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# Stress, Adaptation and Nutrition

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**Abstract:** In recent years, the problem of increasing of organism adaptation to stresses by using of food minor substances is one of the priorities of modern physiology and food biochemistry. Studies on micronutrient influence on adaptive abilities of stressed rats were conducted. Three groups of white male Wistar rats 10 animals each weighing 130-160 grams were formed: first group- intact, second group- intact+ stress and received isotonic solution of sodium chloride in equal volumes, third group- experimental animals, received biologically active additive 'Eramin' by gavage during 14 days before stress at a dose of 0.01g per rat in the form of aqueous solution. Stress was simulated by swimming lasting 45 minutes per day for 5 days in water at 27-28°C. It was discovered that additional invasion of flavonoids, microelements and other biologically active substances in the form of biologically active additive 'Eramin' in the organisms of stressed rats increases resistance to extreme factors, in particular, does not cause increase of lymphoid organs mass, structure changes in the adrenal cortex, stabilizes secretory activity of glucoproductive cells, weakens lipid peroxidation.

**Key words:** Adaptation · Stress · Diet · Cortisol · Thymus · Lipid Peroxidation

## INTRODUCTION

In recent years, the problem of increasing of organism adaptation to stresses by using of food minor substances is one of the priorities of modern physiology and food biochemistry. Adaptation abilities of organism allow maintaining homeostasis during stress [1], adaptive reaction depends on stress-factor impact and is lying within the range- from simple reaction to interaction of all systems of organism [2, 3].

In order to ground micronutrient impact on the adaptation process it is rational to stop at the characteristics of physiological mechanism of stress developing.

For the first time, the definition 'stress' was suggested by W.B.Cannon [4]. The founder of stress doctrine Canadian physiologist Selye, numerous Russian and foreign scientists mark out three stages of stress development: anxiety, resistance and exhaustion.

At the stage of anxiety, while adrenaline is releasing, mobilization of energy reserves occurs, activity of phosphorylase in the liver increases, glycogen disintegration accelerates and blood glucose level increases. The glycogen reserves exhaust and the glycogenesis is carried out by metabolism of non-carbohydrate compounds, such as pyruvate, lactate, glucogenic amino acids. Under the action of catecholamine not only glycogen disintegration accelerates, but blood insulin level rises, resistance weakens. Disruption of the nitrogen balance in tissues is noticed, the sizes of lymphoid system organs decrease, adrenals increase, body weight decreases. Hemo concentration occurs, blood vessel penetrability rises, neutrophilia, lympho- and eosinopenia arises.

If the stress-factor action weakens or the stressor was not too strong, the stage of anxiety turns into the stage of resistance. Under the action of adrenalin ACTH-releasing-factor discharges from hypothalamus and then goes into adenohypophysis stimulating synthesis of ACTH. Glucocorticoids, mineralocorticoids and androgens release into blood. Products of hypatalamic hypophisic-paranephric system suppress the inflammatory immune response, inhibit somatotropin and gonadal steroid production. In a case of adipose tissue catabolism and anabolism of bones and muscles, action of these hormones weakens. In the period of stress, power consumption increases and glucogenesisand free fatty acids become the main source of carbohydrates. Change of carbohydrate type of energy metabolism to fat occurs. Synthesis begins to predominate the disintegration processes, white blood picture and body weight recovers.

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As extreme factor impact increases, the resistance stage transfers into the stage of exhaustion. Corticosteroids bind with transcortin protein and their arrival of hypothalamus delays. Hormone making intensifies, that leads to exhaustion of the hypatalamic hypophisic-paranephric system. Quantity of noradrenaline in hypothalamus reduces, adrenalin is not produced, adrenal cortex function weakens, disintegration of proteins and lipids intensifies, dystrophic changes appear, nitrogene balance becomes negative, lymphocytosis and eosinophilia are observed, alkali reserves decrease, acidosis arises due to accumulation of lactic acid and ketone bodies. Under the long-term exposure of the stressor, glycogen reserves are completely exhausted and deep hypoglycemia can lead to death.

In the opinion of Nobel Laureat I. P. Pavlov and modern researches, adrenocortical activity is just a part of stress manifestation and its main regulators are neural and endocrine systems [5]. According to the data M. Pshennikova homeostasis regulation in the period of stress-factors impact is carried by central link and two periphery branches of the stress-system. The central link is situated in the brain and is presented by neurons of hypothalamus paraventricular core (corticotropin-realising-hormone-neurons, arginine-vasopressin-neurons and noradrenalin-neurons). The hypatalamic-hypophisic-adrenal and parasympatyc neural systems belong to periphery branches of the stress-system. The stress-system interacts with mezacortical and mezalymbical dopamine systems [6].

