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# COMPARATIVE STUDY OF THE BIOSYNTHESIS OF PROTEINS OF RAT LIVER MITOCHONDRIA AT PHYSIOLOGICAL AGING AND THE MODEL OF "ACCELERATED AGING", INFLUENCE ON THIS INDICATOR OF SOME PLANT PREPARATIONS

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**ABSTRACT**
It has been determined that quercetin and its supramolecular complex have the ability to stimulate the translation processes in mitochondria of rat liver in the model of "accelerated aging", as well as rats of different ages. Liver functions, requiring energy consumption and protein synthesis, enzymatic activities of subcellular structures, etc., suffer secondarily.

**KEYWORDS:** mitochondria, quercetin, physiological aging, accelerated aging, polyphenols, glycyrrhizic acid, rat liver.

## 1. INTRODUCTION

Mitochondria are universal organelles of the overwhelming majority of eukaryotic cells, and their main functions are the synthesis of adenosine triphosphoric acid (ATP), regulation of ion homeostasis, lipid metabolism and participation in apoptotic cell death. However, for all the diversity of shapes and sizes, the general principle of the structural organization of mitochondria is the same. In a complex hierarchy of intracellular structures, mitochondria occupy a special "semi-autonomous" position, as far as they have their own genome, as well as a complete set of enzymes necessary for DNA replication and for the synthesis of RNA and proteins.[1]

Evaluating the influence of age-related alterations on the efficiency of mitochondrial function, scientists noted a significant decrease in the production of ATP in the cells of the muscles of old cells, i.e. mitochondrial dysfunction.[2,3] Over the past decades, scientists have suggested that mitochondria are the cause of aging, but the real interest in them has appeared with the understanding that mitochondria are more than just a source of energy for the cell. In addition to the main function, these organelles can perform other functions. So, they protect cells from a very dangerous form of oxygen-free radicals, control chemical reactions inside the cell and also cause the natural death of a damaged or old cell. The influence of free radicals has long been attributed to the causes of aging and mitochondria serve as the primary source of free radicals and the source of basic protection against them.[4]

Alterations in old animals with mitochondria include a significant decrease of the membrane potential (difference in charges on the inner and outer sides of the inner mitochondrial membrane, through which work is carried out to synthesize of ATP – universal energy currency of the cell). For example, in old rats the membrane potential is reduced by 40% in comparison with the membrane potential in young animals. In the mitochondrial membrane, the level of cardiolipin – an important phospholipid, this is a cofactor for a number of important mitochondrial transport proteins, amount of coenzyme Q10 and carnitine decreases that is important for beta-oxidation of fatty acids.[5]

In previous studies, we found out that with increasing age, as well as on the model of "accelerated aging" in rats, there was an increase in the process of lipid peroxidation (LPO), as well as a decrease in the energy parameters of mitochondria, as a result of which the ATP synthesis fell.[6]

Obviously, with increasing age due to the above disorders, mutations accumulate in mitochondrial genes, the synthesis of proteins decreases, organelles begin to work less efficiently.

In this regard, the study of the influence of compounds that have antioxidant activity on the biosynthesis of mitochondrial proteins is of great interest.

The purpose of this study was to study the effect of glycyrrhizic acid (GA) isolated from the licorice root,

quercetin (Q) and a supramolecular complex (GA + Q), developed on the basis of GA and Q on the biosynthesis of proteins of liver mitochondria of rats with different ages and rats with the "accelerated aging".

## 2. MATERIALS AND METHODS

White outbred rats aged 3, 6, 12, 15 months were used in the research. All animals were divided into 13 groups. The first group was the control group (young, 3 months old), the second group was the "adult" model, corresponding to the age of 6 months, the third group was "adult" rats received polyphenol Q at a dose of 30 mg per kg of body weight of the animal; the fourth – "adult" rats, received GA at a dose of 25 mg/kg; the fifth – "adults" who received supramolecular complex GA + Q at a dose of 10 mg/kg; the sixth group-model "old", corresponding to the age of 12 months, the seventh, eighth and ninth groups – "elderly" rats, who received Q and GA, as well as a complex of GA + Q; the tenth model is "old", corresponding to the age of 15 months, the eleventh, twelfth and thirteenth groups are "old" rats, who received respectively Q, GA and GA + Q. The fourteenth group consisted of animals with the model of "accelerated aging". The fifteenth, sixteenth and seventeenth groups consisted of irradiated rats treated with Q, GA and GA + Q, respectively. To obtain the model of "accelerated aging", 6-month-old rats were subjected to a single X-ray irradiation at a dose of 2 Gray on the RUM-17 (dose rate 0.87 Gray/min, at 15 mA, 180 kV). Herbal preparations were administered to experimental rats for 7 days.

