

**THE ANTIOXIDANT EFFECT OF NATURAL POLYPHENOLIC COMPLEXES  
OF GRAPE WINE IN THE RAT PERIPHERAL NERVOUS SYSTEM UNDER  
STREPTOZOTOCIN-INDUCED DIABETES MELLITUS**

**A. Gnatush<sup>1</sup>, V. Drel<sup>1</sup>, N. Hanay<sup>2</sup>, A. Yalaneckyy<sup>2</sup>, V. Mizin<sup>3</sup>, N. Sybirna<sup>1</sup>**

*<sup>1</sup>Ivan Franko National University of Lviv  
4, Hrushevskiyi St., Lviv 79005, Ukraine  
e-mail: gnatuk88@ukr.net*

*<sup>2</sup>National Institute for Vine and Wine "Magarach"  
31, Kirov St., Yalta, Crimea 98600, Ukraine*

*<sup>3</sup>Crimean University for the Humanities  
2, Sevastopolska St., Yalta, Crimea 98635, Ukraine*

It has been established, that the specimen of natural polyphenols complexes of grape wine contribute to the normalization of the antioxidant enzyme system (superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase) of the sciatic nerves, dorsal root ganglia and spinal cord of rats, whose activity **is disrupted as a result of oxidative-nitrosative stress** development of which is characteristic for diabetes mellitus. Significant increase in body weight of control rats and animals with diabetes under consumption of specimen by 36% and 18% **accordingly has been established. The results indicate the perspectives** of application of specimen of natural polyphenols complexes of grape wine for the prevention and treatment of diabetes mellitus complications.

*Keywords:* diabetes mellitus, oxidative-nitrosative stress, the specimen of natural polyphenols complexes of grape wine, diabetic neuropathy, antioxidant protection.

Diabetes mellitus (DM) - is one of the most common, not infection diseases, which are characterized by the development of micro- and macrovascular complications that can often lead to disability. According to World Health Organization, in 2010 for over 290 million people suffer from diabetes. In Ukraine more than 1 million patients with DM are registred.

In 40% of patients with diabetes that control blood glucose level and take antidiabetic drugs chronic complications in the peripheral nervous system are developed [16]. Diabetic neuropathy (DN) is one of the most common complications of diabetes [9, 10, 24].

Hyperglycemia is the main established pathogenetic factor for the development of DM, which occurs against the background of insulin deficiency, which is determinant of the diagnosis of type 1 DM. The violation of the electron transport chain that leads to the overproduction of superoxide anion, which, interacting with other reactive oxygen species (ROS), activates free radical oxidation leads to oxidative stress (OS) [11]. OS, in its turn, leads to the disruption of cellular homeostasis, accumulation of molecules with altered structure, damages the structure of lipids, proteins and DNA. In response to DNA damage the nuclear enzyme poly(ADP-ribose) polymerase (PARP-1) is activated. Poly-ADP-ribosilation of numerous nuclear proteins takes place causing significant energy depletion of cells with the participation of the PARP-1. Under certain conditions, it can cause cell death [23] (it is proved that PARP-1 can poly-ADP-ribosilate glyceraldehyde 3-phosphate dehydrogenase (the enzyme of glycolysis) that leads to the inhibition of glycolytic glucose utilization at the level of glyceraldehyde 3-phosphate formation, with

subsequent accumulation of intermediate products of glycolysis). This leads to the activation of a number of signaling and metabolic pathways. Such changes in metabolism (accumulation of fructose, sorbitol, methylglyoxal, advanced glycation end products etc) is a trigger for the development of DN. Primary metabolic changes occurring in nerve fibers in the beginning cause disruption of their functions, and eventually lead to changes in their structure. In particular, the activation of the polyol pathway in nervous tissue with the characteristic accumulation of sorbitol and fructose which consistently causes a decrease in activity of  $\text{Na}^+/\text{K}^+$ -ATPase and the level of mioinozytol, leads to the retention of  $\text{Na}^+$  and water, swelling of the myelin sheath, its further demyelination and reduction of motor and sensory nerve conduction velocity of the peripheral nervous system [10].