Meerson F. [7] regards adaptation as a complex of neurohormonal and cell regulatory changes, presence of 'stress-limit systems' and 'protection mediator', what corresponds to methodological platform of H. Selye. This conception is not supported by the other physiologists [8, 9]. According to their data, stress leads to inhibition of thymic-lymphatic system, weakening of activity of endocrine glands which characterized by lymphopenia, secretion of ACTH and glucorticoids is increased against the background of immune depression.

Popov S. [10] considers stress as cognitive activation that is activation of brain structure and stress level as activation extent.

There is an opinion that stress leads to destabilization of genetic apparatus of gametal and somatic cells, inhibiting reproduction and immunity [11].

Nowadays, stress is regarded with the conception of free-radical theory, in accordance with which oxidation of free radicals, which leads to disorder of biological membrane functions (barrier, receptor and catalytic). In order to weaken the free radicals activity, antioxidants are implied, particularly, flavonoids, vitamins (tokopherol) and selenium-containing compounds.

Great attention in the mechanism of 'oxidative stress' development is paid to the influence of biologically active additive, in particular, selenium on the genes able to weaken the processes of peroxidation. Study of micronutrient influence on the genes, regulating adaptation abilities, is the subject of nutriogenomic. Under decreasing of antioxidants level in the organism, activation of vitagenesarises, which monitor antioxidant-proaxidant balance in a cell, including monitor the ferment of antioxidant protection – catalase. Presence of cofactors- mineral substances (selenium, zinc, manganese, copper) in the organism performs important role for synthesis of necessary ferments.

Among the priorities of the mechanism of oxidative stress development there are heat shock proteins – chaperones (HSP), amount of which is increasing in response for stress. HSP protect receptors of immune cells from disorder caused by free radicals, what prevents immunosuppression and maintains immune competence [12-15].

Stress protection is provided by proteins-sirtuins (genes SIRT) by the means of formation weakening and deleting of free radicals by deacytilation of superoxide dismutase and is ocytratde-hydro genase. Sirtuins eliminate disorder of the DNA cells caused by free radicals [16].

Thereby, in order to prevent negative impact of free radicals on the organism and to weaken 'oxidative stress' it is necessary to provide admission of antioxidants and mineral substances to the organism. In this case, using of biologically active additive can be efficient and economically available method of stress prevention.

So developing a biologically active additive 'Eramin' -extract of Lucerne, mineralized (State registration certificate No RU77.99.11.003.Å.047016.19.11 issued on 29.09.2011) [17].

'Eramin' contains lutheolyn, iron, manganese, chrome, copper, molybdenum and selenium.

Studying of influence of the biologically active additive on the organisms of stressed white rats was the task.

## MATERIALS AND METHODS

To solve the problems of the experiment created three groups of albino rats male Wistar weighing 130-160 g of 10 individuals each. Group 1 - intact, 2 - intact + stress and received isotonic sodium chloride solution in equivalent

volumes, 3 - experimental animals in the diet included for up to 14 days of stressing inside gavage BAA "Eramin" at a dose of 0.01 g per animal in an aqueous solution. Stress simulated swim of 45 minutes per day for 5 days at 27-28°C t water.

The efficacy of dietary supplements "Eramin" the stage of resistance (5 days of stress exposure). The animals were kept in a vivarium Ural State Academy of Veterinary Medicine 10 animals in a cage under the same conditions of light, temperature and food regimes. The experiment was conducted in accordance with the requirements of normative legal acts regulating the execution of studies on the safety and efficacy of pharmacological agents in the Russian Federation (Order "On approval of rules for laboratory practice" No 267 of 19.06.2003) and the rules of international legal and ethical use of animals.

White rats received obschevivarny diet recommended by Order of the Minister of Health from 1179 number 10.10.83. After ether anesthesia the animals were decapitated with blood sampling.

Cortisol levels were determined using ready-made kit reagents "Steroid - cortisol EIA". Lipid peroxidation activity was assessed by the accumulation Malanova dialdehyde (MDA) - the product of thiobarbituric acid. Extraction of diene conjugates (DC) - heptane-isopropanol. Selenium concentration - stripping voltammetry. EK mass of internal organs - electronic scales AND EK -1200. State of the gastric mucosa - visually.

The results obtained were processed using a standard computer program Microsoft Exsel XP, Statistica 8,0.

