the presence of numerous side effects leads to the search for possibilities of different methods of influence, phytotherapy in particular, on the tumor and the body as a whole.

Phytotherapy is an important complement to post-stage treatment of cancer patients and allows the maximum individualization of therapy, taking into account the peculiarities of the organism, the role of individual systems in the development of the disease, and metabolism. Herbal preparations compensate the general condition of cancer patients, especially during combined treatment with chemotherapy, radiotherapy, preparation for surgery and period after operation.

Low toxicity of plant products and a wide range of their effects on the body allow long and successful using of medicinal plants, especially as a symptomatic remedy in combination with other modern treatments.

The first result that should be achieved by a purposeful treatment by means of remedies on the basis of medicinal plants is: reduced severity of pain syndrome, improved sleep, compensation of neurotic condition. Against the ground of severe pain, even a slight relief of the patient's condition is of great importance for the control of ailment. Peripheral action of phytotherapy in the site of spasm, edema, tissue compression and irritation of nerve endings are an important complement to central effects of analgesics that are prescribed to patients with oncological disease.

The possibilities of phytotherapy can achieve the effect associated with improving the function of the body or system. The use of herbal remedies in the prevention of relapses and metastases of tumors is of a particular interest. Moreover, the complex use of herbs, diet and medicines is very important for long-term cancer prevention. Immunomodulatory effect of herbal preparations is one of the essential factors of oncology and antiretroviral therapy.

Modern methods of secondary prevention, including complex and long-term use of herbal medicine, are not sufficiently developed. Therefore, there is a need for additional research and the administration of medicines on the basis of medicinal raw material into standard therapies.

Shchudrova T.S.

AMELIORATION OF GENTAMICIN-INDUCED KIDNEY INJURY BY SYNTHETIC PEPTIDE

Department of Pharmacology
Higher state educational establishment of Ukraine
«Bukovinian State Medical University»

Acute kidney injury of different degree occurs in one third of patients treated with gentamicin for more than 1 week, being the reason for serious limitation of its use (A. Muthuraman et al., 2011). Search for drugs able to mitigate the toxic effects of aminoglycosides is an active area of research (B.H. Ali et al., 2011).

The aim of our study was to estimate the nephroprotective potential of tripeptide EDL (L-glutamyl-L-aspartyl-leucine) synthesized in the St.-Peterburg Institute of Bioregulation and Gerontology (RF) on a model of gentamicin-induced kidney injury in rats.

Experimental study was conducted on 21 non-linear white rats weighting 150-180 g, divided into three groups (n=7): I group – control, II group – animals with gentamicin-induced kidney injury caused by administration of 4% gentamicin sulfate solution in dose 80 mg/kg once a day during 6 days. Animals of the III group received EDL (3 μg/kg, i.p.) after each gentamicin injection. Kidney function was assessed by diuresis, glomerular filtration rate (GFR), plasma creatinine concentration, urine protein excretion and fractional excretion of sodium. Histopathological examination by light microscopy was conducted to confirm the research results. Data were compared by Mann-Whitney test using SPSS Statistics 17.0.

Administration of gentamicin during 6 days resulted in the toxic kidney injury, manifested in the decrease of diuresis by 54% ($p<0.01$), increase of plasma creatinine concentration by 3.3 times on the background decrease of GFR by 73% ($p<0.01$) and significant proteinuria with an increase of protein excretion by 57% ($p<0.01$) comparing to control. Proximal tubular injury caused an increase of fractional sodium excretion up to 4.55% ($p<0.01$). Biochemical data correlate with histopathological findings: vacuolar degeneration affected 30%, epithelial necrosis – 70% of proximal tubular cells, the lumen of the tubules were filled with hyaline casts, glomerular congestion and their partial atrophy were also observed. Co-treatment with EDL decreased the severity of renal injury realized in preclusion of oliguria (increase of diuresis by 72% ($p<0.01$) comparing to untreated animals), prevention of retention azotemia (decrease of plasma creatinine concentration by 2.7 times, $p<0.01$), reduction of proteinuria by 3.4 times ($p<0.05$) and normalization of sodium fractional excretion (to 0.87%, $p<0.01$). Protective effect of peptide is confirmed by the absence of epithelial necrosis, glomerular atrophy, luminal hyaline casts and potentially reversible hydropic swelling of 80% of the proximal tubular cells.

Obtained results suggest the therapeutic potential of tripeptide EDL under the conditions of gentamicin-induced kidney injury confirmed by the amelioration of excretory kidney function and histopathological changes.

Stepanchuk V.V.

CIRCADIAN CHRONORHYTHMS OF FREE RADICAL OXIDATION **UNDER CONDITIONS OF LEAD POISONING AND IMMOBILIZING STRESS IN ALBINO RATS**

Department of Pharmaceutical Botany and Pharmacognosy
Higher State Education Establishment of Ukraine
«Bukovinian State Medical University»

Oxidative stress represents an imbalance between the production and manifestation of reactive oxygen species and a biological system's ability to readily detoxify the reactive intermediates or to repair the resulting damage.