In parallel, there is total destruction of the organism by ROS that in addition to DNA damage, causes damage of axons membrane structures of peripheral nerve fibers and the results in damage of the structures and functions of nerve cells. In addition to the direct damaging effects, accumulation of ROS affects the energy metabolism in neurocytes and development of endoneurial hypoxia. Such a comprehensive total damage causes demyelination and degeneration of nerve fibers, reduces their functional activity [10].

Imbalance between production of free radicals and the activity of enzymes of antioxidant system which is reduced under DM is made by significant contribution into formation of late diabetic complications [4]. Strengthening of the work of antioxidant system by exogenous antioxidants has a protective effect on all body systems and reduces the "area of damage".

Researches into natural antioxidant - polyphenol complexes of grape wine, including proanthocyanidins, derived flavan-3-ols and several other derivatives of flavonoids which are effective in preventing cardiovascular diseases, have become promising recently [19]. It is known that polyphenols of grape wine are able to interact with plasma proteins and cellular elements of blood, prevent premature oxidation of their molecular complexes, which occurs under the oxidative and nitrative stress. Significant bactericidal and antiviral effect of the given substances has been shown [12]. The protective effects of the polyphenols complexes of grape wine on some systems and organs under oxidative stress and during the metabolic syndrome have been detected [20, 21].

As protective properties of natural grape polyphenol complexes under streptozotocin-induced DM and their effect on the enzymic antioxidant system during the development of neuropathy have been investigated very little, the goal of our work has been to investigate the protective antioxidant effect of polyphenol complexes of grape wine on the enzymatic antioxidant system in the tissues of peripheral nervous system of Wistar rats under streptozotocin-induced diabetes mellitus.

### Materials and methods

All animal care and procedures were carried out in accordance with the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes Directive of 24 November 1986 (86/609/ECC) and were approved by Bioethics Committee of Ivan Franko National University of Lviv Protocol for Animal Studies, Lviv, Ukraine. Male Wistar rats, of 190–210 g body weight, were fed a standard rat chow and had access to water ad libitum.

The specimen of natural polyphenols complexes of grape wine (speciment) was received by evaporation of red wine in rotary evaporators LABOROTA 4000 (Heidolph, Germany) at 36 °C. Amount of polyphenols determined by the Lowry method.

The red wine was made by the classical technology from Cabernet Sauvignon (clone C337/S04C3) grapes and contained phenolic compounds 2309.31 mg/l, proanthocyanidines 936.0 mg/l and pigment polymers 443.8 mg/l.

Wistar rats were separated into four groups of seven animals each: Group 1 – normal untreated control; Group 2 – polyphenols treated; Group 3 – STZ treated and Group 4 – polyphenol and STZ treated. The STZ treatment was a single i.p. injection of 50 mg/kg body weight. The specimen treatment was an oral dose (300 ml/70 kg body weight/day) that constituted 23.5 mg/kg body weight/day, administered daily for 2 weeks prior to the STZ injection and daily for 4 weeks after the STZ injection. Group 2 received specimen of natural polyphenols complexes of grape wine for 6 weeks. Blood samples for glucose measurements were taken from the tail vein, 72 h after the STZ injection and the day prior to the study termination. All the rats with blood glucose of 14 mmol/l or more were considered diabetic. The level of glucose in the blood was determined by Aviva Accu Check glucose meter.

The animals were sedated by CO<sub>2</sub> and immediately killed by cervical dislocation. Selected tissues were frozen immediately in liquid nitrogen. Tissues homogenization was carried out using hand homogenizers in the presence of 0.1 M phosphate buffer (1:10 wt/vol) pH 7.0 on the ice. Homogenized samples of spinal cord were centrifuged for 30 min at speed of 14000 g at 4 °C. After removal of a thin lipid layer recentrifuged for 15 min at 10000 g at 4 °C. Samples of sciatic nerves and dorsal root ganglia were centrifuged for 20 min at 10000 g at 4 °C.

The activity of superoxide dismutase (SOD) was determined by Chevari method [8], catalase (CAT) – by the Corolyk method [3], glutathione peroxidase (GPO) – by Moin method [5], glutathione reductase (GR) – by Goldberg method [14]. MDA level was analyzed with 2-thiobarbituric acid by Timyrbulatov method [7]. The concentration of protein was determined by Lowry method [18]

Data are expressed as mean ± SD. Differences among experimental groups were determined by ANOVA (analysis of variance), and the significance of between-group differences was assessed by Student–Newman–Keul’s multiple range test. Significance was defined at  $P \leq 0.05$ .

