

UDC 577.343+602.643:54-126

**IN VITRO AND IN VIVO INVESTIGATION OF POLYELECTROLYTES**

M. Kozak<sup>1</sup>, PhD, D. Ostapiv<sup>1</sup>, Dr., N. Mitina<sup>2</sup>, Dr., O. Zaichenko<sup>2</sup>, Dr., V. Vlizlo<sup>1</sup>, Dr.  
mariya\_kozak@yahoo.com

<sup>1</sup>Institute of Animal Biology NAAS, Lviv, Ukraine

<sup>2</sup>National University "Lviv Polytechnics", Lviv, Ukraine

Transmissible spongiform encephalopathies are a group of neurodegenerative diseases that affect both humans and animals. There are different causes, ranging from prion infection and genetic mutations to unknown factors. The effective treatment and specific prevention do not exist. The disease is always fatal. Different approaches for treating or slowing down disease progression are studied. The antisense oligodeoxynucleotides (asODN) to the PrP<sup>C</sup> mRNA reduced the content of PrP<sup>C</sup>, which is a substrate for an infectious prion protein (PrP<sup>Sc</sup>).

The purpose of the research was to identify risks for animal health from cationic polyelectrolytes as a carrier of the therapeutic asODNs.

Low molecular weight water soluble homopolymer dimethylaminoethyl methacrylate (polyDMAEM) was used. On its basis a series of syntheses were conducted in which the following oligomers were obtained: D1, D2, D3, MP-27, MP-2, MP-3. The ability of polymers to bind oligonucleotide was characterized by the method of free diffusion in an agarose gel. *In vitro* studies (survival of cells and oxidative-reduction processes in them) were performed with cell (bull sperm cells). *In vivo* experiments were performed with two groups of *Rattus norvegicus* var. *Alba*, Wistar lines — control and experimental (n=15). Animals of the experimental group were injected into the tail vein with polymer-asODN complex.

It has been established that polyelectrolytes, which are characterized by positive charge, form complexes with asODN. MP-27 has shown the lowest cytotoxicity when complexed with asODN. The cell survival was 120 h. It was found that polymer D1 enhanced the oxygen uptake in cells by 14.7 %, and D3, on the contrary, reduced it by 18.7 %. The adding of NaF under the action of D1 decreases oxygen uptake by 2.34 times. The addition of inhibitors (amytal, sodium azide and EDTA) also reduced the oxygen consumption by 25 times of its initial value. The obtained data indicate that D1 enhances the processes of glycolysis and is the most sensitive to the inhibitor of this process. NaF together with D2 reduced oxygen uptake by 21.1 % and the addition of EDTA depressed this process by 59 times. Polymer D3 itself can inhibit the oxidative processes in cells. It was also found that inhibitors of the oxygen uptake had a stronger effect on cells that were exposed to polymeric compounds compared to the control. It has been established that all polymers with the name MP, which are derivatives of the D1 sample, increase the oxygen consumption by 18.0 % (MP-27), by 37.1 % (MP-2) and by 2.6 times for MP-3. MP-27 has the least cytotoxicity and the smallest impact on the oxidation-reduction processes in cells. Therefore, MP-27 has been selected for *in vivo* studies. The hematological parameters in rats were within normal limits. It was established that the number of erythrocytes decreased by 8.5 %, and the hemoglobin concentration — by 6.5 %, the number of leukocytes was  $13.4 \pm 2.1 \cdot 10^9/L$ . Any changes in creatinine and urea content were not detected. The ALT activity increased by 35 % as compared to the control.

MP-27 influences on vital functions of cells and the whole body the least and therefore has a promising future in research.