Mitochodria from liver of irradiated rats and rats of different ages were isolated by a well-known method of differential centrifugation.[7] The synthesis of proteins in mitochondria of the liver was judged by the inclusion of $C^{14}$-leucine in mitochondrial proteins.[8] The protein in the mitochondria was determined by.[9]

## 3. RESULTS AND DISCUSSION

After the determination of the protective action of Q and its supramolecular complex of GA + Q on the energy-producing processes taking place in the mitochondria of the liver of the "elderly" and "old", as well as model rats with "accelerated aging"[6], it was necessary to determine whether the observed effect of polyphenols linked with direct alteration in the synthesis of mitochondrial proteins? It is known that mitochondria possess an autonomous system of transcription and translation. Approximately 30 mitochondrial proteins are synthesized in the organelles themselves. These are enzymes and proteins that perform various functions in the mitochondria.[10]

Table 1 presents the results on the effect of these compounds on the biosynthesis of proteins of liver mitochondria in rats of various ages. From the data presented, it can be seen that with age there is a decrease in the incorporation of labeled leucine into proteins in mitochondria, which is consistent with the existing opinion about the specific damage with age not only of the nuclear but also of the mitochondrial genomes.[11]

Administration of GA, Q, as well as supramolecular complex GA + Q into rats had an ambiguous effect on the synthesis of mitochondrial proteins. Thus, GA insignificantly increased the inclusion of the label in the mitochondrial proteins of the liver of "elderly" and "old" animals. The administration of Q also did not cause a complete restoration of the functioning of the protein-synthesizing system of mitochondria of the "elderly" and "old" animals, although it increased the biosynthesis of proteins by 11 and 19%, respectively. Under the action of the complex GA + Q, a great stimulation of the synthesis of mitochondrial proteins was observed in these groups of animals and was 15 and 28%.

These data are agreed with results, well-known in the literature on polyphenol stimulation of the level of mRNA responsible for the synthesis of subunits of cytochrome oxidase[12], as well as with data obtained from other models. Thus, in vivo administration of polyphenols increased the maximum rate of respiration achieved in the presence of the substrate of ADP and phosphate, which, in the opinion of the authors, was caused by an increase in polyphenols in the synthesis of mitochondrial proteins.[13]

**Table 1: Alteration in the synthesis of liver mitochondria proteins in rats of different ages and the influence of various polyphenols on this index (M±m; n=7).**

| № | Animal groups | Inclusion of $C^{14}$-leucine into mitochondrial proteins (imp/min/mg of protein) | % of alteration |
|---|---|---|---|
| 1 | Control (3 months old rats) | 1709±31 | 100 |
| 2 | Adult (6 months old rats) | 1845±47 | 108 |
| 3 | Adult +GA | 1931±71 | 113 |
| 4 | Adult +Q | 2045,7±21 | 119,7 |
| 5 | Adult +(GA+Q) | 2127,7±36,3 | 124,5 |
| 6 | Old (12 months old rats) | 1493,8±54 | 87,4 |
| 7 | Old +GA | 1658±33 | 97 |
| 8 | Old +Q | 1681,6±29 | 98,4 |
| 9 | Old +(GA+Q) | 1749,8 ±62 | 102,4 |
| 10 | Old (15 months old rats) | 1194,5±27 | 69,8 |
| 11 | Old + GA | 1396,9±23 | 81,7 |
| 12 | Old + Q | 1508±34 | 88,2 |
| 13 | Old +(GA+Q) | 1675±59 | 98 |

In the next series of experiments, we studied the alterations in the synthesis of mitochondrial proteins in the model of "accelerated aging". The data are presented in Table 2.

**Table 2: Alteration of the synthesis of proteins in mitochondria in the liver of model rats with "accelerated aging" and the influence of various polyphenols on this index (M±m; n=7).**

| № | Animal groups | Inclusion of $C^{14}$-leucine into mitochondrial proteins (imp/min/mg of protein) | % of alteration |
|---|---|---|---|
| 1 | Control (3 months old rats) | 1709±31 | 100 |
| 2 | Adult (6 months old rats) | 1845±47 | 108 |
| 3 | Adult + irradiation | 1105,4±63 | 64,7 |
| 4 | Adult irradiated + GA | 1339,5±54 | 78,4 |
| 5 | Adult irradiated + Q | 1467,9±62 | 85,9 |
| 6 | Adult irradiated + (GA+Q) | 1574,8±54 | 92,2 |

Table 2 shows that irradiation of "adult" rats leads to a significant decrease in the inclusion of labeled leucine into mitochondrial proteins (by 30.2%). These data are comparable and even exceed the results obtained on "old" 15 months old animals. Flavonoid quercetin and its supramolecular complex GA + Q positively influence the system of mitochondrial translation of irradiated rats and increase its activity, although we did not mention the full restoration of the synthesis of mitochondrial proteins. As in experiments with rats of various ages, in our experiments with model animals, the supramolecular complex GA + Q was most effective. It is possible that in the later stages of aging, not only lipid but also protein part of the membrane structures are exposed to damaging effects, while GA + Q interacts favorably with enzymes and prevents the action of pathogenic factors.

Thus, based on the conducted experiments on research of the effect of polyphenols on the synthesis of mitochondrial proteins, data have been obtained that suggest that quercetin and its supramolecular complex have the ability to stimulate the translation processes in mitochondria of rat liver in the model of "accelerated aging", as well as rats of different ages. Inhibition of the protein-synthetic function of mitochondria in liver lesions leads, in the opinion of some researchers, to a decrease in oxidative phosphorylation. Liver functions, requiring energy consumption and protein synthesis, enzymatic activities of subcellular structures, etc., suffer secondarily.

The results obtained in our experiments on the alterations in the biosynthesis of proteins in mitochondria of rat liver cells of different ages under the influence of herbal preparations are in complete agreement with the literature data and indicates the need for the use of such compounds that exert a protective effect on mitochondria.

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