### Results and discussion

At the end of the experiment, the final body weight of control rats and rats consuming the specimen of natural polyphenol complexes of grapes grew by 36%, compared with the body weight of animals before the experiment (Table 1). In contrast to the control groups, the body weight of rats with diabetes slightly decreased. At the same time the body weight of rats with diabetes which consumed the specimen increased by 18%. In groups of rats with streptozotocin-induced diabetes mellitus this phenomenon can be explained by the fact that diabetes is characterized by “overproduction” of urea. The latter, due to osmotic diuresis, was excreted from the body with the necessary for this amount of water and electrolyte K<sup>+</sup> and Na<sup>+</sup> ions [15]. This process leads to dehydration, which further increases due to the induction of the release of free fatty acids from adipocytes and the followed by conversion to ketone bodies (acetoacetate and β-hydroxybutyrate) leading to ketoacidosis [1]. Ketone bodies “provoke” an increase in osmotic diuresis and loss of electrolytes [17]. Such changes of the level in body water can help to affect the general metabolism and body weight.

The indices of body weight in groups of rats with streptozotocin-induced diabetes mellitus that consumed the specimen significantly increased to control values. Obtained data are consistent with our previous results of using red wine [1, 2]. Unfortunately, the polyphenols complexes of grape wine in studied concentrations do not have corrective effect on blood glucose both in control and groups with DM, because the concentration of glucose in the blood of infected animals has increased throughout the experiment (Table 1).

Possibly, the protective effect of polyphenols complexes is detected by reducing the level of ketone bodies on the stage of their utilization, or excretion from the body system of glomeru-

lus and tubules of the kidneys that is followed by stimulation of reabsorption of electrolytes and water from primary urine [1].

Table 1

Body weight and blood glucose concentration in control and diabetic rats with or without polyphenol speciment consumption (M±m. n=5-7)

indicators Rodent group	Blood glucose (mmol/l)		Body weight (g)	
	Initial §	Final	Initial §	Final
C	5.72±0.46	6.2±0.51	206±16.1	279±19.6
C+S	5.92±0.16	6.3±0.19	202±17.35	276±20
D	18.54±0.89**	26.82±2.23**	200±6.78	209±30**
D+S	20±0.29**	26.88±1.87**	198±6.41	234±10.47*, #

**Comments.** C – control; C+S – control+ speciment of polyphenols; D – diabetic; D+S – diabetic+ speciment of polyphenols. \*, \*\* P<0.05 and < 0.01 against the control group. # P<0.05 against the control and diabetic group without polyphenol speciment consumption. § – 3rd day after induction of diabetes.

The presence of increased of the level of ketone bodies is directly connected with the intensification of free radical oxidation in the body that is typical for DM [22]. The consequences that come, depend on various factors, but primarily, they are determined by the coordinated functioning of enzymes of antioxidant system, among which the main role belongs to superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase.

Under diabetes mellitus the activity of enzymes of antioxidant system in the tissues of the peripheral nervous system has decreased, that indicates to the OS and the development of neuropathy in this tissue [13].

The activity of SOD in the group of rats with DM has decreased (by 40%, 25.8% and 32% in the sciatic nerve, dorsal root ganglia and spinal cord, respectively) (Fig. 1).

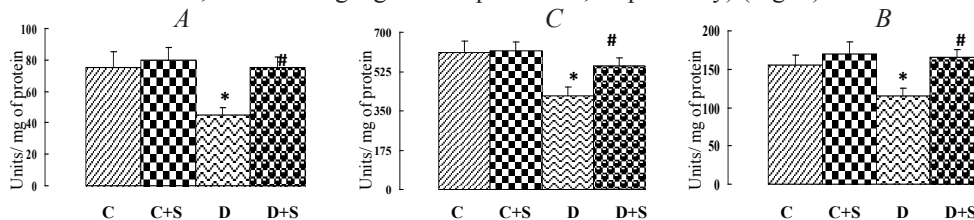


Fig. 1. The activity of superoxide dismutase in peripheral nervous system: *A* – in sciatic nerve, *B* – in spinal cord, *C* – in dorsal spinal ganglia. C – control; C+S – control + speciment of polyphenols; D – diabetic; D+S – diabetic + speciment of polyphenols, (M ± m, n = 5–7). \*P<0.05 compared with controls. #P<0.05 compared with diabetic rats without speciment of polyphenols consumption.

