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Gudkova, O.O., Krysiuk, I.P., and Shandrenko, S.G.

Palladin Institute of Biochemistry of the NAS of Ukraine,
9, Leontovicha St., Kyiv, 01601, Ukraine,
+380 44 234 59 74, +380 44 279 63 65, secretar@biochem.kiev.ua

INNOVATIVE PROPOSALS ON THE IMPLEMENTATION OF DIETARY SUPPLEMENTS FOR DIABETES MELLITUS AND HELICOBACTERIOSIS

Introduction. *Diabetes mellitus and gastrointestinal tract pathology are among the most common pathology of modern society. In Ukraine, the number of patients with all types of diabetes increases, with gastrointestinal tract diseases caused by Helicobacter pylori showing intensive upward dynamics because of transmission in domestic conditions.*

Problems. *Therefore, two dietary supplements for the prevention and mitigation of diabetes mellitus and stomach helicobacteriosis have been developed on the basis of fundamental research conducted in the Palladin Institute of Biochemistry of the NAS of Ukraine.*

Purpose. *To evaluate the effectiveness of these dietary supplements.*

Materials and Methods. *The effectiveness of developed nutritional supplements has been confirmed by in vivo experiments. The degree of H. pylori infection ingress has been determined by non-invasive direct urease test using Helicotester device.*

Results. *The results have shown a high efficacy of the developed dietary supplements. Thus, the dietary supplement for diabetes reduces the content of toxic components, such as total amount of aldehydes, carbonyl groups and postsynthetic modification of proteins, which can suppress development of diabetes complications. The dietary supplement for helicobacteriosis has been proved to enable reducing the degree of H. pylori infection ingress in stomach, which can effectively prevent the development of gastrointestinal tract diseases.*

Conclusions. *The developed dietary supplements contain cheap and stable long-storable components, enable to effectively reduce the content of toxic components in the patients with diabetes and manifestations of certain gastrointestinal tract diseases, to improve the functioning of the body, and to maintain its working capacity and health.*

The authors are looking for investors to application of these dietary supplements to production.

Keywords: dietary supplements, diabetes, helicobacteriosis, glycine, lysine, N-acetyl cysteine, urea, and silver nitrate.

Today, the World Health Organization has recognized diabetes as a disease that has reached a global epidemic. According to official statistics, in Ukraine, about 1.3 million patients have been diagnosed diabetes, but their actual number is assumed to be 2—2.5 times higher, as a significant part of patients with diabetes finds out the diagnosis at the stages of formation of persistent signs of pathology.

Helicobacteriosis of the stomach is a condition with an elevated titer of *Helicobacter pylori* in the specified organ. In 1994, the International Agency for the Study of Cancer (IARC) concluded in 1994 that *H. pylori* (that lives in the lower (pyloric) stomach) had a causal linkage to gastric carcinogenesis and is a definite carcinogen in humans (there have been obtained clinical evidence linking *H. pylori* to gastric cancer). Increased infectivity *H. pylori* is also thought to be the cause of such diseases of the stomach and duodenum as gastritis and ulcers.

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Complex nutritional supplements for prevention, reduction of negative consequences of the development of pathologies of different genesis, and for maintenance of the normal state of health of different ages are developed based on fundamental research conducted at the Department for Metabolic Regulation of Palladin Institute of Biochemistry of the NAS of Ukraine. For the time being, the following supplements "Complex dietary supplement for patients with diabetes" and "Complex dietary supplement for patients with helicobacteriosis" have been completely developed [1, 2]. Below, there is a description of characteristics and effectiveness of these additives.

Complex dietary supplement for patients with hyper-carbonyl state

Diabetes mellitus may have severe complications, in particular, angiopathy, retinopathy, polyneuropathy, diabetic foot, which may result in cardiovascular disease, acute and chronic renal disease, cognitive impairment, loss of vision, limb amputation and, eventually, premature death [3, 4].

