

## THE INCREASE OF LIVING ORGANISMS RESISTANCE THROUGH APPLICATION OF BIOLOGICAL ACTIVE SUBSTANCES

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### ABSTRACT

At present, people need to face with thousands of toxic substances, pollutants and sickly products. Because of the big sensitivity level for diseases appearance, application of biological active substances could may represent the best solution. Bee products can be a major wellhead for obtaining of some essential bio-products, which are sources of pharmaceutical, aromatic and industrial compounds. A long time ago, herbal plants and bee products were used by people in metabolism regulation, immune system improvement and increase of mental skills.

**Key words:** impact, resistance, immunity, health, diseases.

### Introduction

Recently, World Health Organization estimates that about 80% of people around the world are interested by pharmaceutical drugs with natural origin, which utilization increased in the last 30 years for medical purposes. Biological active substances are one of the most popular categories of nutritive products that are consumed by people at present. They contain essential substances, which are necessary for maintaining a good health state. Biological active substances can regulate the metabolism of organism, can increase the metal skills and improve the immune system. They act as antioxidants for free radicals eliminating, grow the level of energy, low the answer on stress and prevent diseases caused by vitamin or mineral deficiency.

The biological active substances are used for:

- Fast supplement in biological active substances deficiency, that are not arrive in organism in sufficient quantities;
- Increase the organism resistance;
- Preventive maintenance of metabolic processes;
- Immune system regeneration;
- Prevention of chronic diseases;
- Reduction of toxins level in organism.

In the last time, a series of natural products were increasingly studied by chemical and biological point of view for their stimulation effects of some organism functions. A particular category of such extracts is created by those which have immunomodulation, anti-inflammatory, antioxidant qualities, and those that represent in traditional medicine of some countries, the basic concepts in

therapeutic techniques and methodologies for some diseases.

The Republic of Moldova disposes by a considerable potential of local stock, necessary for elaboration and implementation of new apitherapeutic drugs. These are confirmed through research results based on local stock usage – extract from beeproducts, realized by “Human and Animal Ecophysiology” Laboratory inside of Scientific Researches Center “Life of Sciences” at Moldova State University.

Propolis is presented as a product with an extraordinary therapeutic value, being appreciated as one of the most efficient natural compounds with effect of regulation, maintenance and health’s body improvement.

The main particularities of this compound are bacteriostatic and bactericidal actions. Propolis inhibits the activity, and also kills a quite wide spectrum of different microorganisms, including hepatitis viruses, trichomonas, tuberculous bacilli, candidiasis. It is worth to notice that intestinal microflora does not suffer, so it can’t be a dysbiosis. This property has both liquids: alcohol and aqueous propolis.

In the XXI century, scientists revealed that propolis sterilizes almost complet beehive, inhibits the virus growth and prevents the recurrence of viral infection. The simultaneous reception of propolis with antibiotics improves their action.

Propolis affected not only bad microorganisms, but also phagocytosis, improving this process that consists in unknown material elimination by body with special cells – phagocytes. This fact low the organism toxicity. In this way,

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propolis increases immunity and the gamma globules level.

This natural compound is considered an excellent local anesthetic, especially in liquid alcohol, being widely used:

- in the treatment of gums, mouth and teeth affections;
- in otitis;
- in case of eye burns or injuries;
- in the cure of injuries, burns or frostbites.

Anesthesia begins at 5-10 minutes right after propolis application and can hold out from 45 minutes to 2 hours.

It was demonstrated that propolis helps to establish blood coagulation process. This fact has a special significance for complications treatment and prevention after strokes and heart attack, because in such conditions the blood coagulation level increases very much. The coagulation process growth with age, this natural compound is also useful for people after 50 years old.

Propolis fortifies capillary walls damaged by injuries, cuts, bruises, nose or gums bleeding. It has also the ability to increase the skin permeability, healing abscesses and suppurations with a rapid resorption. Propolis helps to reduce pruritus in psoriasis, after bites, burns and fungal diseases. It plays a dermatoplastic role, restoring the mucous membranes that cover up the body organs, and also prevents scar evolution.

Propolis is known as well for antitumor and antioxidant properties. It limits the tumor process, normalizes respiration process at cell level and establishes the cell reproduction in our body.

