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The effects of antioxidants on metabolic changes under conditions of noise action

M. Melkonyan, A. Manukyan, S. Karapetyan, T. Meliqyan and K. Kocharyan

Yerevan state Medical University after M. Heratsi, Koryun str 2, Department of Medical Chemistry, 3741 Yerevan, Armenia
magda.melkonyan@meduni.am

The aim of the current review is to present the effects of antioxidant alfa-tocopherol and several bioactive compounds as preventive measures against hazardous effect of noise action on living systems. The previously obtained results testify to the noticeable decrease of the main endogenous antioxidant α-tocopherol content, lipid peroxidation processes activity increase both in the tissues of experimental animals under noise action and in the blood of the female employed in high noise level conditions. Correlation of changes of the studied parameters with increase of atherogenity index in the blood of employees, confirms our assumption of the leading role of the disorders in pro- and antioxidant systems in the development of different pathological states, particularly atherosclerosis and heart diseases under the noise action. The introduction of α-tocopherolacetate has had a considerably expressed regulatory effect on the studied parameters both in experimental animals and people. Our investigations also revealed regulatory effects of several compounds, possessing adaptogenic and immunostimulating properties on the studied parameters in tissues of white rats in acute acoustic stress conditions. The results obtained testify that the functional activity of the studied compounds in certain extent depend on their effects on the pro-and antioxidant systems in tissues.

1 Introductin

The problem of acoustic stress in modern conditions of economically developed countries has become extremely topical, as more and more people live and work in high environmental noise: long term transportation noise from road, rail or air traffic, noise of equipment, facilities, widely used in the home and workplace, excessively loud music, a dramatic change in sound level of commercials that, eventually, depending on the duration of exposure, level and other characteristics of the noise not only leads to impairment of the auditory organ of varying degrees, but also to an increase in morbidity, development of a number of pathologies, including hypertension, atherosclerosis, ischemic heart disease, myocardial infarction [1,2,3,5,8,10,11,26,28,32,33,35]. Taking into consideration the important role of activation of free radical oxidation processes, oxidative stress (OS) development and lipid peroxidation (LPO) processes intensification in the pathogenesis of the diseases listed above [7,12], it was studied the LPO intensity and the state of the antioxidant activity of the tissues for the elucidation of possible biochemical mechanisms of hazardous effects of noise. The LPO processes have an important physiological value for the vital functions of cells, they take place in all tissues with the low intensity and are regulated by antioxidant system [4,34]. The activation of oxidation processes leads to violations of the lipid and protein components of membranes and membrane structure, particularly to intensification of unsaturated fatty acids (FA) peroxidation, which leads to the qualitative and quantitative changes in the phospholipids (PL) spectra, conformational changes of membrane proteins, chemical modification of nucleic acids, membrane proteins, including lipiddepending enzymes activity, the transmembrane transport of metabolites, the external signal transfer, ligand-receptor interactions, and the normal functioning of cells in general on the background of antioxidative activity disorders [27,29,34].

Our recent investigations have revealed pronounced shifts in pro-antioxidant system in different tissues of experimental animals under the noise action, the changes in the structure and functional activity of biological membranes, particularly mitochondrial and erythrocytes, the development of OS [13,14,15,17,23], in which the steady-state balance is disturbed and prooxidant processes are dominated creating preconditions of organic lesions. It was shown that action of noise leads due to LPO processes activation to α-tocopherol (α-T, vitamin E) content exhaustion in tissues. The intensity and direction of the observed changes of LPO processes, α-T content, PL and FA compositions depend on the duration of noise action [20, 23], as well as sex and level of noise [17,18]. The study of comparative action of exposed noise of different level and duration on organism revealed development of α-T deficit in tissues of white rats, more expressed in male-rats than in female, as well as prevalence of effects of duration on the level of noise, which was chosen based on the ISO R1999 recommendations. To reveal possible universal mechanism of disorders development in the tissues of different organisms in the conditions of noise action and taking into account all above mentioned, the study of LPO processes intensity in the blood of female workers of the textile mill was carried out. Results obtained demonstrate pronounced changes in the lipid components and antioxidant status of blood of employees, similar those, observed in experimental animals. It was revealed, particularly intensification of LPO processes, decrease of α–T content in plasma and EM. The observations were held in direction of clearing up the diagnostical importance of displaces of the lipid metabolism, mentioned above.