Steady increase in the sugar (glucose) content in patient's blood (hyperglycemia) plays a key role in the development of complications. Since glucose belongs to the monosaccharides that are aldehydes, carbonyl compounds with a high reactivity, the development of diabetes is accompanied with an increase in the content of these compounds in the body (the hyper-carbonyl state). The reaction of carbonyl compounds with proteins and nucleic acids leads to the formation of end products of glycation, which, in turn, causes changes in the regulation, transport, reception, protection, and structure of cells and extracellular matrix, which in the future may cause disorders of systems and organs and numerous diseases. N-carboxymethyl lysine is one of the end products of glycation. Its concentration in blood serum correlates with the content of glucose, and therefore it is a bio-marker of diabetes mellitus and its complications. Recently, this indicator has been used to characterize the degree of development of diabetes mellitus concomitant diseases (pathology of vessels, kidneys, retina, bone and connective tissues, etc.) [5]. Therefore, reducing the amount of generated reactive aldehydes and the intensity of protein modification in the body of patients with diabetes mellitus is important for maintaining a satisfactory state of patient's health and ability to work.

In order to reduce the adverse effects of the formation of excess amount of aldehydes and their modified proteins under conditions of diabetes mellitus, a biologically active nutritional supplement consisting of L-lysine, L-glycine, and N-acetyl cysteine has been created. The first component effectively reduces the intensity of aldehydes interaction with the body's proteins, since it is actively involved in the formation of aldehyde-dependent modifications of proteins in the body. In addition, lysine has shown immunomodulatory and antiviral, antidepressant, and anxiolytic effects [6, 7]. L-lysine and L-glycine are structural components of the collagen molecule (collagen is the basic material of bone and connective tissue) and one of the targets in the case of diabetes development. N-acetyl cysteine is part of a nutritional supplement as a donor of SH-groups that are acceptors of aldehydes and thus provide antioxidant protection and lower the hyper-carbonyl content.

The effectiveness of the proposed dietary supplement has been confirmed by studies conducted in the Department of Metabolic Regulation of the Palladin Institute of Biochemistry of the NAS of Ukraine on the model of diabetes mellitus type I [8] in rats. The use of dietary supplement has been shown to decreases the content of toxic components and their products, in particular, aldehydes (5.7 times), carbonyl groups of proteins (1.27 times), TBC products (3.4 times), and carboxymethyl lysine in plasma (2.25 times) in the liver of rats. Also, the level of antioxidant protection increases as the content of SH-groups grows 1.7 times, with the indicators approaching those of healthy animals.

Complex dietary supplement for patients with helicobacteriosis

Maintenance of *H. pylori* titer within the norm is a means of prevention of gastrointestinal tract diseases. The pathogenic effect of the bacterium on the organism is caused by increased activity of urease enzyme [9], due to which urea (the main product of nitrogen metabolism) in the stomach is converted into ammonia that locally changes the medium reaction from pH 2.0 to alkaline values (pH 4.8—7.4). As a result, in the sites of bacteria localization on the stomach mucous membrane there appears an inflammation that subsequently may evolve into an ulcer [10].

A dietary supplement that improves the gastrointestinal tract functioning and maintains a satisfactory state of health and the ability to work in patients of different ages, who are infected with *H. pylori*, has been developed for correcting the microbiocenosis composition. The supplement contains two components, a solution of silver nitrate and urea powder. Therefore, as compared with other existing supplements, it is more stable to storage, since the active substances are packed separately and only two components are used.

Silver nitrate acts on *H. pylori* cells that colonize the stomach due to specific inhibition of bacterial urease activity by silver ions. To suppress the activity of one molecule of this enzyme, four Ag^{2+} ions are enough [11]. However, silver reacts with chlorine ions, a large number of which are present in the stomach, and forms insoluble silver chloride. To restore the silver solubility ammonium ions are required, so the second component of the supplement is urea.

