decreased on day 21 ($P < 0.05$). Inhibitory effect on SOD was probable caused by metabolites which were excreted by *T. spiralis* larvae during their hematogenous migration. This phenomenon can be explained as evolutionary mechanism of parasites to reduce nonspecific resistance of a host organism and facilitate larvae penetration through sarcoplasma of muscular fibres. But on day 30 it increased and reached 192.4 ± 17.8 units / mg Hb ($P < 0.05$) compared with the levels of the control group and remained high during the whole observation period (Fig. 1.).
Catalase activity in this group throughout the entire experiment, except day 60, was significantly higher compared with the control group levels, and it reached a maximum value on day 30 (1.36 ± 0.10 units / g Hb; $P < 0.001$). It is necessary to note that the decreasing activity of one enzyme (more often SOD) with simultaneous decreasing activity of another indicate intensification of the LPP and can be one of criteria for a homeostatis disturbance of the antioxidant status (Akhmedov DR 1994; Miroshnichenko 1992). In the group with untreated Trichinellosis (T), the same effect was observed on day 21 post infection (Fig. 1, 2). At the same time, the MDA level in blood serum in this group was at its maximum (Table 1). The MDA concentration in group T on day 30 was also high, but Catalase and SOD activity increased and almost twice exceeded the values of group C - which, can be probably perceived as an adaptation reaction of host organism, since during the subsequent periods of observation, the condition of functional activity of both enzymes remained coordinated, and MDA concentration decreased. The peak of the explored characteristics coincides with the peak of biological activity of the *Trichinella spiralis* larvae, 21 – 30 days post infection, which corresponds with the period of larvae migration through blood system, their penetration into skeletal muscles and encystation (Bekish, 1978; Senutaite, 1990). Afterwards, when cyst capsule is formed, parasite

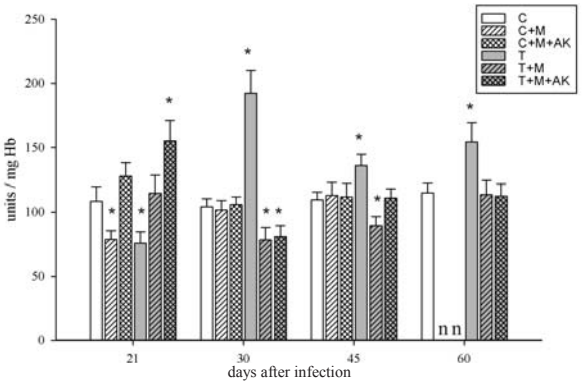

Fig.1. Activity of superoxide dismutase (SOD) in the blood serum of the laboratory rats

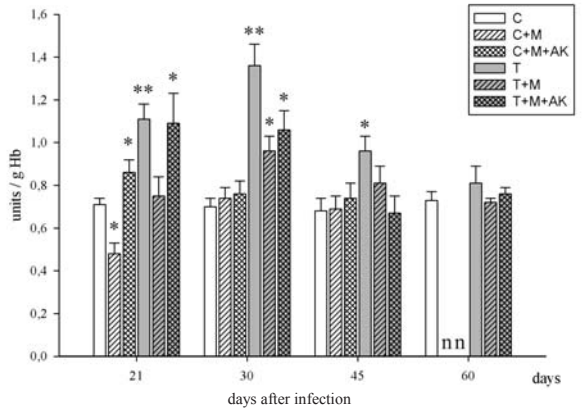

Fig.2. Activity of catalase (CAT) in the blood serum of the laboratory rats

Table 1. Malonic dialdehyde (MDA) concentration (nmol/ml) in the blood serum of laboratory rats depending on the method of treatment

Groups / Days	21	30	45	60
C	2.02±0.09	2.08±0.06	1.93±0.08	2.00±0.08
C+M	3.74±0.39*	2.84±0.19*	2.10±0.08	---
C+M+AK	2.61±0.11**	2.16±0.20	2.06±0.23	---
T	4.12±0.28**	3.06±0.31*	2.26±0.23	2.17±0.16
T+M	4.08±0.34**	3.87±0.19**	2.32±0.14*	1.97±0.17
T+M+AK	2.78±0.17*	2.29±0.07*	1.97±0.12	2.04±0.10