Developing deficit of antioxidants and, in particular, α–T, can be the reason of enhanced complaints of poor health, dizziness, annoyance and fatigue under conditions of high noise environment at the work place. Therefore maintenance of antioxidant status of organism by intake of antioxidants can considerably promote his resistibility. Requirement of healthy man in the antioxidants is variable and in a great deal determined by the intensity of physical work, degree of tension of psychical processes features of influencing factors. Living organisms requirement in antioxidants can considerably grow under conditions of many unfavourable physical and chemical factors.

All this testifies to the necessity of usage of antioxidants in the conditions of noise influence. Nowadays the natural antioxidants have found a large usage in the clinical practice, especially α-T, possessing a large spectrum of activity. Use of antioxidants requires the scientific-based prescriptions in regard to dosage, duration of intake or administration, taking into account the results of biochemical analysis of the mentioned parameters in people.

The main aim of the carried out investigations and the present paper is to review the effects of prophylactic usage of α-T–acetate by the employees working in high level

noise environment and also review the effects of several compounds, possessing adaptogenic, antistressor and immunostimulating properties on the LPO processes in white rat's in acute acoustic stress conditions (acute exposure of noise).

2 Experimental procedure

Investigations were carried out on white rats of both sexes weighing 150-200 g with a general feeding in vivarium. The animals were divided into 5 groups: rats of the 1-th group serve as a control, rats of the 2, 3, 4, 5, 6-th groups underwent noise influence (91 dB(A) and 97 dB(A)) with maximal energy in the region of average and high frequency. For 91 dB(A) level the duration and periods of noise influence were consequently 2hr, 8 hr, and 7, 28 and 56 days, each day 8 hr noise exposition; for 97 dB(A) duration was consequently 15min., 2 hr, 7x2 hr, 28x2 hr, 56x2hr., which were chosen according to ISO R1999 recommendations. Occupational safety organizations recommend that for every additional 3 dB(A), the maximum exposure time is reduced by a factor 2. The noise was obtained by white noise generator joint with attenuator. The acoustic system supplied the reproduction in the range of 63-16000Hz.

The first injection of α-T–acetate (α –Ta, 1mg/kg) was given 18 hr before first noise action. Injections were repeated every 48 hr.

It was studied LPO processes intensity (ascorbate-depended, ADP and NADPH-depended inducible LPO) and antioxidative activity of different tissues (brain, heart, liver, blood), particularly content of α–T, activity of enzymes of antiradical protection.

For revealing more effective compounds under conditions of acute acoustic stress, the effects of synthetic peptide (SP), analogous to the part of immunophyline, delta-sleep peptide (DSIP), and newly synthesized α_2-adrenoblocker "beditine" (synthesized in the Institute of Fine Organic Chemistry, Republic of Armenia [31]) on the LPO processes, antioxidative state of tissues, membrane PL metabolism, LPO intensity under conditions of noise influence were studied. SP (2mkg/kg), DSIP (120 mkg/kg) and "beditine" (2.0 mg/kg) were injected intraperitoneally before the noise action. The animals underwent 91 dB(A) noise influence during 2 ,8 or 16 hours. Determination of LPO processes, antioxidant activity, content of total lipids (TL), total cholesterol (TCh), low-density lipoproteids (LDLP), high-density lipoproteids (HDLP) as well as Ch-LDLP and Ch-HDLP in blood of women workers of textile mill (age range 24-60 years, Yerevan, Armenia), working under conditions of 87-90dB(A) noise level also was performed. The women didn't use ear protectors, because they felt annoyed or uncomfortable. The contingent under study was divided into 3 groups depending on the work experience: I group – up to 10 years (in Figures-a), II - 10-20 years (in Figures-b), III - over 20 years (in Figures-c). Women working at the same enterprise but under different low noise levels in the working place served as control groups.

After blood test all the female workers were given capsules of α -Ta in a dose 100 mg three times per week.

The next biochemical inspection of blood was produced after one year of systematic usage of α -Ta.