Having been ingested, in the stomach, urea is converted into ammonia by means of catalytic urease activity of *H. pylori*. In this case, in the acidic medium of gastric juice, the concentration of ammonium ions increases. The ammonium ions react with silver chloride forming a complex water-soluble compound that facilitates the release of silver cations (Ag^{2+}). Urea, both in itself and in acidic environment, is toxic to *H. pylori* bacteria [12]. As a strong antioxidant it protects the gastric mucosa cells from the action of free radicals, including those resulting from the *H. pylori* products [13].

The effectiveness of the developed nutritional supplement has been confirmed by studies conducted at the Department of Metabolism Regulation of the Palladin Institute of Biochemistry of the NAS of Ukraine, with volunteers who were tested for *H. pylori* infection by a noninvasive direct urease test using *Helicotester* device (certificate of state registration No. 13543/2014) involved. The presence of these bacteria in the stomach was estimated by an increase in time of ammonia concentration in the samples of air taken from the oral cavity of patients who administered urea. The analysis results varied from "–" (a negative result), to "+++" (the highest degree of helicobacteriosis). The volunteers who had a positive test result "+++" administered three times a day the recommended daily dose of supplement for three weeks. After that, the test was repeated to determine the helicobacteriosis degree. The results ranged from "–" to "+".

Thus, based on the above results, one can conclude that *the complex dietary supplement for patients with hyper-carbonyl state* [2] contains cheap and stable to storage components and enables to effectively reduce the intensity of the hyper-carbonyl state, which leads to a significant decrease in the content of protein modifications that are not part for the essential nature of human organism in the patients with diabetes mellitus, which helps to improve the functioning of the body, to maintain the ability to work and the general state of health and, accordingly, to reduce the risk of complicated diabetes.

The developed and patented *complex dietary supplement for patients with helicobacteriosis* [1] contains cheap and stable to storage components, enables to effectively prevent and to correct the stomach microbiocenosis in the patients infected with *H. pylori* and thereby to improve the functioning of the gastrointestinal tract, to maintain the ability to work and the general state health, and to reduce the risk of gastric cancer caused by *H. pylori*.

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О.О. Гудкова, І.П. Крисюк, С.Г. Шандренко
Інститут біохімії ім. О.В. Палладіна НАН України,
вул. Леонтовича, 9, Київ, 01601, Україна,
+380 44 234 5974, +380 44 279 6365, secretar@biochem.kiev.ua

ІННОВАЦІЙНІ ПРОПОЗИЦІЇ ДЛЯ ВПРОВАДЖЕННЯ КОМПЛЕКСНИХ ДІЄТИЧНИХ ДОБАВОК ПРИ ЦУКРОВОМУ ДІАБЕТІ ТА ХЕЛІКОБАКТЕРІОЗІ ШЛУНКА

Вступ. Захворювання на цукровий діабет та патології шлунково-кишкового тракту є одними з найбільш поширених захворювань сучасного суспільства. В Україні зростає кількість хворих на діабет, а захворювання шлунково-кишкового тракту, ініційовані *Helicobacter pylori*, мають стрімку динаміку зростання через побутовий характер розповсюдження бактерії.

Проблематика. В Інституті біохімії ім. О.В. Палладіна НАН України на основі результатів фундаментальних досліджень розроблено дієтичні добавки для профілактики та зменшення негативних наслідків цукрового діабету («Комплексна дієтична добавка при гіперкарбонільному стані») та патології шлунково- кишкового тракту («Комплексна дієтична добавка при хелікобактеріозі»).

Мета. Оцінити ефективність застосування розроблених дієтичних добавок.

Матеріали й методи. Ефективність розроблених харчових добавок підтверджено дослідами *in vivo*. Ступінь інфікованості *H. pylori* визначали методом неінвазивного прямого уреазного тесту за допомогою апарату «Геліkотестер».