Decrease in the activity of SOD is directly associated with the accumulation of superoxide anion, which is typical for most tissues under DM conditions. Violations of the mechanism of utilization of this anion leads to the formation of other oxidant – peroxynitrite (ONOO<sup>-</sup>), which interacting with proteins, nitrite them by tyrosine, altering their biological properties [25]. Besides the peroxynitrite, the formation of products of protonation of nitric oxide (NO<sup>+</sup>, NO<sup>•</sup>, NO<sub>2</sub><sup>-</sup>, NO<sub>3</sub><sup>-</sup>, NO<sub>2</sub>), which are especially dangerous for the enzymes, because they can modify amino acid residues of proteins that can be manifested in the decrease of the activity of SOD has been reported. The direct interaction of NO with Cu<sub>2</sub><sup>+</sup> in the active center of SOD causes inhibition of it activity. It is complemented by the non enzymatic glycosylation of amino acid residues, part of which is included in the active center of the enzyme, which also affects the superoxide dismutase activity.

Under consumption of speciment of natural polyphenols complexes of grape wine by the rats treated by DM the activity of SOD in the sciatic nerve, dorsal root ganglia and spinal cord

have been respectively increased by 67.6%, 43.5% and 32.5% compared with a group of diabetic rats without consumption of specimen (Fig. 1). It is caused by antioxidant properties of natural polyphenols complexes of grape wine that are scavengers of ROS. Polyphenols are able to “weight down” on a newly created ROS, particularly superoxide anion, which reduces the formation of dangerous compounds, including peroxynitrite [1].

Under DM, catalase activity has decreased in all tissues of the peripheral nervous system: the sciatic nerve - by 27% in the spinal cord by 20.5% and dorsal ganglia by 38.6% compared to controls. Specimen consumption did not affect catalase activity in nondiabetic rats. A decrease in the activity of this enzyme can be explained by similar mechanisms to SOD. Additionally, nitric oxide can directly contact with ferum-porphyrine complex of catalase, forming nitric derivatives. The appearance of heme-NO complexes prevents binding of H<sub>2</sub>O<sub>2</sub> in the active center of catalase, and hence its expansion. Nitrite ions are also able to directly communicate with ferum of heme of enzyme that can cause the decrease in the activity of the enzyme [20].

Under consumption of the specimen by the rats with streptozotocin-induced diabetes mellitus, the activity of CAT increase. Particularly, in the sciatic nerve by 43.7%, in the spinal cord and dorsal ganglia of 24.2% and 44% respectively (Fig. 2). It almost corresponds to the values of activity enzyme in the control group. The use of natural antioxidants leads to a decrease in free-flow oxidation and, as a result - increases the activity of the enzyme. This mechanism is common to all enzymes of antioxidant system.

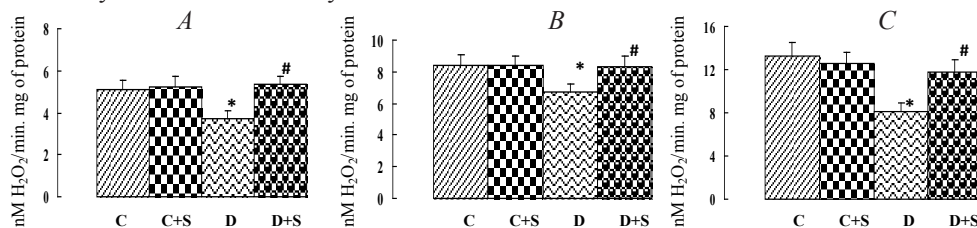


Fig. 2. The activity of catalase in peripheral nervous system: *A* – in sciatic nerve, *B* – in spinal cord, *C* – in dorsal spinal ganglia. C – control; C+S – control+ specimen of polyphenols; D – diabetic; D+S – diabetic+ specimen of polyphenols, ( $M \pm m$ ,  $n = 5-7$ ). \* $P < 0.05$  compared with controls. # $P < 0.05$  compared with diabetic rats without specimen of polyphenols consumption.