3 Results and discussion

3.1 Effects of compounds possessing antioxidation properties on the oxidation processes in tissues of white rats

Taking into account close connection between intensity of LPO processes, α-T content and structural disorders under high noise action conditions, the effect of α–Ta administration was studied to prevent significant changes in the studied parameters. The efficiency of the α–Ta acetate usage especially obvious during longterm action of noise (during 8 weeks, every day 8hr, 91dB(A)). The long term systematic usage of α-T in dose 1 mg /kg mass showed the normalizing effect almost on all studied parameters in all studied tissues [14,16]. Of particular interest are effects in the heart tissue and in blood (Table 1). These results are especially important due to numerous data concerning a high level of atherosclerosis, hypertension, ischemic heart disease, myocardial infarction in the people underwent noise action [6].

Table 1: The α–T content in the heart tissue (nmoles/g) of white male rats under the noise (91 dB(A)) action (I) and α–Ta administration (II). (p = * < 0.001, ** < 0.05).

	1	2	3	4	5	6
I	37,1 ±0,6	40,0± 1,0**	40,3± 1,2**	41,2± 1,4*	30,6± 1,9**	34,8 ± 2,8
II		33,6 ± 1,1	28,1± 07*	27,4± 2,1*	45,6± 1,7**	46,3 1,3*

Especially must be noted the hypolipidemic effect in blood plasma, developed on the background of the usage of α–Ta [16].

The research of compounds possessing more expressed regulatory effect under conditions of acute acoustic stress is of utmost importance. Among the studied compounds, such as SP, DSIP and α_2-adrenoblocker "beditine", it was "beditine" which revealed more significant preventive effect on the changes development in the studied parameters under conditions of acute acoustic stress [9, 22, 24, 25].

Nowadays a great attention is paid to the problems of permissible level and duration of noise action in environment.

We also compared these data and the data obtained in the result of higher level noise (97 dB(A), the duration of which was shortened for 4 times, according to recommendation ISO R1999. The data obtained are the evidence of equality absence in the observed biochemical changes in different tissues in mentioned conditions. More over, the higher efficiency of exogenous α-TA influence on metabolism has been found in animal tissues under the higher level of acting noise (and shorter time) and it proves that the time factor dominates in these conditions [13, 17].

3.2 Efficiency of the α–Ta usage by female workers of textile mill

In the EM the activation of ADP and NADPH processes is estimated in the 1st and 3rd groups, which according to our

conclusions can be characterized subsequently as phases of activation and exhaustion. The α-TA usage improved all recorded significant changes in studied parameters almost in all groups [19, 21]. The exception is NADPH- inducible LPO processes intensity increase against the background of α-T content increase in the EM of the 1-st group, which is, in our opinion, in accordance with common rule: the higher level of α–T in membranes the richer are PL in polyunsaturated FA, main substrates of LPO (Figure 1).

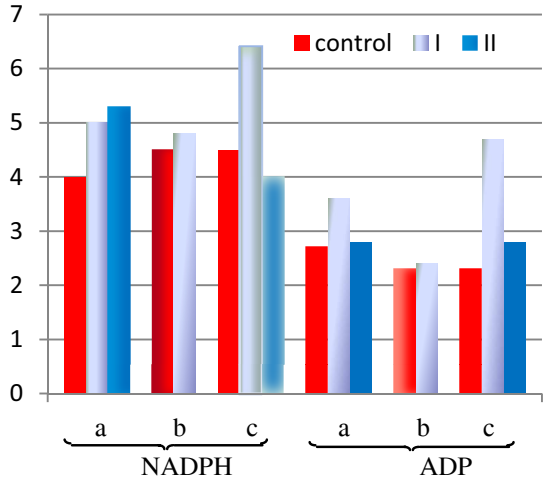

Figure1: The intensity of Ascorbate- and NADPH-dependent LPO processes in the EM of female workers. I- before α-Ta intake, II – after 1 year of α–Ta intake

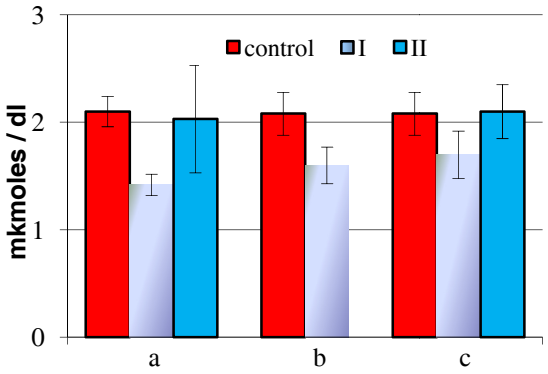

Figure 2: The level of α–T (mkmol/dl) in the blood plasma of female workers.