Specialists in herbal medicine are resolute convinced of the fact that the most effective method for propolis administration remains the tincture. The propolis tincture represents the alcoholic extract of propolis, which was obtained after his preparation at cold temperature. Among herbal and bee products that are administrated in the oral form, alcoholic and hydro-alcoholic liquids are very easy assimilated by organism in a short period of time.

One from the multiple benefits of the propolis tincture is the antihyperglycemic action. The studies show that propolis tincture administration on the background of diabetes mellitus can stabilize the blood sugar level. This property takes place due to some elements from chemical composition of propolis as: vitamin PP, vitamin C, flavones. Vitamin PP interferes in carbohydrates and lipid metabolism as prostetic group; vitamin C contributes on growth of defense body capacity through leucocytes activation and immune response stimulation; flavones with a very

wide spectrum, have an antihistamine, antihyaluronidase and anti-inflammatory effect.

The researchers [3] were demonstrated that ability to manage the blood glucose level and to control the exact process of glucose and lipids metabolism, ultimately inducing more poor results about lipids peroxidation and free radicals at rats with experimental diabetes. According to scientific researches, propolis represents a real food stimulant.

The effects on immune system include activation of macrophages, modulation of lymphocytes and antibodies proliferation, cytokines production, as well as inhibition of transcription factors. In this way propolis constitutes one of the bee products, that has an essential role in treatment and prevention of some human diseases, due to the context with amino acids, proteins, hydrocarbons, enzymes, flavones, microelements etc. The above examples suggest the possibility of propolis tincture usage for management of carbohydrates metabolism, amelioration of inflammatory problems to diabetic people, and also beneficial role on immune system.

The propolis tincture shows positive effects in body detoxification and revitalization due to his content. Also, plays a role in prevention of some complications, which appear at diabetic patients as cardiovascular affections. There is an interrelation between the phenomenon of leukocytosis and diabetes mellitus, the increase of leukocytes number in blood being the important cause of subsequent complications by this pathology.

At diabetic patients lows in distinctive way the capacity of granulocytes non-specific and specific defense. Also declines the lymphocytes number caused by apoptosis. This phenomenon has a rate twice more increased than the health subjects. The lymphocytes apoptosis provokes the deficiency of immune response and induces a lot of pathologies. In case of insulin administration at patients with type 1 diabetes was noticed an increase of leukocytes number. In case of ketosis and diabetic coma, the leukocytosis is usually raised, being accompanied by lymphopenia and eosinopenia.

In an initiated study that took place in the period: march 2015-2016, were emphasized the following effects on leukocytes at diabetic patients with type 2, between 40-60 years old of both sexes: in case of untreated diabetes the leukocytes execute an aberrant chemotaxis, an increased susceptibility at bacterial infections and releases lysosomal enzymes [1]. Researchers support that diabetic persons have an increased risk to catch much more severe and frequent infections than healthy people. This predisposition on infections is determined by hyperglycemia and faulty immune system.

According to a study [2], in case of experimental diabetes on rats was studied the frequency of DNA fragmentation at lymphocytes. After analysis of lymph nodes was found that DNA fragmentation at rats was twice increased, aught suggests that diabetes induces the lymphocytes apoptosis. Modifications of cellular immunity can be in relation with some metabolic changes – the base for research of leukocyte status in organism.

Recent were execute investigations (November 2016) on diabetes type 1, which demonstrated inflammatory effects and progresses in disease evolution, the results being published in American Journal of Pathology. It was noticed that diabetes type 1 changes the innervation and the immune function of bone marrow. This causes the increase of monocytes level, involving inflammatory signals in sympathetic centers at rats. The scientists were demonstrated that use of minocycline, an antibiotic which crosses blood brain barrier, reduces inflammatory responses by animal brain in diabetes type 1. This fact can prevent the diabetes complications at humans [4].