The work of glutathione system (GS) is especially important under OS. GS effectively protects cells from the effects of ROS and therefore the violation of its normal work - serious consequences for the organism have been observed. Glutathione system eliminates ROS directly, or as the “second line of defense” after SOD and CAT, complements and completes the work of the “first line” and correctes its errors. [6].

Apart from CAT, the neutralization of hydrogen peroxide is also carried out by GPO, whose affinity to H<sub>2</sub>O<sub>2</sub> is significantly higher than in catalase. Under DM the activity of GPO and GR in the sciatic nerve, spinal cord and dorsal ganglia is reduced by 33%, 34.7%, 30% and 37.2%, 30.5%, 15%, respectively (Fig. 3). GPO activity depends on the content of reduced glutathione, the level of which is supported by intracellular concentration of GR. As for glutathione reductase functioning is determined by the level of reduced nicotinamide coenzymes. The energy depletion of the body, which causes deficiency of energy substrates that has directly proportional effect on the efficiency of protective systems, has been observed under DM. There is no effective protection without enough quantity of energy substrates.

Under consumption of the specimen of natural polyphenols complexes of grape wine has been observed the recovery of activity of GPO and GR in the sciatic nerve, spinal cord and dorsal

ganglia by 33.3%, 60.5%, 35.8% and 24.3%, 43.7%, 17%, respectively, compared with animals with DM without specimen consumption (Fig. 3). This increase in the activity of the HR can be explained by improvement of the energy of the body that may be caused by the protective effect of natural polyphenols complexes.

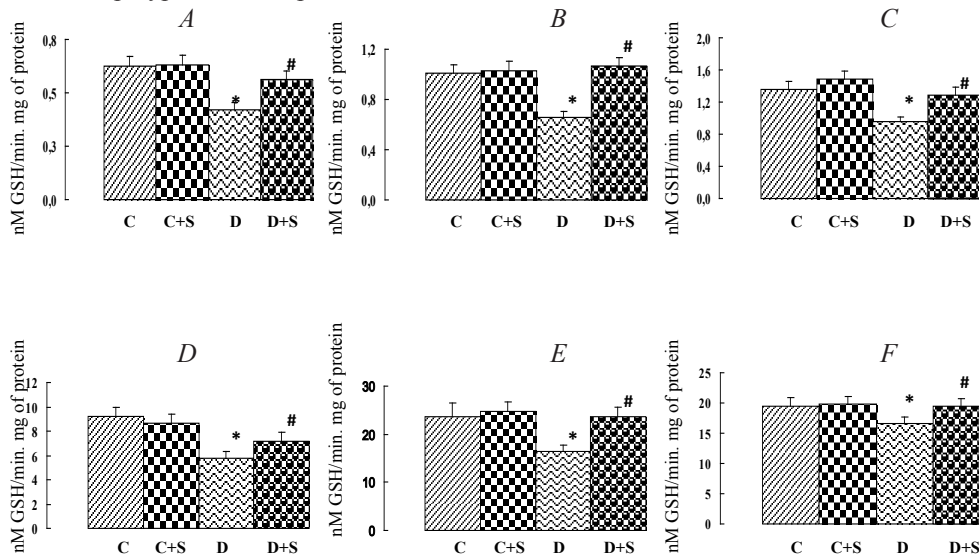


Fig. 3. The activity of antioxidant glutathione system in peripheral nervous system: *A* – activity GPO in sciatic nerve, *B* – activity GPO in spinal cord, *C* – activity GPO in dorsal spinal ganglia, *D* – activity GR in sciatic nerve, *E* – activity GR in spinal cord, *F* – activity GR in dorsal spinal ganglia, ( $M \pm m$ ,  $n = 5-7$ ). \* $P < 0.05$  compared with controls. # $P < 0.05$  compared with diabetic rats without specimen of polyphenols consumption.