***P*<0.001; **P*<0.05 compared to the control group levels

C - control group; C+M - *Trichinella*-free rats administered mebendazole; C+M+AK - *Trichinella*-free rats administered mebendazole and AKβ vitamin complex; T - rats experimentally infected with *T. spiralis* without treatment; T+M - rats experimentally infected with *T. spiralis* with mebendazole treatment; T+M+AK - rats experimentally infected with *T. spiralis* and administered mebendazole and AKβ vitamin complex.* - significant difference in compare to control group with $p < 0.05$; ** - significant difference in compare to control group with $p < 0.01$; n - none data measured

Table 2. Body weight changes (g) in laboratory rats depending on the method of treatment

Groups / Days	14	21	30	45	60
C	199.9 ± 1.80	213.1 ± 2.59	225.2 ± 2.31	247.8 ± 2.60	271.1 ± 4.95
C+M	200.8 ± 2.0	171.1 ± 1.29**	220.6 ± 3.10	241.4 ± 5.37	xxx
C+M+AK	200.1 ± 1.89	198.6 ± 2.95**	222.7 ± 2.61	245.0 ± 3.81	xxx
T	188.3 ± 2.77*	215.4 ± 3.0	213.6 ± 3.64*	252.2 ± 3.03	275.6 ± 4.41
T+M	187.6 ± 1.86**	166.3 ± 1.77**	162.9 ± 3.47**	198.4 ± 3.50**	264.8 ± 8.44
T+M+AK	185.7 ± 2.14**	181.8 ± 2.47**	179.5 ± 2.88**	215.0 ± 2.39**	268.9 ± 3.64

**P < 0.001; *P < 0.05 compared to the control group levels
Legends in the Table 1.

activity is reduced and disease comes to the long-term chronic phase without expressed clinical signs.

The dynamics of metabolism value changes correlated with the picture of clinical status of experimental animals. The condition of the rats in the T group during all experiments was satisfactory. At 3-4 weeks post infection, the rats in the T group had slight diarrhea and their rates of weight gains were lower compared with the control group (Table 2), but their appetite (food consumption) and behaviour activity was the same as in control C group. The fact that there was no incidence of the animal deaths indicates a sufficiently high level of the compensatory-adaptive reactions of the host organism with experimental Trichinellosis.

In T + M group, the greatest changes of investigated parameters were observed on days 21-30 of the experiment. A double increase in MDA concentration on day 21 and the absence of distinctions in activity of antioxidant enzymes regarding the values of group C with the subsequent expressed separation of the SOD and Catalase activity on day 30 (Chart 1, b) indicate the decline of compensatory reactions of animal organisms treated by anthelmintic.

Our observations show that Wistar rats are susceptible to mebendazole and they bore the treatment badly. To the 21st day of experiment, most animals expressed signs of dyspepsia and intoxication: apathy, sedentary, abdominal swelling, liquid stool (in severe cases with yellow-greenish mucus), dim and tousled coat. To the 30th day of experiment, the rats in T + M group had significant loss of body weight (to 23 %; $P < 0.001$) compared with body weight to the 14th day of experiment, 23 animals (38.3 %) died from day 20 to day 28 of the experiment. In the C + M group, during the same period of the experiment the rats have also significant loss of body weight (to 11 %; $P < 0.001$) compared with body weight in the control group although mortality in this experimental group was only 20 % (6 experimental animals).

To the 21th day of experiment, in animals from the control group which were treated only with Mebendazole (C+M), a significant decrease in SOD and Catalase activity was observed, compared to the control group (C), 72.5% and 67.5 % , respectively, ($P < 0.05$). At later periods of observation, this data did not significantly differ from group C. But the MDA concentration in C + M group was reduced only to 45 days of the experiment. Analysis of dynamics of the examined indexes in the groups of C + M and T + M compared to indexes in the group C brought us to conclusion that mebendazole can directly inhibit SOD and CAT in erythrocytes. It was shown by significant changes between groups C and C + M on day 21 ($P < 0.05$) (Fig. 1, 2). It appropriately leads to increase in MDA concentration ($P < 0.05$) (Table 1), to disturbance of tissue metabolism and subsequent intoxication of laboratory animals, to microhemocirculatory disorders - which appears to be additional burden factor markedly worsen prognosis of anthelmintic therapy effect. In our opinion this is how it is possible to explain the cases of animal deaths in the group T + M (Tolstoj *et al.*, 2007).