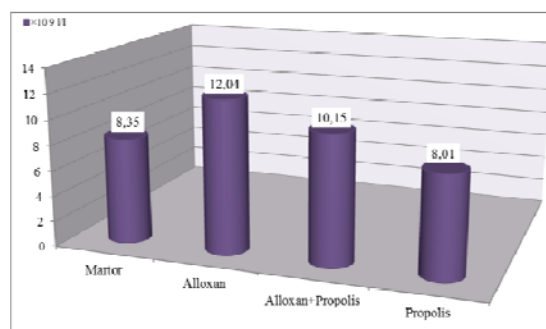
According to American researchers [2], in diabetes type 1 and 2 induced by alloxan on rats with a rich caloric diet, the leukocytes are strong recruited, having a reduce function in inflammation. Also, it was observed that phagocyte activity of rat leukocytes after inoculation with *Staphylococcus aureus*, being reduced towards the control group.

In case of investigations at “Human and Animal Ecophysiology” Laboratory, a special attention attracts the leukocytes changes in experimental diabetes. Comparing the Martor group with Propolis group is observed the fact that propolis tincture has the same effects on organism as physiological solution with small differences (Table 1).

**Table 1** - The propolis tincture influence on number of leukocytes on the alloxanic diabetes background

Indices	Martor	Alloxan	Propolis	Alloxan +Propolis
Number	30	30	30	30
Leukocytes ( $\times 10^9$ l/l)	8,35± 0,03	12,04± 0,21	8,01± 0,15	10,15± 0,17

Analyzing the experimental groups it can be observed that number of leukocytes increases in Alloxan group at  $12,04 \pm 0,21 \times 10^9$  l/l towards Martor group. This growth have place due to metabolic changes which are occurred in organism after experimental diabetes installation.



**Fig. 1** - Leukocytes level ( $\times 10^9$  l/l) in blood at propolis tincture administration on the experimental diabetes background

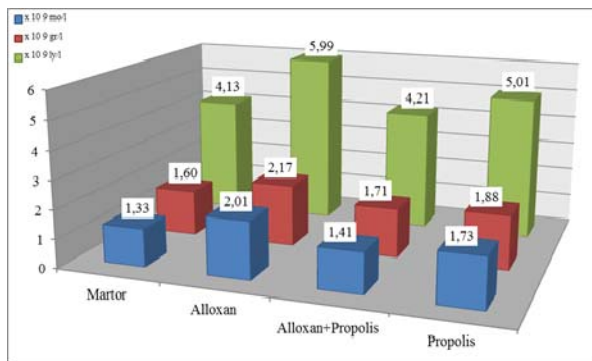
The big number of leukocytes at initialstages of diabetes demonstrates the body fight for homeostasis maintenance in several pathology. So results were obtained and by other scientists that can not to contradict us, because in late stages of diabetes evolution takes place an immunity discount followed by decrease of leukocytes number.

**Table 2** - The propolis tincture influence on white blood cell indices on the alloxanic diabetes background

Indices	Martor	Alloxan	Propolis	Alloxan +Propolis
Number	30	30	30	30
Lymphocytes ( $\times 10^9$ ly/l)	4,13± 0,11	5,99± 0,20	4,21± 0,39	5,01± 0,87
Monocytes ( $\times 10^9$ mo/l)	1,33± 0,08	2,01± 0,07	1,41± 0,02	1,73± 0,42
Granulocytes ( $\times 10^9$ gr/l)	1,60± 0,80	2,17± 0,11	1,71± 0,51	1,88± 0,12

The white blood cells stick to endothelial cell via classic molecules of adherence: ICAM-1 (intercellular adhesion molecule-1) for blood vessels. Leukocytes accumulation is making in time, predominantly being monocytes and neutrophils. The level of these adhesion molecules increases with diabetes mellitus induction and is correlated with growth of white blood cells number.

The debut of diabetes vascular dysfunctions agrees with the growth of leukocytes number. At beginning, the dysfunction is subclinical or undetectable through clinical and paraclinical methods because of low sensitivity of diagnostic methods. When diabetic rats are treated with propolis tincture, the leukocyte adherence is suppressed, hematoretinian barrier is restored and endothelial damage is prevented.



**Fig. 2** - The level of white blood cell indices at propolis tincture administration on the experimental diabetes background

A big part of lymphocytes gets in blood through lymphatic vessels. A small part is lost in intestinal lumen and in lungs, others are phagocytosed, but the most lymphocytes deeper proliferates after the contact with specific antigens, and some of them are converted in producing antibodies cells, being dispersed in the body tissues.