Thus, change of the activity of antioxidant enzymes system underlies in the neurodegenerative processes that occurs in the peripheral nervous system and is indicator of DN. Evidence of this is the accumulation of primary and secondary products of oxidation. The one of the main marker of lipid peroxidation is the presence of sulfocarbaniide-positive products. Thus, under DM, their concentrations has increased in the sciatic nerve by 85%, in the spinal cord and in the dorsal root ganglia by 59.3% and 66.5%, respectively (Fig. 4). The level of this product has decreased by 37.7%, 25% and 35.3% respectively under consumption of specimen.

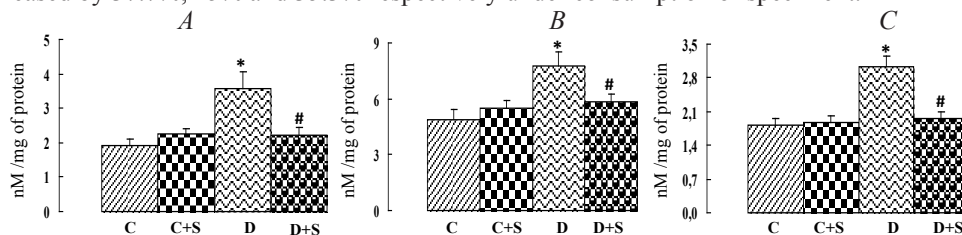


Fig. 4. TBK-positive content of LPO products in peripheral nervous system: *A* – in sciatic nerve, *B* – in spinal cord, *C* – in dorsal spinal ganglia. C – control; C+S – control+ specimen of polyphenols; D – diabetic; D+S – diabetic+ specimen of polyphenols, ( $M \pm m$ ,  $n = 5-7$ ). \* $P < 0.05$  compared with controls. # $P < 0.05$  compared with diabetic rats without specimen of polyphenols consumption.

Thus, natural polyphenols complexes of grape wine have a significant antidiabetic effect on the level of the whole organism: they protect it from the dehydration, by the way of increase in the activity of antioxidant enzyme system in the tissues of peripheral nervous system. Particularly, the activity of SOD, CAT, GPO and GR in groups with DM with specimen consumption normalizes to control values. The level of sulfocarbaniide-positive products decreases to control values.

Biochemical mechanisms of action of natural polyphenol complexes of grape wine are the subject of further research, but certainly these natural complexes can be used in the treatment of complications of diabetes and the development of new antidiabetic drugs.

*We express our sincere gratitude to the Western Ukrainian Biomedical Research Center (WUBMRC, 2011-2012), for a grant provided to conduct our researches.*

#### REFERENCES

1. Дрель В. Р., Гнатуш А. Р., Яланецький А. Я. та ін. Поліфеноли виноградних вин запобігають накопиченню нітротирозину та активації PARP-1 у сітківці ока шурів із стрептозотозиніндукованим цукровим діабетом // Медична хімія. 2010. Т. 1. № 42. С. 25-33.
2. Дрель В. Р., Гнатуш А. Р., Яланецький А. Я. та ін. Протекторна дія виноградних вин за нітрозативного стресу, зумовленого експериментальним цукровим діабетом // Укр. біохім. журнал. 2010. Т. 82. № 1. С. 108-116.
3. Королюк М. А., Иванова И. Г., Майорова И. Г. Метод определения активности каталазы // Лаб. дело. 1988. № 1. С. 16-18.
4. Меньшикова Е. Б., Ланкин В. З., Зенков Н. К. и др. Окислительный стресс. Прооксиданты и антиоксиданты. Москва, 2006. С. 411-413.
5. Моин В. М. Простой и специфический метод определения активности глутатионпероксидазы в эритроцитах // Лаб. дело. 1986. № 12. С. 124-126.
6. Сибірня Н. О., Маєвська О. М., Барська М. Л. Дослідження окремих біохімічних показників за умов оксидативного стресу. Львів: Видавничий центр ЛНУ ім. І. Франка, 2006. 60 с.
7. Тимирбулатов Р. А., Селезнев Е. И. Метод повышения интенсивности свободнорадикального окисления липидсодержащих компонентов крови и его диагностическое значение // Лаб. дело. 1981. № 4. С. 209-211.
8. Чевари С.И, Андял Т. Д., Штиренгер Д. А. Определение антиоксидантных параметров крови и их диагностическое значение в преклонном возрасте // Лаб. дело. 1991. № 10. С. 9-13.
9. Boulton A., Malik R., Arezzo J. et al. Diabetic Somatic Neuropathies // Diabetes Care. 2004. № 27. P. 1458-1486.
10. Boulton A., Vinik A., Arezzo J. Diabetic neuropathies: a statement by the American Diabetes Association // Diabetes Care. 2005. № 28. P. 956-962.
11. Brownlee M. The pathobiology of diabetic complications: a unifying mechanism // Diabetes. 2005. Vol. 54. № 6. P. 1615-1625.
12. Daglia M., Papetti A., Grisoli P. et al. Antibacterial activity of red and white wine against oral streptococci // Agric. Food Chem. 2007. Vol. 55. № 13. P. 5038-5042.
13. Feldman E. Oxidative stress and diabetic neuropathy: a new understanding of an old problem // J. Clin. Invest. 2003. Vol. 111. № 4. P. 431-433.
14. Goldberg D., Spooner R., Bergmeyer H. Methods of Enzymatic Analysis, 3rd ed // Verlag Chemie. 1983. Vol. 5. № 3. P. 258-265.
15. Gouni-Berthold I, Krone W. Diabetic ketoacidosis and hyperosmolar hyperglycemic State // Med. Klin. (Munich). 2006. Vol. 101. № 1. P. 100-105.