## RESULTS

Experimental animals, received biologically active additive 'Eramin' by gavage during 14 days before stress at a dose of 0.01g per rat in the form of aqueous solution. Stress was simulated by swimming lasting 45 minutes per day for 5 days in water at 27-28°C.

The efficiency of the biologically active additive 'Eramin' was studied during the resistance stage (5 days of stress-impact). The animals were kept in the vivarium of Ural State Academy of veterinary medicine in cages 10 rats in each under the equal light, nutritional and temperature conditions. The experiment was conducted in accordance to requirements of the normative legal acts, regulating research conducting on safety and effectiveness of pharmacological substances in Russian Federation (Order of the Ministry of Health of Russian Federation 'About Adopting the Rules of Laboratory Practice' No267 issued on 19.06.2003) and international rules of legal and ethical norms of using animals.

The white rats received ration, common for the vivarium, which is recommended by the Order of Ministry of Health of the USSR No 1179 issued on 10.10.83. After ether anesthesia of the animals were decapitated with blood sampling. Table 1 presents weight of thymus, adrenal and state of mucous coat of stomach of male-rats.

As result of stress impact reliable decrease of thymus weight was observed – in the second group by 34.9%, in the third group by 10.7%. In animals of the second group, the weight of the right adrenal reliably increased by 47.2%, hypertrophy adrenal cortex was observed, due to expanding of the zonafasciculate by 20.5% comparing with the first group. On the background with the biologically active additive 'Eramin' (3rd group) pathologic changes in the adrenals are less evident, which corresponds with cortisol level 63,4±3,2 nmol/l, in the second group - 84,5±3,7 nmol/l, in the first group- 42,5±2,8 nmol/l. It was noticed, that stress caused multiple hemorrhages on the mucous coat of stomach in the second group of animals.

In the Table 2 the content of POL in the blood plasma of the rats is presented.

During studying of the lipid peroxidation it was discovered that the content of MDA in the blood plasma of the rats of the second group was on the levelof 105.2nmol/ml and it was reliably higher by 53.8% comparing with the control group (68.4 nmol/ml). Inhibiting effect of 'Eramin' on the POL processes was noticed. The content of MDA in the blood plasma of the rats of the third group was 87.4 nmol/mlthat was higher then control group by 27.8%.

The content of DC- peroxidation products in the blood plasma of the second group was higher than the animals of the intact group by 46.9%. Invasion of the antioxidants to the rats' organisms in the form of 'Eramin' stabilizes the processes of free-radicals lipid oxidation during stress adaptation. The content of DC in the third group was on the level of 26.3 nmol/ml, what was reliably higher control by 15.3%. Stabilization of the peroxidation processes is explained by the chemical composition of the biologically active additive 'Eramin' chrolophyll, flavonoids (lutheolyn, rutin), organic acids (succinic, fumaric, oxalic), macro- and microelements (iron, copper, zinc, selenium). Flavonoids intensify activity of oxiredutase and peroxide ferments. Protein ceruloplasmin is the main antioxidant of plasma, binding superoxide ion-radical with the help of copper ions and reduces oxygen to water. Microelements- zinc, copper,

Table 1: Thymus weight, adrenal weight and state of mucous coat of stomach of male-rats (n=10)

| Group | Thymus weight, mg | Right adrenal weight, mg | State of mucous coat of stomach |
|---|---|---|---|
| 1 | 128,5±3,2 | 12,5 | No changes |
| 2 | 83,6±2,5** | 18,4** | Multiple hemorrhages |
| 3 | 114,7±3,0* | 15,8* | Single hemorrhages |

*p=0,05; **p=0,01

Table 2: The content of POL in the blood plasma of the rats, nmol/ml

| Group | MDA | DC |
|---|---|---|
| 1 | 68,4±5,3 | 22,8±1,5 |
| 2 | 105,2±7,1** | 33,5±2,1* |
| 3 | 87,4±6,2* | 26,3±1,8* |

iron are a part of antioxidant ferments [18]. Activity of Se-glutathione peroxidase depends on presence of selenium in the organism [19-23]. The content of selenium in the blood plasma of the animals of the second group was 164.3±5.2 mkg/l and does not reliably differ from control animals (172.5±5.4 mkg/l), whereas the rats additionally receiving 'Eramin' had level of selenium of 284.8±7.5 mkg/lor 161.9%.

## DISCUSSION

Using of the biologically active additive 'Eramin' in the ration of the stressed rats:

- Increases resistance to extreme factors;
- Does not cause decrease of lymphoid organs weight, structural changes in the adrenal cortex in the period of stress and stabilizes secretary activity of glucoproductive cells;
- Weakens lipid peroxidation.

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