After research investigations were identified the results about the number variation of lymphocytes in induced alloxanic diabetes on the background of propolis tincture administration. So, it was observed a number increase of lymphocytes in Alloxan group ( $5,99 \pm 0,20 \times 10^9$  ly/l) with 15% more than control group ( $4,13 \pm 0,11 \times 10^9$  ly/l). Administration of propolis tincture on the alloxanic diabetes background leads to a relative balance of this parameter until  $5,01 \pm 0,87$  ly/l. The modifications that appear during progression of alloxanic diabetes is the base reason for thoroughgoing investigations study, emphasizing the need of methods and processes elaboration in directed maintenance for suffering organism by diabetes. The increase of circulating lymphocytes takes place in some acute and chronic infections, but in our research case it's also about in experimental diabetes.

Monocytes are big blood cells with very fine grains, which are produced in bone marrow and in lymphopoietic organs. They stay in the circulation only about 24 hours, after that migrate in tissues where transformed in macrophages and kill the bacteria. The number of monocytes varies from control group:  $1,33 \pm 0,08 \times 10^9$  mo/l, to alloxanic group:  $2,01 \pm 0,07 \times 10^9$  mo/l. In alloxanic diabetes on the background of the propolis tincture administration is attested a relative monocytes amelioration up to  $1,73 \pm 0,42 \times 10^9$  mo/l. Similar results were obtained and from other researchers. This is a proof about stimulation role of propolis tincture on the background of experimental diabetes.

Granulocytes plays a big role in initial anti-infectious organism defense through phagocytose and microorganism digestion, but their inappropriate activation can lead to destruction of normal tissues through enzymes and pathogens liberation. With infection appearance are produced chemotactic agents that determine neutrophils migration to the infection focus and activation of their defensive functions with phagocytose of respectively agent, followed by granules liberation in phagocytose vesicle and destruction of the infectious agent. This effect is frequently associated with the increase of neutrophils production and release from bone marrow.

On the background of experimental diabetes we noticed an increase of granulocytes number – process that is called granulopoiesis. It takes place at the bone marrow level. It's considered that neutrophil, eosinophil and basophil granulocytes follow the same model of proliferation, differentiation, maturation and in blood liberation. In addition to bone marrow, the neutrophil granulocytes can be found in tissues, where some of them circulating in the blood vessels and others adhere at the vascular endothelium. The growth of circulating neutrophils is due to their liberation from bone marrow or mobilization of neutrophils from the border.

In our investigation is attested an increase of granulocytes number from  $1,60 \pm 0,80 \times 10^9$  gr/l at control group to  $2,17 \pm 0,11 \times 10^9$  gr/l at alloxanic group. The administration of propolis tincture on the experimental diabetes background led to a normalization of this parameter till  $1,88 \pm 0,12 \times 10^9$  gr/l.

The changes about white blood cells in diabetes mellitus represent a big problem, the reason being illustrated in multiple investigations at this field. It was demonstrated the beneficial effect of propolis tincture on this indices not only in our investigations but also in other studies. Comparing the obtained results from different experimental groups we can see that the number of leukocyte indices in alloxanic diabetes has a significant increase, but administration of propolis tincture on the experimental diabetes background attested a relative equilibration of them.

The use of natural remedies based on apitherapeutical drugs became nowadays a highly requested branch. In this way, apitherapy stimulates the body defensive system, such that organism fights alone against the malady, this thing representing a holistic approach. Herbal medicine can be estimated as insufficiently strong in some of affections and can't be set to all persons, depending on disease

severity and complications. However, on the base of obtained results we can mention that propolis tincture used a long period of time in an adequate dosage can improve the situation at diabetic persons.

### **Rezumat**

În prezent, oamenii sunt nevoiți să se confrunte cu o mulțime de substanțe toxice, poluanți și produse dăunătoare sănătății. Din cauza sensibilității crescute de apariție a maladiilor, aplicarea substanțelor biologic active poate reprezenta una din cele mai bune soluții. Produsele apicole pot fi o sursă promițătoare de obținere a unor bio-produse esențiale, care conțin compuși farmaceutici, aromatici și industriali. Cu mult timp în urmă, plantele medicinale și produsele apicole erau utilizate pentru reglarea metabolismului,

fortificarea sistemului imun și creșterea abilităților cognitive

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