16. King H., Aubert R. E., Herman W. H. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections // *Diabetes Care*. 1998. Vol. 21. № 9. P. 1414–1431.
17. Kitabchi A., Umpierrez G., Fisher J., et al. Thirty years of personal experience in hyperglycemic crises: diabetic ketoacidosis and hyperglycemic hyperosmolar state // *Journal of Clinical Endocrinology and Metabolism*. 2008. Vol. 93. № 5. P. 1541–1552.
18. Lowry O., Rosenbraugh M., Pori A. Protein measurement with the Folin phenol reagent // *Biol. Chem.* 1951. Vol. 193. № 1. P. 265–275.
19. Marfella R., Cacciapuoti F., Siniscalchi M. et al. Effect of moderate red wine intake on cardiac prognosis after recent acute myocardial infarction of subjects with Type 2 diabetes mellitus // *Diabet Med*. 2006. Vol. 23. № 9. P. 974–981.
20. Montilla P., Barcos M., Munoz M. et al. Red wine prevents brain oxidative stress and nephropathy in streptozotocin-induced diabetic rats // *Biochem. Mol. Biol.* 2005. Vol. 38. № 5. P. 539–544.
21. Napoli C., Balestrieri M., Sica V. et al. Beneficial effects of low doses of red wine consumption on perturbed shear stress-induced atherogenesis // *Heart Vessels*. 2008. Vol. 23. № 2. P. 124–133.
22. Naso F., Dias A., Porawski M. et al. Hepatic nitrosative stress in experimental diabetes // *Experimental Diabetes Research*. 2011. P. 1–6.
23. Pacher P., Beckman J. S., Liaudet L. Role of nitrosative stress and peroxynitrite in the pathogenesis of diabetic complications. Emerging new therapeutical strategies // *Physiol. Rev.* 2007. Vol. 87. № 1. P. 315–424.
24. Sumner C., Sheth S., Griffin J. et al. The spectrum of neuropathy in diabetes and impaired glucose tolerance // *Neurology*. 2003. № 60. P. 108–111.
25. Viktor Drel, Nataliya Sybirna. Protective effects of polyphenolics in red wine on diabetes associated oxidative/nitrate stress in streptozotocin-diabetic rats // *Cell Biol. Int.* 2010. 34. P. 1147–1153.