Simultaneously significant decrease of α-T content in the EM and the plasma is estimated. The intensity of changes depends on the experience of work: the decrease of α–T content is mostly expressed in female workers of group one (Figure 2, 3). The decreased level of α–T observed also in EM in all groups of employees before α–Ta usage.

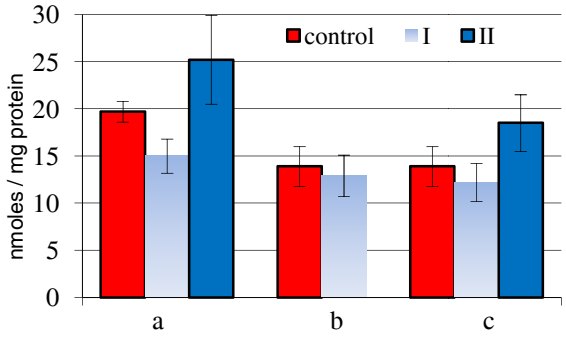

Figure 3: The α–T content in the EM of female workers

As shown in the Figures 2 and 3, in the result of α-Ta intake the α-T content in plasma and EM returns to normal level. The results only of few representatives of the 2-nd group having used α-Ta (complaints in this group, on the whole, were less expressed), are not verified and aren`t represented here. The value of index TCh/α-T is more informative data about composition of membranes and is higher compared with control level in all groups. The increase level of Ch in membranes is evidence of changes in the membrane viscosity, which is one of the most important characteristic of membranes, determining membranes and membrane-bonded proteins functional activity.

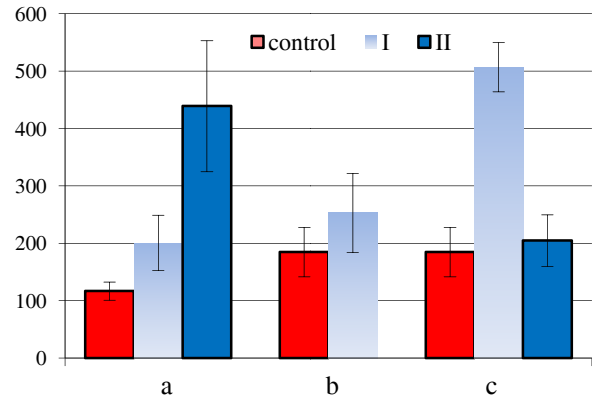

Figure 4: The the ratio TCh /α–T of the EM of female workers.

It must be noted that the arranged preventive intake of α-Ta draws nearer not only the level of α-T, but the coefficient TCh/α-T in the employees of the 3rd group (Figure 4). There is no doubt that the decrease of level of the major lipid soluble antioxidant of the plasma, α-T, may lead to serious disturbances in the metabolism of lipoptoteids of the plasma and structural-functional integrity of the biomembrans. At the same time growth of the level of TL, mainly due to plasma TCh contents observed. The α-TA usage leads to the normalization of TL level, but at the same time the Ch level increase is observed in group 1 [27]. It can be mentioned that the decrease of α – T is more expressed in the 1st group, but TCh is decreased in the 3rd group [19].

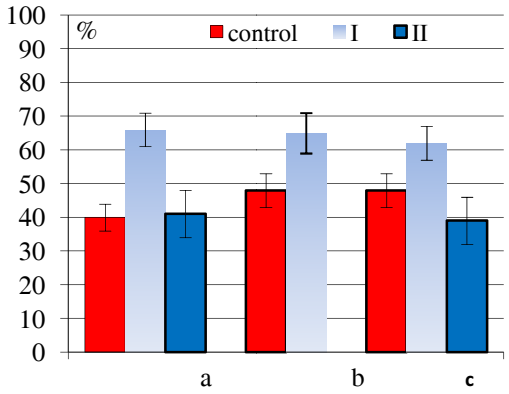

Figure 5: The cholesterole of low density lipoproteides (Ch-LDLP) in blood plasma of female workers.

