BIOTECHNOLOGY

UDC 547.9:678.048 (045)

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LYMPHOCYTIC CHALONES IS A NEW CLASS OF NATURAL ANTIOXIDANTS

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Abstract. *The analysis of biological properties of lymphocytic chalones, regulators of cell proliferation, indicates the prospect of the creation of these new antioxidant preparations for the correction and normalization of immunological reactions in current adverse conditions of environment.*

Keywords: antioxidants; free radical reactions; immunological reactions; lipid peroxidation; lymphocytic chalones.

1. Introduction

Number of immunomodulators used in medicine today is great, but it's mostly synthetic drugs with side effects.

Therefore, there are constant searches for substances that have no toxic, mutagenic, carcinogenic effects on the body and have focused influence on the immune system.

Such requirements are met by the biologically active substances of natural origin — lymphocytic chalones, from which the creation of new immunopharmacological tools will provide new facts that are important for the determination of the functioning and regulation of the immune reactivity.

Creation of the immunopharmacological means for the treatment and prevention of diseases highlight the search for medicines that provide effective results in diagnostics of immunopathological states of the organism, determination of the immunodeficiency level.

2. Literature analysis

In 1970–1980 a new class of biologically active substances — chalones derived from 20 kinds of tissues was revealed.

A number of studies [3, 6, 13, 17, 19, 21] describe chalones properties: they are exempt from differentiated cells and inhibit their proliferation.

The action of chalones is tissue-specific and phase-specific but not species-specific.

Chalones are not toxic, their action is reversed.

All this indicates general biological character of chalones regulation directed to support interstitial homeostasis and shows the universality of chalones regulation of cell proliferation.

Lymphocytic chalones were discovered in 1970s [6, 7, 13, 14, 17, 18].

It was shown that the spleen and thymus chalones inhibit proliferation of PHA-stimulated lymphocytes in vitro, decrease lymphocyte proliferation in the follicles of the spleen, lymph nodes, the number of retarded plaque forming cells prolongs graft transplants leather. Like all chalones, lymphocytic ones have tissue specificity but not species specificity.

3. Role of free radical reactions in the organism

Free radical reactions play one of the most important roles in the regulation of cell proliferation.

E.B. Burlakova in 60–80 years of XX century [5] put forward a hypothesis about the role of free radical mechanisms in the regulation of cell proliferation.

This mechanism describes one or more stages of free radical processes, the intensity of which depends on the process of reproduction.

The intensity of these shares is primarily due to the content of natural inhibitors.

Changing number of natural inhibitors or changes in the speed of initiation of free radical reactions regulate those metabolic processes related to cell proliferation.

The author suggests that a steady state of a living organism ratio of natural inhibitors to the concentration of free radicals is the largest constant.

The growth of free radicals inhibits cell proliferation and inhibits the growth of natural inhibitors of free radicals, which in turn leads to an increase in proliferating cells.

Thus, in many actively prolifferating tissues high quantities of antioxidants are found [4].

The presence of free-radical steps in the mechanism of the regulation does not preclude other ways and second ionic or molecular mechanisms.

Setting interconnection and interdependence of these pathways can approach the solution of the question of regulation of cell reproduction and control those diseases that are dependent on the violation of this mechanism [4].

Rate of cell processes associated with the intensity of oxidative reactions in lipids, number of AO changes the speed of cell proliferation [5].

Antioxidant activity of lipids increases before DNA synthesis, but during the process of synthesis it takes a minimum value and then increases when DNA ends.

It is possible that derived changes in antioxidative activity of lipids in vivo and in vitro are specific and logical when the cell divides [1].

Antioxidants are substances that can inhibit the oxidation.

The natural antioxidants or bio-antioxidants include substances of plant or animal origin that impede the development of free radical oxidation. In experiments in vitro antioxidative properties have different biologically active substances:

— tocopherol;
— steroid hormones;
— ubiquinone;
— phospholipids.

Reducing or failure in the body of certain natural antioxidants actually leads to the intensification of oxidative processes in lipids and until their oxidation products appear in larger quantities than normal.

Antiradical activity characterizes the possibility of compounds to react with free radicals and antioxidative activity determines the ability of these compounds to inhibit the oxidation process [4, 5].

Free-radical oxidation in the tissues of living organisms is normal in general biological regularity [23]. Tissues in living organisms are of 2 types of oxidation processes: enzymatic and non- enzymatic.

Multiple-enzymatic oxidation eliminates oxidative addition of oxygen to the substrate. Energy is released in small portions (6–10 kcal at each stage electron cascade).

The final products of biological oxidation are inactive compounds most often are H_2O and CO_2.

When non- enzymatic, free radicals continuously generated free radicals.

There is a direct oxidative addition of oxygen to the substrate.

In this case, the formation of toxic oxy-dependent products (free radicals, peroxides, aldehydes, ketones, etc.), much of which is in electrically-agilated state, which are then transferred to the ground state.

This process is accompanied by chemiluminescence in the visible or near-ultraviolet region.

The intensity of free radical changes under the action of the original product reactants (energy substrate or oxygen) or reaction products (radicals, peroxides).

A classic factor that generates free radicals throughout the body is ionizing radiation.

Changing the intensity of free radical oxidation by redistribution of tissue antioxidants is one of the mechanisms that provide the autoregulation of cells [22]. Free radical mechanisms are very labile, because they can change in one direction or another.

This allows dynamic responsive to the influence of different factors. In this regard there is a great similarity of free radical mechanism in the regulation of cell proliferation and adaptation of Selye syndrome [2].

