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Smart biomaterials based on Laponite®: acute toxicity and influence on the redox state and enzyme activity in the organs of the detoxification system of mice

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Background. Laponite® (Lap) is a synthetic disc-shaped material with thickenss of h ≈ 1 nm and diameter of d ≈ 25 nm. Lap is widely used in many industrial fields and medical applications. The medical application of Lap includes long-acting drugs, and in particular, anticancer drugs. **Aim.** The work aims to prepare smart biomaterials (thermosensitive Poly(N-isopropylacrylamide)–based hydrogels cross-linked by acid-activated Lap (aLap) doped with doxorubicin (Dox) (aLap+Dox/hydrogel)), to determine and compare the indicators of its acute toxicity, and to estimate its effects on the level of generation of superoxide radicals (SR), activity of ribonucleases (RNases), ornithine decarboxylase (ODC) and gelatinase (matrix metalloproteinases-2 and -9 (MMP-2 and -9)) in liver and kidney tissues of C57Bl/6 mice. **Methods.** Experimental animals (mice) were injected intra-peritoneally with 1, 2, 4, 8, 12 and 14 mg/kg of Dox or aLap+Dox/hydrogel (equivalent to 1, 2, 4, 8, 12 and 14 mg/kg free Dox). Mice of the control groups received aLap/hydrogel and normal saline in equivalent volumes. Observation was conducted for 14 days and the lethal doses were obtained from probit analysis. In order to collect the tissues, the part of the mice was removed from the experiment by euthanasia on the 5th day after the injection. Electron-paramagnetic resonance, zymography in polyacrylamide gel, and biochemical techniques were used for analysis. **Results.** It was determined that LD_{50} and LD_{84} for Dox was 10.8±1.0 and 19.2±1.8 mg/kg. We have found that the highest of the studied doses of the aLap+Dox/hydrogel did not cause the death of animals. Behavioral signs of intoxication of varying intensity, in contrast to control mice, were observed in both groups. For injection with Dox the rate of SR generation in the liver and kidney tissues of mice was higher (by 1.4, and 1.27 times, respectively, $p < 0.05$), as compare with injection of aLap+Dox/hydrogel. The total activity of RNases and ODC in the liver tissue was also significantly higher (by 1.7 and 1.4 times, respectively) as compare with injection of aLap+Dox/hydrogel. The similar positive trends were observed in the total activity of gelatinases. When Dox was administered, the total activity of gelatinases in the liver and kidney tissues of mice was 38.0±7.1 and 33.7±4.5 a.u. respectively, and was higher compared to the injection of aLap+Dox/hydrogel (21.3±4.9 and 20.1±4.1 a.u., $p < 0.05$). **Conclusions.** Dox in aLap-based/hydrogels exhibits significantly less overall toxicity compared to the traditional Dox drug. It can be explained by the successive release of the incorporated drug during the degradation of the hydrogels in the conditions of the animal organisms. Therefore, the aLap+Dox/hydrogels are the promising carriers of incorporated antitumor drugs. **Grants.** The National Research Foundation of Ukraine, Project No 2022.01/0039, 2024.

Keywords: Laponite®, acute toxicity, doxorubicin, C57/Bl6 mice, superoxide radicals.