It was shown that informative value of various lipid indicators and indexes in healthy subjects and in patients with ischemic heart disease in 10 investigated biochemical

indicators the first places belong to the atherogenity index, TCh and the percent of HDLP-Ch in TCh. The cholesterol atherogenity index and HDLP-Ch percent in TCh were closely correlated with the severity of angiographically proved changes in the coronary arteries [30].

After systematic α-TA intake by female workers the level of this parameters in some cases almost completely returns to the norm and the coefficient of atherogenity drops lower than the control level, which can undoubtedly be an objective index of efficiency of the α–Ta usage as preventive measure against hazardous effect of high level noise (Figures 5,6).

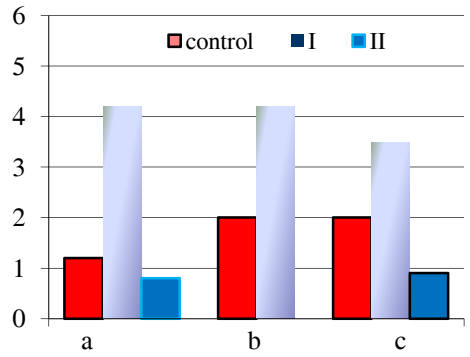

Figure 6: The ratio Ch-LDLP/Ch-HDLP in blood plasma of female workers.

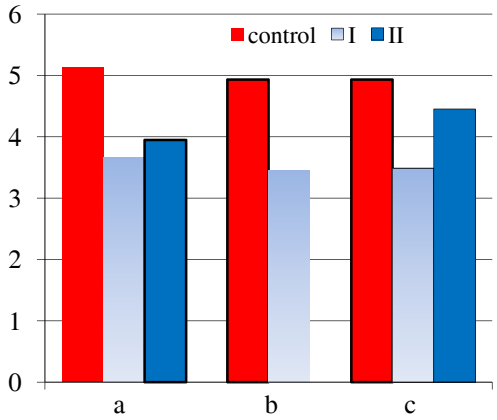

Figure 7: The ratio α–tocopherole/cholesterole (α–T/Ch) in blood plasma of female workers.

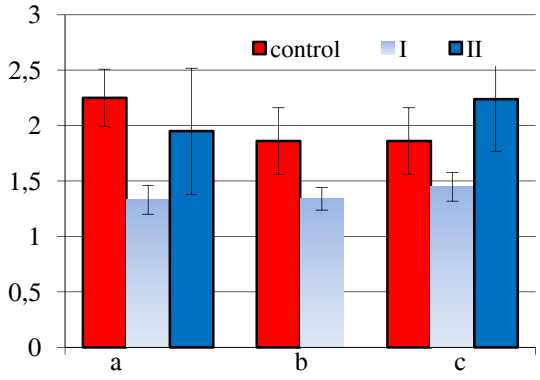

Figure 8: The ratio α–tocopherole/ total lipids (α–T/TL) in blood plasma of female workers.

The coefficients α-T/TL (Figure 7) and α-T/CH (Figure 8), that are in our opinion more objective criteria for estimating level of saturation of plasma lipids by antioxidants, which were low before α-Ta intake, are significantly increased in the case. It means that lipid phase is become rich of antioxidant and reliably protected.

It is necessary to note that the usage of α-Ta during a year promoted working activity increase, decrease of duration of its temporal loss, as well as complaints of poor health, annoyance, giddiness and fatigue.

4 Conclusion

The observed changes testify that the noise action leads to reconstruction of membranes and plasma lipids against the background of the antioxidant deficiency development in all the studied tissues in experimental animals. For prevention oxidation intensification under conditions of acute acoustic stress α_2-adrenoblocker "beditine" is more effective. The usage of α-Ta has had a considerable expressed regulatory and preventive effect both on experimental animals and people under long term exposure to noise. The revealed regulatory influence of α-Ta on the LPO processes, antioxidative activity of tissues, structural and blood plasma lipid composition under conditions of noise action depends both on the level of acting noise and duration of action. After one year of α-T-acetate intake by female workers decrease of complaints on dizziness, annoyance, anxiety and fatigue along with improved content of α–T, lipid components of blood plasma and EM are recorded. Among the revealed data a sharp decrease of ratio Ch-LDLP/Ch-HDLP (index of atherogenity), which is one of the well known diagnostic indices of atherosclerosis and heart disease development is the most important one. The results of the observations prove that the determination of LPO intensity, α-T, Ch and lipoproteins content of plasma are very important both for estimating the depth of pathological changes due to harmful action of noise as well as for estimating the necessity of wide usage of α-Ta. The presented data could serve as a basis for working out health protecting measures and used in practice of occupational medicine and industrial hygiene.

