

## THE INFLUENCE OF COMPLEX LIPOSOMAL ANTIOXIDANT PREPARATIONS ON BIOLOGICAL OXIDATIVE STRESS MARKERS IN ISCHEMIC HEART DISEASE

Pylypenko D.M.<sup>1</sup>, Gorbach T.V.<sup>2</sup>, Krasnopolsky Yu.M.<sup>1</sup>

<sup>1</sup>National Technical University "Kharkiv Polytechnic Institute", Ukraine

<sup>2</sup>Kharkiv National Medical University, Department of Biochemistry, Ukraine

Lipid peroxidation processes are observed in many diseases, in particular in ischemic heart disease (IHD), indicating the decrease in activity of antioxidant defense system of an organism [1, 2]. Antioxidant therapy is actively studied in cardiology that requires the development of new effective pharmaceutical forms of antioxidants. Currently, studies aimed at the creation of liposomal (LS) forms of natural lipophilic antioxidants are conducted: quercetin (QUER), curcumin (CUR), coenzyme Q10 (Q10), etc. [3, 4]. The creation of LS form of drugs is a promising area in medicine, since it make it possible to create injectable water-soluble form of lipophilic compounds that allows for increasing their bioavailability.

The aim of the work was investigation of biochemical oxidative stress markers in blood serum of rats with IHD, treated with LS antioxidant preparations, containing QUER, CUR, Q10 and complexes of them.

**Materials and methods.** The study of the effectiveness of LS preparations was performed on IHD model of rats, simulated according to the method [5]. Experimental animals were divided into the following groups (n=6): 1 – intact animals; 2 – rats with experimental IHD; 3 – rats with experimental IHD, treated with LS-QUER; 4 – rats with experimental IHD, treated with LS-Q10; 5 – rats with experimental IHD, treated with LS-CUR; 6 – rats with experimental IHD, treated with complex LS form, containing QUER and CUR; 7 – rats with experimental IHD, treated with complex LS form, containing QUER and Q10. All LS preparations were intravenously administered at a dose of 10 mg/kg for 5 days. The following oxidative stress markers were determined in rat blood serum: total antioxidant activity, levels of malondialdehyde (MDA), conjugated dienes (CD), protein peroxidation and SH-groups [6].

**Results.** An increase in the content of MDA (by 180 %) %, CD (by 73 %), protein peroxidation (by 164 %) and a decrease in the levels of total antioxidant activity (by 40 %) and SH-groups (by 45 %) were observed in blood serum of rats with IHD compared to intact animals ( $p < 0.01$ ). The changes in the levels of antioxidant markers obtained in the study are consistent with the experimental and clinical data available in the literature [1, 2, 7].

When studying the effectiveness of LS forms of QUER, CUR and Q10, it was shown that this antioxidants demonstrated a different influence on the studied biochemical markers. For instance, the decrease in the levels of MDA and CD was the most effective in the groups of rats, treated with LS-QUER (by 56 % and 33 %, respectively) and with LS-Q10 (by 45 % and 33 %, respectively), while the use of LS-CUR reduced the levels of these markers to a lesser extent (by 30 % and 13 %, respectively) ( $p < 0.001$ ). An increase in the content of SH-groups was noticed in groups of LS-CUR and LS-Q10, while the use of LS-QUER was not effective in this case. However, the use of LS-QUER allowed for reducing the level of protein peroxidation to the level of intact animals. All LS preparations increased the level of total antioxidant activity at least 50 % compared to rats with IHD. Moreover, for the most part LS monopreparations, containing individual antioxidant (QUER, CUR or Q10), have not led to normalization of studied biological markers levels to the level of intact animals. In order to enhance the effectiveness of antioxidant defense, complex LS preparation, containing two antioxidants (CUR and QUER, or QUER and Q10), were used, and complex preparations were more effective compared to LS form of monopreparations.

It was shown, that QUER, CUR and Q10 have different mechanisms of antioxidant activity and exhibit higher effectiveness in complex using. Consequently, it is suggested that antioxidant effect could be explained by synergetic activity of complex antioxidant preparations.

Prospects for further research. Future studies will deal with the influence of complex LS form of antioxidants on the enzymatic antioxidant system and the dose-dependent effect.

## References

---

1. Middleton E.Jr., Kandaswami C., Theoharides T.C. The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer. *Pharmacol. Rev.* 2000; 52(4): 673-751.
  2. Pavlova E.A. The influence of antioxidant therapy on lipid peroxidation and antioxidant protection in ischemic heart disease. *Actual Probl. Transp. Med.* 2017; 1(47): 154-157.
  3. Krasnopolskii, Yu.M., Grigor'eva, A.S., Katsai, A.G. et al. Technologies and perspectives of liposomal Drug Application in clinical practice. *Nanotechnologies in Russia.* 2017; 12: 461-470.
  4. Grygorieva G.S., Krasnopolsky Y.M., Konachovich N.F., Pasychnikova N.V. Method of obtaining active liposomal quercetin-containing product. WO 2016/007114 A1. 2016 Jan 14.
  5. Gaman D.V., Kononenko N.N., Gubina-Vakulik G.I. et al. Features of the morphogenic ultrastructure of the myocardium in experimental myocardial ischemia. *Ukr. Biopharm. J.* 2011; 5: 16-20.
  6. Deryugina A.V., Koryagin A.S., Kopylova S.V., Talamanova M.N. Methods of study stress and adaptive reactions of the body in terms of the blood system. Nizhniy Novgorod: Izd-vo Nizhegorodskogo gosuniversiteta; 2010. 25 p.
  7. Farías J.G., Molina V.M., Carrasco R.A. et al. Antioxidant Therapeutic Strategies for Cardiovascular Conditions Associated with Oxidative Stress. *Nutrients.* 2017; 9(9): 966.
- 

**Key words:** *oxidative stress markers, ischemic heart disease, liposomal antioxidant*