In the T + M + AK group, a high activity of enzymes was observed on day 21 which interchanges with disjunction of their activity to day 30 (Fig. 1, 2). The MDA concentration in this group was on average 124 % compared to the control group (C) ($P < 0.05$). In the C + M + AK group, reliably increasing MDA concentration and catalase activity were shown on day 21 (Table1; Fig. 1.). The SOD activity of C + M + AK, at all observation times, did not significantly differ from control group (Fig. 1.).

The AKβ injection during mebendazole treatment did not fully prevent signs of intoxication, but their clinical signs were expressed to a small extent. In the T + M + AK group, 11 animals died (18.3 %) and in the C + M + AK 2 animals died (6.7 %), compared with 38.3 % in the T + M group and 20 % in the C+M. We did not observe significant differences in changes of animal body weights, between those having been administered with mebendazole and AKβ vitamin complex compared with animals administered only with mebendazole. In our opinion, for minimizing intoxication signs and deaths of animals, AKβ vitamin complex can be administered for a longer period of time.

It is necessary to stress that the experimental animals treated with Mebendazole and AKβ vitamin complex had faster convalescence compared with animals treated only with mebendazole. The dynamics of the enzymatic activity and values of MDA concentration proves this fact. On day 45, all the observed parameters in the group T + M + AK were similar to values in the control group. The body weight gain in this group was on 11 % greater compared to T + M group.

It is apparent that mebendazole can immediately inhibit the activity of SOD and catalase in erythrocytes of the rats. Therefore, on day 21, the monitored values of SOD and catalase in groups C and C + M demonstrated distinct differences ($P < 0.05$). AKβ vitamin complex, which was

administered during the anthelmintic treatment, can considerably reduce this negative factor. The high level of the enzyme activity on day 21 ($P < 0.001$), and the lower level of the MDA concentration in the blood serum on days 21 – 30 ($P < 0.05$) in group C + M + AK compared with the same values in the group C + M prove this fact.

The present study shows that increasing MDA concentration in blood serum and changes of the SOD and Catalase activity in erythrocytes of the laboratory rats with experimental Trichinellosis during the disease progression indicate activation of free radical oxidation processes in infected animals. During the treatment with anthelmintic, the intoxication of the organism was caused not only due the massive destruction of parasites, but also due to mebendazole incidence. Mebendazole in doses of 150 mg/kg of body weight can cause a pro-oxidant effect which is manifested in the reduction of antioxidant enzymes activity and an increase in MDA concentration. This can be one of the reasons for the considerable health impairment and deaths in part of the treated animals.

Using the AKβ vitamin complex during the anthelmintic treatment with mebendazole improves the LPP values and coordination of antioxidant enzymes (SOD and Catalase) function. Moreover, it raised adaptive-compensatory reactions of host organism and reduced the rate of the experimental animal's mortality.

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References

AKHMEDOV, D. R. (1994): Clinical and pathogenetic significance of the antioxidative system in infectious diseases. *Klin. Med.* (Mosk) 72(1): 24-6 (in Russian)

BAGLEY, E. (2000): Products of lipid peroxidation as a direct carcinogen. In *Oncology 2000, Articles of II Oncologists Meeting of countries of the CIS in the Kiev*, p 172 (in Russian)

BEKISH, O. IA. (1978): Biochemical aspects of pathogenesis in trichinellosis. In *Proceedings of the 4th International Congress of Parasitology*, Warszawa, Poland, 4: 271 – 279

BEKISH, O. IA., BEZNOS, T. B., BURAK, I. I. (1980a): Influence of specific therapy of some helminthic infections on character of allergic reactions in the parasitized ghost organism. In *Articles of IX Conference of the Ukrainian Parasitological Society, Kiev*. Part I, pp 68 – 69 (in Russian)

BEKISH, O. IA., BURAK, I. I., OSTREIKO, N. N., ZATVORNICKAIA, V. V. (1980b): Way of trichinellosis modeling in various forms of severity. In: *Modern methods of struggle against parasitic diseases of agricultural animals. Articles of Republican Scientific–Practical Conference. Minsk, Belorussia*, pp 17 – 18 *(*in Russian)

CHISTENKO, G. N., VEDENKO, A. L. (2006): Parasitic disease morbidity in Belorussia. In: *Achievements and trends in the development of modern parasitology. Articles of the 5th Republican Scientific-Practical Conference.* Vitebsk, Belorussia, pp 21 – 25 (in Russian)