References

[1] E. Andreeva – Galanina, S. Alekseev, A. Kadiskin, et al, Noise and Noise disease, Meditzina, Leningrad, 304 (1972)

[2] W. Babish, "Health aspects of extra-aural noise research", Noise & health 6, 69-81(2004)

[3] W. Babisch, "Transportation noise and cardiovascular risk" , Noise Health 8, 1-29 (2006)

[4] E. Burlakova, N. Khrapova, "Lipid peroxidation and natural antioxidants", Uspechi med. chimii, 54 (9), 1540-1548 (1985)

[5] NI Chun-hui, CHEN Zhi-yong, ZHOU Yin, ZHOU Jian-wei, Pan Jing-jing, LIU Nian, WANG Jun, LIANG Chen-ke,ZHANG Zhi-zhong and ZHANG Yu-jun, "Associations of blood pressure and arterial compliance with occupational noise exposure in female workers of textile mill" Chin Med J,120(15),1309-1313 (2007)

[6] L. DeMaio, M. Rouhanizadeh, S. Reddy, A. Sevanian, J. Hwang, T. K. Hsiai, "Oxidized phospholipids mediate occludin expression and phosphorylation in vascular endothelial cells. Am J Physiol Heart Circ Physiol. 290(2), 674-683 (2006)

[7] E. Dubinina, "Products of metabolism of oxygen in functional activity of cells (life and death, creation and destruction)", Physiological and kliniko-biochemical aspects, Medical press, Saint Petersburg, 276-282 (2006)

[8] M. Heinonen-Guzejev, H. S. Vuorinen, H. Mussalo-Rauhamaa, K. Heikkila, M. Koskenvuo, "The association of noise sensitivity with coronary heart and cardiovascular mortality among Finnish adults", Sci Total Environ. Kaprio J. 372, 406-412 (2007)

[9] L. Hunanyan, O. Sotski, L. Khachatryan, E. Shirinyan, M.Melkonyan, [The oxidative modification of white rats serum proteins under the noise and –adrenoblockers influence]. [Published in russian]. Biol J of Armenia, 1 (62),79-83(2010)

[10] H. Ising, B. Kruppa, Health effects caused by noise: Evidence in literature from the past 25 years", Noise & Health 6(22), 5-13(2004)

[11] R. McNamee, G. Burgess, W. M. Dippnall, N. Cherry, Occupational noise exposure and ischemic heart desease mortality, Occup. Environ MED 63, 813-819 (2006)

[12] F. Meerson, "Pathogenesis and prevention of stress and ischemic damages of heart", Medicina, Moscow, 272 (1984)

[13] M. Melkonyan V. Mkhitaryan. E. Melik-Agaeva A Rukhkyan, "The process of lipid peroxidation and α–tocopherol level in white rat tissues under conditions of acoustic stress", Biol. J. of Armenia, 7 (36), 582-587 (1983)

[14] M. Melkonyan, "The lipid peroxidation processes intensity in white rats brain under the acoustic stress conditions", Neurochemistry, USSR 3 (3), 331-332 (1984)

[15] M. Melkonyan, E Melik-Agaeva, A. Arakelyan, "Influence of noise on the processes of lipid peroxidation at acoustic stress", Biol. J of Armenia 8 (37), 668-673 (1984)

[16] M. Melkonyan, V. Mkhitaryan, "Influence of α-tocopherolacetate on some biochemical parameters of blood of white rats in the conditions of stress", Byul. eksper. biol. and medicine 9, Moscow, 270-272 (1985)