Stress agents affect the antioxidant activity and the intensity of free radical reactions and, therefore, the processes of cell division, and the immune reactivity [21].

But if we see only a decrease in the number of natural inhibitors during the action of stress agents, then for free radical mechanism of regulation one part of inhibitors reduces the quantity of inhibitors and increases the intensity of free radical reactions, but the second part in opposite — increases the number of natural inhibitors and, thereby, reduces free radical reactions.

During changes in free radical mechanism the similar phenomenon to stress and antistress can be observed [2, 24].

Changes in free radical mechanism may be temporary, reversible or can move to another level of autoregulation and also may be irreversible and lead to a breach of regulatory functions. Increased level of cholesterol and unsaturated fatty acids protects against free radical processes [16].

4. Antioxidant properties of lymphocytic chalones

In the state of development of the immune response and its suppression of endogenous lymphocytic chalones the range of fatty acid membranes of immune cells was studied.

It was found that during the induction of an immune response on the first day of research in the spectrum of fatty acid membranes lymphocytes have no significant changes while using thymic lymphocyte chalones with a molecular mass of 30–40 and 10 kDa.

Although using the fraction with a molecular weight of 13–17 kDa amounts of unsaturated fatty acids were increased, and saturated fatty acids were decreased. The level of cholesterol on the first day for all test and control groups was reduced approximately 2-fold.

On the third day, in the proliferative phase of the immune response in experimental group's saturation index was decreased by 1.5 times compared to the control.

This trend was in the conditions of use of fractions with a molecular mass of 30–40 kDa and 13–17 kDa.

In experiments in vitro in control there was a decrease of saturated fatty acids and increase of unsaturated fatty acids.

In test samples it was vice versa.

Cholesterol in control and studied samples was within norm.

When using fractions of chalones there was an evident three-time decrease in cholesterol level.

On the fifth day, in the productive phase of the immune response in the experimental and control groups there was no clear pattern in the distribution of fatty acids in the lipid matrix of immune cells. The level of cholesterol in the control samples in vitro fraction with a molecular weight of 30–40 kDa was increased by 6 times, when in use of research fractions with a molecular weight of 30–40 kDa and 10 kDa cholesterol level was decreased 2-fold and was 1.5-fold increased when in use of fractions with a molecular weight of 13–17 kDa.

Range of fatty acids and cholesterol in the membranes of cells was dependent on the phase of the immune response and the molecular weight of thymic lymphocyte chalones used in the experiments.

Thus, in vitro conditions the fractions with a molecular weight 30–40 and 13–17 kDa in the cell membranes mainly increased the polyunsaturated fatty acids and cholesterol and reduced the amount of saturated acids.

Such a clear relationship of fatty acids was observed in the use of fractions with a molecular weight 10 kDa.

During the development of the immune response thymic chalones effect on fatty acid composition and cholesterol content in the membranes of cells was in different directions dependent on the phases of the immune response and molecular weight of chalones [12].

In conducting experiments on a model of antioxidant failure caused by the E-avitaminosis, the violations in lymphocytic chalones system was found that had manifested in the following.

The level of lymphocytic chalones production was increased with antioxidant deficiency and vitamin E, the increased inhibitory activity of lymphocytic chalones (66% and 54%) was recorded in relation to the proliferative activity of lymphocytes and disappeared activity in relation to the synthesis of DNA, that is, in these conditions, may have been produced in chalones acting on pre-mitotic phase of the cell cycle of lymphocytes.

According to the results of gas-liquid chromatography of the lipid complex of lymphocyte membranes it was found that lymphocytic chalones normalized range of fatty acids of lymphocyte membranes, which led to the conclusion about antioxidant properties of lymphocyte chalones [10].

In our studies devoted to evaluation of the antioxidant properties of lymphocytic chalones with stable radical — diphenylpicrylhydrazyl it was found that lymphocytic chalones has high antioxidant properties.

Freshly obtained lymphocytic chalones converts 50% of diphenylpicrylhydrazyl radical form to a non-radical in 7.6 min, and if saving for 6 months — in 5.5 hours [9, 11].

Due to the fact that the maximum production of lymphocytic chalones [8] noted in the inductive phase of the immune response, and the maximum production of products of lipid peroxidation in the proliferative phase Lymphocytic chalones — a new class of natural antioxidants

It is indicates a significant relationship lymphocytic chalones and of lipid peroxidation and has a biological significance for the regulation of free radical processes in conditions of immunological reactions [15].

5. Conclusions

Thus, the analysis of biological properties of lymphocytic chalones, regulators of cell proliferation, indicates the prospect of the creation of these new antioxidant preparations for the correction and normalization of immunological reactions in current adverse conditions of environment.

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Received 10 December 2013.

К. Г. Гаркава. Лімфоцитарні кейлони-новий клас природних антиоксидантів

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Проведено аналіз біологічних властивостей лімфоцитарних нейлонів — регуляторів клітинної проліферації. Показано перспективність створення з них нових антиоксидантних препаратів для корекції та нормалізації імунологічної реакції організму в сучасних несприятливих екологічних умовах.

Ключові слова: антиоксиданти; вільнорадикальні процеси; імунологічна реакція; лімфоцитарні нейлони; перекисне окиснення ліпідів.

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Выполнен анализ биологических свойств лимфоцитарных кейлонів — регуляторов клеточной пролиферации. Показана перспективность создания из них новых антиоксидантных препаратов для корекции и нормализации иммунологической реакции организма в современных негативних екологических условиях.

Ключевые слова: антиоксиданты; иммунологическая реакція; лимфоцитарные кейлоны, перекисное окисление липидов; свободнорадикальные процессы.

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