Результати. Показано високу ефективність розроблених комплексних добавок, оскільки при вживанні дієтичної добавки за цукрового діабету зменшувався вміст токсичних складових (зниження загальної кількості альдегідів, карбонільних груп протеїнів, постсинтетичних модифікацій протеїнів), що, відповідно, гальмує розвиток ускладнень цієї патології, а вживання дієтичної добавки при хелікобактеріозі призводить до зниження рівня інфікованості шлунка бактерією *Helicobacter pylori*, що сприяє профілактиці низки захворювань шлунково-кишкового тракту.

Висновки. Розроблені дієтичні добавки містять дешеві та стійкі до зберігання компоненти, дозволяють ефективно зменшити вміст токсичних складових за цукрового діабету та прояви окремих захворювань шлунково-кишкового тракту, покращити функціонування організму, підтримати його працездатність і загальний стан здоров'я.

Автори шукають зацікавлених осіб для співпраці з питань впровадження у виробництво розроблених дієтичних добавок.

Ключові слова: дієтична добавка, діабет, хелікобактеріоз, гліцин, лізин, *N*-ацетилцистеїн, карбамід, срібла нітрат.

И.П. Крисюк, О.А. Гудкова, С.Г. Шандренко
Институт биохимии им. А.В. Палладина НАН Украины,
ул. Леонтовича, 9, Киев, 01601, Украина,
+380 44 234 5974, +380 44 279 6365, secretar@biochem.kiev.ua

ИННОВАЦИОННЫЕ ПРЕДЛОЖЕНИЯ ДЛЯ ВНЕДРЕНИЯ КОМПЛЕКСНЫХ ДИЕТИЧЕСКИХ ДОБАВОК ПРИ САХАРНОМ ДИАБЕТЕ И ХЕЛИКОБАКТЕРИОЗЕ ЖЕЛУДКА

Введение. Заболевание сахарным диабетом и патологии желудочно-кишечного тракта являются одними из наиболее распространенных заболеваний современного общества. В Украине постоянно растет количество больных диабетом, а заболевания желудочно-кишечного тракта, инициированные инфицированностью *Helicobacter pylori*, имеют динамику стремительного роста в связи с бытовым характером распространения бактерии.

Проблематика. В Институте биохимии им. А.В.Палладина НАН Украины на основании полученых результатов фундаментальных исследований разработаны диетические добавки для профилактики и уменьшения негативных последствий диабета («Комплексная диетическая добавка при гиперкарбонильном состоянии») и патологии желудочно-кишечного тракта («Комплексная диетическая добавка при хеликобактериозе»).

Цель. Оценить эффективность применения разработаных диетических добавок.

Материалы и методы. Эффективность розработаных пищевых добавок подтверждено опытами *in vivo*. Степень инфицированости *H. pylori* определяли методом неинвазивного прямого уреазного теста при помощи аппарата «Геликотестер».

Результаты. Показано высокую эффективность разработанных комплексных добавок, поскольку при употреблении диетической добавки при диабете уменьшалось содержание токсических составляющих (снижение количества альдегидов, карбонильных групп протеинов, постсинтетических модификаций протеинов), что тормозит развитие осложнений этой патологии, а диетическая добавка при хеликобактериозе способна понижать уровень инфицированности желудка бактерией *Helicobacter pylori*, что способствует профилактике ряда заболеваний желудочно-кишечного тракта.

Выводы. Разработанные диетические добавки содержат дешевые и стойкие к хранению компоненты, позволяют эффективно уменьшить содержание токсических составляющих при сахарном диабете и проявления отдельных заболеваний желудочно-кишечного тракта, улучшить функционирование организма, поддержать его работоспособность и общее состояние здоровья.

Авторы ищут заинтересованных лиц для сотрудничества по вопросам внедрения в производство своих разработок.

Ключевые слова: диетическая добавка, диабет, хеликобактериоз, глицин, лизин, N-ацетилцистеин, карбамид, серебра нитрат.