[17] M. Melkonyan, E. Melik-Agaeva, V. Mkhitaryan, "The effect of sex on the intensity of lipid peroxidation processes and antiradical enzymes activity in the conditions of stress", Exp. and clin. medicine 26 (4), 322-328 (1986)

[18] M. Melkonyan, "Sex distinctions in the dynamics of changes of some biochemical parameters of plasma and erythrocytes of white rats in the conditions of acoustic stress", Exp. and clin. medicine (Rus) 276 (I), 21-29 (1987)

[19] M. Melkonyan, "Regulation of weaving workshop employees metabolism of blood lipid (noise level 90dB(A))", Voprosi meditsinkoy chimii 6, 60-62 (1993)

[20] M. Melkonyan, "Dynamics of changes of erythrocyte membrane lipids fatty acid composition in the condition of acoustic stress and α-tocopherolacetate application", Exp. and clin. medicine (Rus) 3 (33), 71-76 (1993)

[21] M. Melkonyan, E. Melik-Agaeva. "Metabolism of lipids of blood of weaving workshop employees working in the conditions of high noise level", Biol. J. of Armenia 1(47),23-27 (1994)

[22] M. Melkonyan, L. Ayvazyan, "Influence of delta-sleep peptide on the lipid peroxidation processes in blood of white rats", Medications and medicine 4, 65-71 (2002)

[23] M. Melkonyan, K.Karageuzyan, G.Hoveyan A., et. al., " Changes in Contents of Phospholipids in Rat Brain under the Action of Noise", Neurochemistry, Netherlands,. Groningen 761-764 (1996)

[24] M. Melkonyan, L., Hunanyan, A. Manukyan, A. Minasyan, N. Hakobyan, J. Javroyan, "The effects of selective alpha-adrenoblocker beditin on the intensity of lipid peroxidation and membrane phospholipids content in acoustic stress conditions" The New Armenian Medical journal 4 (4), 15-24 (2010)

[25] M. Melkonyan, G. Zakaryan, L. Ayvazyan, A. Galoyan, "Antistressor & antioxidant activity of the synthetic N-terminal peptide fragment of immunophilin, under acoustic stress conditions", J. Neurochemistry 20 (4), 276-279 (2003)

[26] S. Nichkov, G. Krivitskaja, Acoustic stress and cerebrovisceral disorders, USSR, Moscow, DDR, Berlin 232 (1969)

[27] E. Pereira, M. Bertolami, A. Faludi, A. Sevanian, D. Abdalla, "Antioxidant effect of simvastatin is not enhanced by its association with alpha-tocopherol in hypercholesterolemic patients", Free Radic Biol Med. 37(9), 1440-1448 (2004)

[28] Proceedings. The 9th Congress of the International commission on the biological effects of Noise. Noise as a Public Health Problem (ICBEN), Foxwoods, CT (2008)

[29] M. Rouhanizadeh, J. Hwang, R.E. Clempus, L. Marcu, B. Lassègue, A. Sevanian, T. K. Hsiai, "Oxidized-1-palmitoyl-2-arachidonoyl-sn-glycero-3-phosphoryl-choline induces vascular endothelial superoxide production: implication of NADPH oxidase", Free Radic Biol Med. 39(11), 1512-1522. (2005)

[30] T. Shipilova, O.Volozh, F. Solodkaya, J. Tagger, V. Pauts, A. Olferiev, "The use of lipid indicators and indexes for assessment of ischaemic heart disease", Cor Vasa. 29(5), 333-340 (1987)

[31] Shirinyan E.A. Collection of researches, 47-56 (1998)

[32] S. Stansfeld, M. Matheson, "Noise pollution nonauditory effects on health", Brit Med Bull 68, 243-257 (2003)

[33] Stansfeld S, Crombie R. Cardiovascular effects of environmental noise: Research in the United Kingdom.Noise Health 13, 229-233 (2011)

[34] Yu. Vladimirov, A. Archakov, "Lipids Peroxidation in Biological Membranes, Nauka, Moscow, 92-152 (1972)

[35] E. van Kempen, H.Kruize, H. Boshuizen, C.Ameling, B. Staatsen, A. de Hollander , The Association between Noise Exposure and Blood Pressure and Ischemic Heart Disease: A Meta-analysis", Environ Health Perspect 3 (110) 307–317 (2002)