DIANZANI, M. U. (1992): Free radicals in physiology and pathology. *Boll. Soc. Ital. Biol. Sper.*, 68 (8-9): 491 – 511

FIGALLOVÁ, V., PROKOPIČ, J. (1987): Effect of vitamins on Trichinella pseudospiralis Garkavi, 1972 infection in mice. *Folia Parasit*., 34 (4): 341 – 346

GAVRILOV, V.B., GAVRILOVA, A. R., MAZHUĽ, L. M. (1987): Methods of determining lipid peroxidation products in the serum using a thiobarbituric acid test. *Vopr. Med. Khim*., 33: 118 – 122 (in Russian)

HALLIWELL, B. (1991): Drug antioxidant effects. A basis for drug selection? *Drugs* 42(4): 569 – 605

HARMAN, D. (1992): Free radical theory of aging: history (a review). *EXS*, 62: 1 – 10

HURNÍKOVÁ, Z., ŠNÁBEL, V., POZIO, E., REITEROVÁ, K., HRČKOVÁ, G., HALÁSOVÁ, D., DUBINSKÝ, P. (2005): First record of Trichinella pseudospiralis in the Slovak Republic found in domestic focus. Vet Parasitol. 128(1 – 2): 91 – 8

KOCIECKA, W. (1996): Wlosen krenty i wlosnica. Volumed, Wroclaw

KOŁODZIEJ-SOBOCIŃSKA, M., DVOROŽŇÁKOVÁ, E., DZIEMIAN, E. (2006): Trichinella spiralis: macrophage activity and antibody response in chronic murine infection. *Exp. Parasitol.*, 112(1): 52 – 62

KOSTIUK, V.A., POTAPOVICH, A.I., KOVALEVA, ZH.V. (1990): A simple and sensitive method of determination of superoxide dismutase activity based on the reaction of quercetin oxidation. *Vopr. Med. Khim.,* 36: 88 – 91 (in Russian)

MAMONTOVA, N. S., BELOBORODOVA, E. I., TIUKALOVA, L. I. (1994): The determination of Catalase activity in chronic alcoholics. *Ter. Arkh*., 66(2): 60 – 63

MIROSHNICHENKO, O.S. (1992): Biogenesis, physiological role and properties of Catalase.
Biopolym. *Cell*, 8(6): 3 – 25

OZERECKOVSKAYA, N. N. (1985): Unsolved problems of trichinosis treatment. In: Articles of All-Union Scientific Conference on human and animal trichinellosis issues in Yerevan, Armennian, pp 19 – 22 (in Russian)

POZIO, E. (2007): World distribution of Trichinella spp. infections in animals and humans. *Vet. Parasitol.*, 149: 3 – 21

POZIO, E., ZARLENGA, D. S. (2005): Recent advances on the taxonomy, systematic and epidemiology of Trichinella. *Int. J. Parasitol.,* 35: 1191 – 1204

RUTKOVSKAYA, ZH. A., MOROZKINA, T. S. (2006): Influence of different doses of carotenes in "AKβ" on the state of the antioxidant system of the organism of rats. Proceedings of the National Academy of Sciences of Belarus, 2: 59 – 62

SENUTAITE, J. (1990): Biochemical changes on the organism during trichinellosis. Mokslas, Vilnius (in Russian)

SMIRNOV, L. D., SUSKOVA, V.S. (1989): Modulation of the immune response by antioxidants (a review). Pharmaceutical Chemistry Journal 23(7): 527 – 537 (in Russian)
TOLSTOJ, V. A., LYTVYNETS, A., LANGROVA, I. (2007): Pro-oxidant effects of Mebendazole in albino rats experimentally infected with *Trichinella spiralis*. *Parasitol. Res.,* 100(6): 1277 – 1280
TOLSTOY, V.A., BUTVILOVSKIY, V.E., DAVYDOV, V.V. (2000): Eosinophilia in rats with experimental trichinellosis durind Mebendazole and anti-oxidant AKβ vitamin complex treatment. In: Tissue helminthiasis: diagnostics, pathogenesis, clinical picture, treatment and epidemiology. Articles of Scientific–Practical Conference. Vitebsk, Belorussia, pp 131 – 137 (in Russian)
VLADIMIROV, YU. A., ARCHAKOV, A.I. (1972): Lipid peroxidation in biological membranes, Nauka, Moscow (in Russian)

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