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ІНСТИТУТ БІОЛОГІЇ КЛІТИНИ НАЦІОНАЛЬНОЇ АКАДЕМІЇ НАУК УКРАЇНИ
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synthesis of ZnO nanoparticles using a leaf extract of *Polymnia (Smallanthus) sonchifolia* and *Catharanthus roseus* and fruits of *Momordica charantia* carried out from $ZnSO_4$ solution.

The results have shown that the glucose treatment was capable to cause an increase in TBARS (by 56 %), methylglyoxal (by 42 %) and rate of hemolysis (by 31 %), but a decrease in total glutathione concentration (by –77 %), and catalase activity (by –51 %) in RBC hemolysate. When glucose-treated RBC were probed with herbal extracts and both manufactured and synthetized zinc-containing compounds, specific response to different co-exposures, but similar to compatible compounds was disclosed. Zinc picolinate is widely-used as dietary zinc supplement in general had no effect on the studied parameters except of TBARS and hemolysis. Meanwhile ZnO nanoparticles caused significant elevation of TBARS (by 70 %) and catalase activity (up to five fold), but a decrease in total glutathione concentration (by –60 %). *P. sonchifolia* didn't provoke significant variation of investigated parameters with one exception when compared to glucose-treated cells. Meantime *Momordica* which is well-known nutraceutical with metabolic and antiglycemic effects and tested *Catharanthus roseus* both in herbal extract form and ZnO-herbal complex have caused the decreased in TBARS and rate of hemolysis, and the increased in catalase and glutathione up to control baseline. *Momordica* extract, ZnO-*Momordica* and ZnO-*Catharanthus* complexes provoked the most prominent changes when compared to the glucose treatment alone and brought values in most cases back to control level. The principal component analysis revealed clear separation of control and glucose exposed group due to their opposite locations along the first principal component. Also, there were three mutually distanced clusters. One of them, that included *Momordica* extract, ZnO-*Momordica* and ZnO-*Catharanthus* treated groups were situated near control group, the next, zinc picolinate treated RBC - near glucose exposed group and the last one, which collected *Polymnia,* ZnO-*Polymnia* and ZnO nanparticles formed mediated cluster. These results have pointed to the necessity of further investigations of antihyperglycemic activity of *Momordica* and *Catharanthus* and mechanistic explanation of their potentials.

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Khoma V.[1], Gnatyshyna L.[1,2], Horyn O.[1], Lahita V.[2], Mishchuk O.[3], Stoliar O.[1]

BIOCHEMICAL RESPONSES OF BIVALVE MOLLUSK IN THE CO-EXPOSURE TO DICLOFENAC, NIFEDIPINE AND GLYPHOSATE ARE DISTORTED BY HEATING

[1] Ternopil National Pedagogical University
2, M. Kryvonosa Str., 46027 Ternopil, Ukraine
[2] I. Ya. Horbachevsky Ternopil State Medical University
1, MaidanVoli, 46001 Ternopil, Ukraine
[3] Rowan University
201 Mullica Hill Rd, Glassboro, NJ 08028, USA
e-mail: Oksana.Stolyar@tnpu.edu.ua

Recently the priority list of the freshwater pollutants was changed: instead of the toxic metals the main pollutants became pharmaceuticals. They are continually get into surface waters at low concentrations (ng–µg per L) even despite the wastewater treatment plants activities. In the rivers, they are combining with the agrochemical substances causing the complex impact on the aquatic animals and on the final consumers of water, higher vertebrates and human. Moreover, their complex impact could be strengthened by the climate changing. The aim of this study was to evaluate the biochemical responses in the sentinel aquatic organism to these substances in the separate exposures and their modulations in the co-exposure. Bivalves as the sessile bio-filters are the most recognized bioindicators for the early forecast of the environmental impact. For the current study, we selected the most utilized substances that are discharged in the surface waters. We treated the mussels *Unio tumidus*, collected in the rural area, with non-steroidal anti-inflammatory drug diclofenac (voltaren) (D, 600 ng L^{-1}), cardiac drug Ca-channel blocker nifedipine (N, 700 ng L^{-1}), or organophosphorus pesticide glyphosate (round up) (G, 33.8 µg L^{-1}) separately at the temperature 18 °C and jointly at the temperatures 18 °C (DNG) and 25 °C (DNG+T) during 14 days. The utilised concentrations were correspondent to the levels indicated in the effluents of the municipal sewage treatment plants and/or surface waters. The responses of stress cytotoxicity were evaluated in the digestive gland.

The exposures caused some almost common responses that attest the high vulnerability of mollusks to these xenobiotics, unlike their low sensitivity to toxic metals. The antioxidant activity was down-regulated: total superoxide dismutase activity decreased in the exposures to D, G and DNG. The level of the lipid peroxidation detected as the TBARS increased in all exposures except DNG, and the concentration of the protein carbonyl groups was enhances in the exposures to G, DNG and DNG+T. The level of glutathione (GSH) was less sensitive: total GSH level increased only by exposures to DNG and DNG+T and did not changed in the other cases, whereas GSSG concentration and GSH/GSSG ratio did not change significantly in any exposure. The depletion of cholinesterase is the typical response to the organophosphorus compound. Indeed, this response was observed in the G and DNG groups, confirming this specificity, but it was absent in the DNG+T group. The activity of cathepsin D within the lysosomes increased in the exposure to D, but decreased by the effect of N and G (by four times). Nevertheless, the co-exposure did not changed this activity. Importantly, the efflux of Cathepsin D from the lysosomes in digestive gland magnified in the co-exposure DNG+T by two times. These results showed that the selected pharmaceutics caused less prominent responses, compared to glyphosate. Its impact was particularly strong and evident both in the single and combine exposures. In general, co-

exposure to selected substances causes mostly synergetic interaction at the 18 °C and antagonistic interactions when they are combined with the heating in this animal model system.