Disturbances in the normal redox state of tissues can cause toxic effects through the production of peroxides and free radicals that damage all components of the cell including proteins, lipids, and DNA. Some reactive oxidative species can even act as messengers in redox signaling.

Oxidative stress plays an important role in pathogenesis of many metabolic disorders including atherosclerosis, Parkinson's disease, heart failure, myocardial infarction, Alzheimer's disease, fragile X syndrome, chronic fatigue syndrome and many others. Therefore, effective antioxidant therapy should be an essential component of their treatment. Circadian chronorhythms of free radical homeostasis in the erythrocytes of mature and old albino rats are examined in the experiment. Desynchronosis in activity of pro- and antioxidation systems is found to occur under influence of lead chloride, which is more pronounced in older animals. Under the influence of immobilizing stress desynchronosis in the free radicals indices of homeostasis and decreasing of antioxidative enzymes activity were found to occur in the experiment.

Enzymatic activity was found to possess significant dependence on the age of the animals. The depth of the changes revealed was considerably higher in the erythrocytes of old albino rats. The reduction of the activity of these enzymes considering the control was a characteristic tendency.

Zamorskii I.I.

NEPHROPROTECTIVE EFFECTS OF ANTITHROMBIN DNA APTAMERS IN ACUTE KIDNEY INJURY

Department of Pharmacology
Higher state educational establishment of Ukraine
«Bukovinian State Medical University»

Aptamers are small single-stranded molecules of DNA / RNA, sized in 30-60 nucleotides with high affinity and specificity to a selected target. These substances are obtained by the methods of combinatorial chemistry of nucleic acids SELEX (Systematic Evolution of Ligands by Exponential enrichment) (Spiridonova V.A., 2010). Single-stranded aptameric molecules of nucleic acids have highly ranked tertiary structure that allows them to form stable and specific complexes with different targets, including thrombin. The objective of this work was to study the effect of antithrombin DNA aptamers (Spiridonova V.A. et al., 2015) on the course of experimental acute kidney injury (AKI) due to rhabdomyolysis.

Rhabdomyolytic AKI was simulated in mature male non-linear white rats by intramuscular injection of hyperosmotic 50% glycerol solution at a dose of 10 ml / kg. DNA aptamers (TVA15, TVA31 and RE31) were injected intraperitoneally at a dose of 0.5 mg / kg daily for 3 days until the disease was simulated. The renal function was evaluated under conditions of water load (5% of body weight) in terms of urine output, glomerular filtration rate, proteinuria, creatinine concentration in plasma and urine excretion of ammonia and titrated acids in the urine. General protective effects of antithrombotic DNA aptamers were also evaluated for the survival of animals with this AKI model.

Introduction of different DNA aptamers showed nephroprotective effects of the studied compounds. Thus, when aptamer TVA31was administered, creatinine in blood plasma, protein and values of titrated acids in the urine remained at the level of control, changing compared to the data obtained in simulated disease by 24.4%, 22.3% and by 2,8 times respectively (180%, $p<0.05$). At the same time under the influence of TVA31 aptamer in the rats with simulated pathology the urine output increased by1.5 times ($p<0.05$) compared to those animals, in which AKI was simulated without aptamers. In this case the glomerular filtration rate increased significantly as well. The survival rate of the animals in the group with simulated pathology within 7 days was 85.7%, and after the application of all studied DNA aptamers – 100% ($p<0.05$).

Zeleniuk V.H., Rovinskii O.O.

ESTIMATION OF THE INFLUENCE OF STATINS ON THE ENERGY SUPPLY OF CELLS IN ISCHEMIC ACUTE RENAL FAILURE

Department of Pharmacy
Higher State Educational Establishment of Ukraine
"Bukovinian State Medical University"

One of the approaches of pharmacotherapy of acute kidney injury (AKI) is the use of drugs with antioxidant properties. Statins can prevent lipid peroxidation and disturbances of the mitochondrial energy generation. Thus, our research study was targeted at the examination of the impact of statins on the linkage between oxidative stress and impaired energy metabolism under the conditions of AKI.

The experiment was carried out on 40 white nonlinear male rats weighing 140-180 g. Statins (atorvastatin, simvastatin and lovastatin) in the dose of 20 mg/kg were administered intragastrically daily for 3 days before the surgery. Renal ischemia-reperfusion injury was simulated during anesthesia: median laparotomy followed by 75-minute clamping of the left renal pedicle and reperfusion for 24 h. The renal function was assessed immediately after reperfusion under the conditions of induced diuresis.

Activation of free radical oxidation led to the energy metabolism imbalance and decrease in the activity of succinate-coenzyme Q reductase (SQR) in the kidney tissue of untreated animals by 2.6 times. The latter was verified by an inversed correlation ($r=-0.88$) between the content of malondialdehyde in the kidney tissue and the SQR activity, as well as by the direct correlation ($r = 0.72$) between the activity of glutathione peroxidase and SQR. Concerning the antioxidant effects of statins it was managed to achieve the activation of SQR: by 2.2 times (atorvastatin), by 1.7 times (lovastatin), and by 2.3 times (simvastatin). Furthermore, the prevention of kidney damage was achieved due to