Стаття: надійшла до редакції 23.08.12

доопрацьована 24.10.12

прийнята до друку 29.10.12

**ПРИРОДНІ ПОЛІФЕНОЛЬНІ КОМПЛЕКСИ ВИНОГРАДУ ЗАПОБІГАЮТЬ  
РОЗВИТКОВІ ОКСИДАТИВНОГО СТРЕСУ В ТКАНИНАХ ПЕРИФЕРИЧНОЇ  
НЕРВОВОЇ СИСТЕМИ ЩУРІВ ЗІ СТРЕПТОЗОТОЦИН-ІНДУКОВАНИМ  
ЦУКРОВИМ ДІАБЕТОМ**

**А. Гнатуш<sup>1</sup>, В. Дрель<sup>1</sup>, Н. Ганай<sup>2</sup>, А. Яланецький<sup>2</sup>,  
В. Мізін<sup>3</sup>, Н. Сибірна<sup>1</sup>**

<sup>1</sup>Львівський національний університет імені Івана Франка,  
вул. Грушевського, 4, Львів 79005, Україна  
e-mail: gnatuk88@ukr.net

<sup>2</sup>Національний інститут винограду та вина “Магарач”,  
вул. Кірова, 31, Ялта, АР Крим 98600, Україна

<sup>3</sup>Кримський державний гуманітарний університет  
вул. Севастопольська, 2, Ялта, АР Крим 98635, Україна

Встановлено, що препарат природних поліфенольних комплексів винограду



сприяє нормалізації роботи ензимів системи антиоксидантного захисту (супероксиддисмутази, каталази, глутатіонпероксидази і глутатіонредуктази) сідничного нерва, дорсальних спинномозкових гангліїв та спинного мозку щурів, чия активність порушується унаслідок оксидативно-нітративного стресу, розвиток якого є характерним для цукрового діабету 1-го типу. Встановлено достовірне зростання маси тіла контрольних щурів і тварин із цукровим діабетом, що споживали препарат поліфенольних комплексів винограду на 36 і 18% відповідно. **Отримані результати свідчать про перспективність застосування препаратів природних поліфенольних комплексів винограду для профілактики та лікування ускладнень цукрового діабету 1-го типу.**

*Ключові слова:* цукровий діабет, оксидативно-нітративний стрес, препарат природних поліфенольних комплексів винограду, діабетична нейропатія, антиоксидантний захист.

## АНТИОКСИДАНТНИЙ ЕФФЕКТ ПРИРОДНИХ ПОЛИФЕНОЛЬНИХ КОМПЛЕКСОВ ВИНОГРАДА В ПЕРИФЕРИЧЕСКОЙ НЕРВНОЙ СИСТЕМЕ КРЫС СО СТРЕПТОЗОЦИН-ИНДУЦИРОВАННЫМ САХАРНЫМ ДИАБЕТОМ

А. Гнатуш<sup>1</sup>, В. Дрель<sup>1</sup>, Н. Ганай<sup>2</sup>, А. Яланецкий<sup>2</sup>,  
В. Мизин<sup>3</sup>, Н. Сибирная<sup>1</sup>

<sup>1</sup>Львовский национальный университет имени Ивана Франко,  
ул. Грушевского, 4, Львов 79005, Украина  
e-mail: gnatik88@ukr.net

<sup>2</sup>Национальный институт винограда и вина "Магарач",  
ул. Кирова, 31, Ялта, АР Крым, 98600, Украина

<sup>3</sup>Крымский государственный гуманитарный университет  
ул. Севастопольская, 2, Ялта, АР Крым 98635, Украина

Установлено, что препарат природных полифенольных комплексов винограда способствует нормализации работы энзимов системы антиоксидантной защиты (супероксиддисмутаза, каталаза, глутатионпероксидаза и глутатионредуктаза) седалищного нерва, дорсальных спинномозговых ганглиев и спинного мозга крыс, чья активность нарушается вследствие оксидативно-нитративного стресса, развитие которого характерно для сахарного диабета 1-го типа. Установлено достоверное возрастание массы тела контрольных крыс и животных с сахарным диабетом, потреблявших препарат полифенольных комплексов винограда на 36 и 18% соответственно. Полученные результаты свидетельствуют о перспективности **применения препаратов** природных полифенольных комплексов винограда для профилактики и лечения осложнений сахарного диабета 1-го типа.

*Ключевые слова:* сахарный диабет, оксидативно-нитративный стресс, препарат природных полифенольных комплексов винограда, диабетическая нейропатия, антиоксидантная защита.