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Korniy N.[1], Goyal A.[1], Hoffmann M.[2], Samatova E.[1], Peske F.[1], Pöhlmann S.[2, 3], Rodnina M. V.[1]

MODULATION OF HIV-1 GAG/GAG-POL FRAMESHIFTING BY TRNA ABUNDANCE

[1] Department of Physical Biochemistry, Max Planck Institute for Biophysical Chemistry
Am Fassberg 11, 37077 Göttingen, Germany
[2] Infection Biology Unit, German Primate Center
Kellnerweg 4, 37077 Göttingen, Germany
[3] Faculty of Biology and Psychology, University of Göttingen
2, Wilhelm-Weber-Str., 37073 Göttingen, Germany
e-mail: natalia.korniy-1@mpibpc.mpg.de

–1 Programmed ribosome frameshifting (–1PRF) is a recoding event that causes a change of open reading frame and translation of an mRNA molecule into two proteins with an identical N-terminus but different C-termini. –1PRF is governed by two major regulatory elements in the mRNA, the so-called slippery sequence (i.e. the place where the actual recoding event takes place) and an mRNA secondary structure element downstream of the slippery sequence. The biological significance of –1PRF is to enlarge the coding capacity of the genome and to regulate gene expression. –1PRF is found in all kingdoms of life, but it is especially common for viruses where it mostly regulates the production of viral replicative enzymes; impairment in –1PRF prevents viral reproduction, particle formation and propagation. Despite crucial importance of –1PRF for viral replication, its underlying molecular mechanism remains obscure for the majority of viruses. –1PRF is responsible for production of the Gag-Pol fusion polyprotein in human immunodeficiency virus type 1 (HIV-1). The frameshifting efficiency at the gag-pol slippery site determines the Gag to Gag-Pol ratio, which is essential for HIV-1 infectivity and structure. Here we show that frameshifting is modulated by Leu-tRNA$^{Leu(UUA)}$ that reads the UUA codon of the slippery site. Leu-tRNA$^{Leu(UUA)}$ is rare in human cells. Depending on its availability, a constant Gag to Gag-Pol ratio is achieved by switching between two frameshifting mechanisms. At high Leu-tRNA$^{Leu(UUA)}$ concentration frameshifting is suppressed, offering options for new approaches in antiviral drug development. A second potential slippery site downstream of the first one is normally inefficient but can also support –1-frameshifting when altered by a compensatory resistance mutation in response to current antiviral drug therapy. Together these different regimes allow the virus to maintain a constant –1-frameshifting efficiency thus ensuring successful virus propagation.

Korotaieva E. I., Dolhikh G. V., Maslak G. S., Chernenko G. P.

LEVEL OF INTERCELLULAR AND SURFACE FIBRONECTIN OF LYMPHOCYTES IN PATIENTS WITH CHRONIC DIFFUSIVE LIVER DISEASES

State Establishment "Dnipropetrovsk Medical Academy of Health Ministry of Ukraine"
9, V. Vernadsky Str., 49044 Dnipro, Ukraine
e-mail: annadolgih100@gmail.com

Glycoprotein fibronectin (FN) is an important adhesive substrate that supports the implementation of many fundamental biological processes. Thus, in neoplastic and metabolic origin inflammatory pathological processes, the level of FN varies greatly. Currently, a lot of data on clinical trials of patients with cancer have been published, while biomaterials for the presence of FN in chronic diffuse liver disease have not been studied sufficiently. There is practically no information on the distribution of FNs on cells surface, in particular, plasma lymphocytes in liver pathologies. The aim of the study was to investigate the level of cellular FN within and on surface of lymphocytes of conditionally healthy donors – control group (n = 10) and patients with chronic diffuse liver disease – CDLD (n = 10).

A flow cytometry method with monoclonal antibodies to matrix AF (AbD Serotec, UK) and appropriate antibodies to mouse immunoglobulins, conjugated to fluorosetinizotiocyanate (Millipore, USA) were used. Cell permeabilization was performed with a solution of 0.025 % digitonin (Fluka, Sweden). The data was recorded on a Beckman Soolter flow cytometer EPICS XL (Beckmann Coulter, USA). The density of the exposure was calculated using FCS Express 3 program.

The data obtained after perimabilization of lymphocytes indicate a two-fold decrease in the level of FN in patients with CDLD compared to control group. It is important to note that the amount of this glycoprotein on plasma membrane of blood lymphocytes in patients with CDLD was increased in 2.6 times in relation to control.

It is known that the increase in the level of intercellular FN affects growth of connective tissue in CDLD (Benyon R.C., 2000), and the involvement of lymphocytes in these processes. Consequently, the data obtained complement the current understanding of the development of CDLD.