Modelling of the polyster copolymers degradation in vitro detected by fluorescence and MRI

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Цель и задачи исследования

Purpose of the work: to study the rate and features of the biodegradation of polyester copolymers in model systems for subsequent testing in vivo using MRI and fluorescence methods.

Copolymers

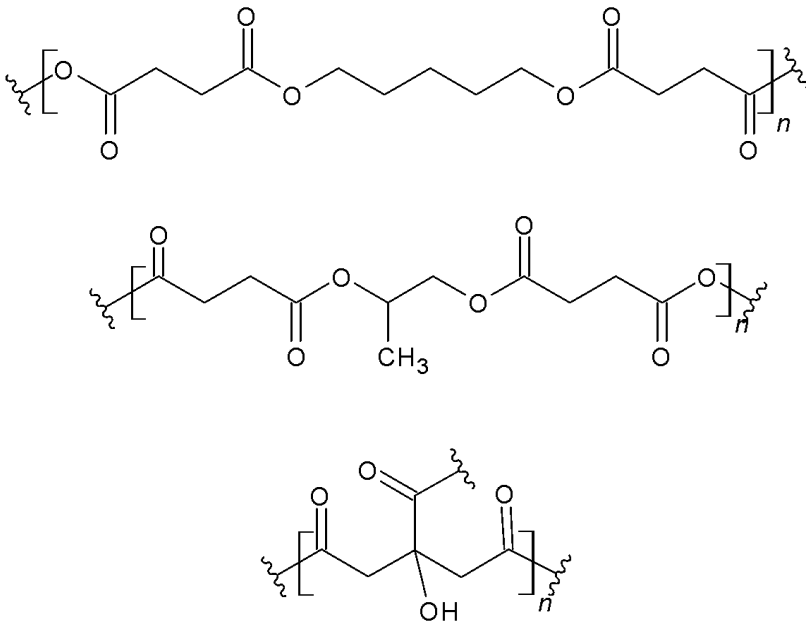
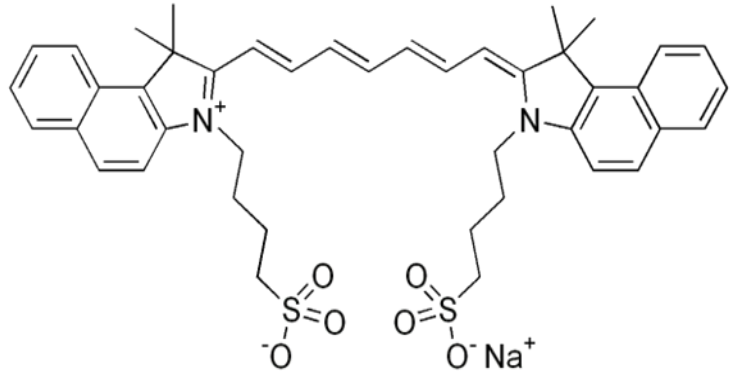
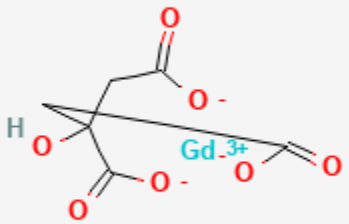


Рисунок 3 – флуоресцентная и парамагнитная метки

ICG

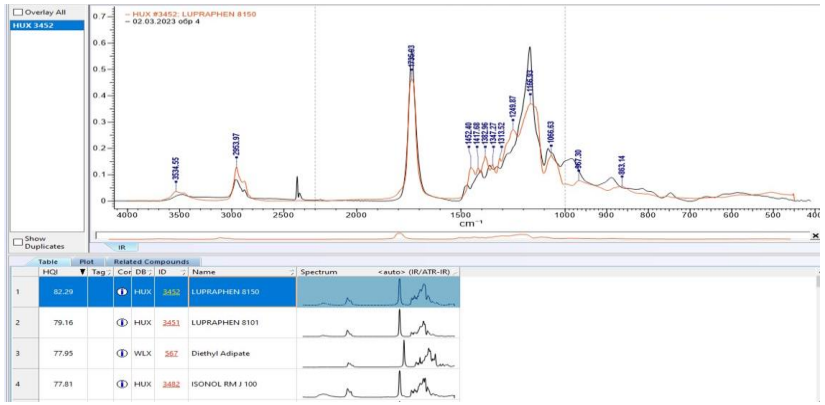


Gd citrate

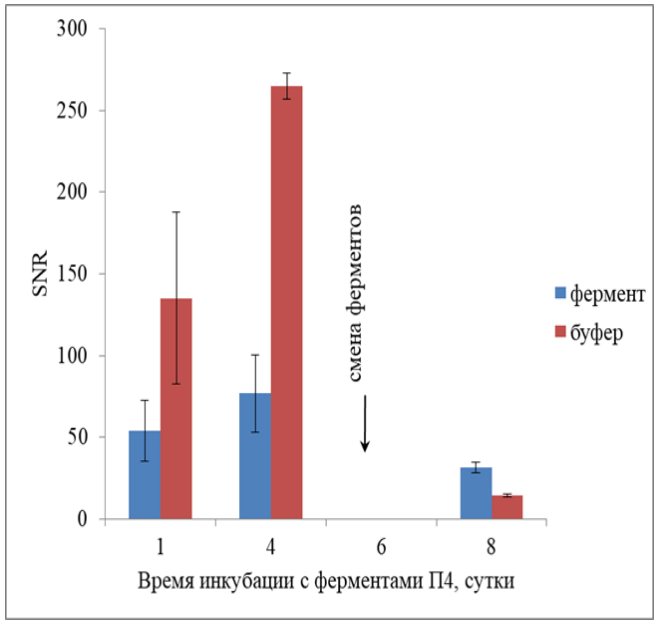


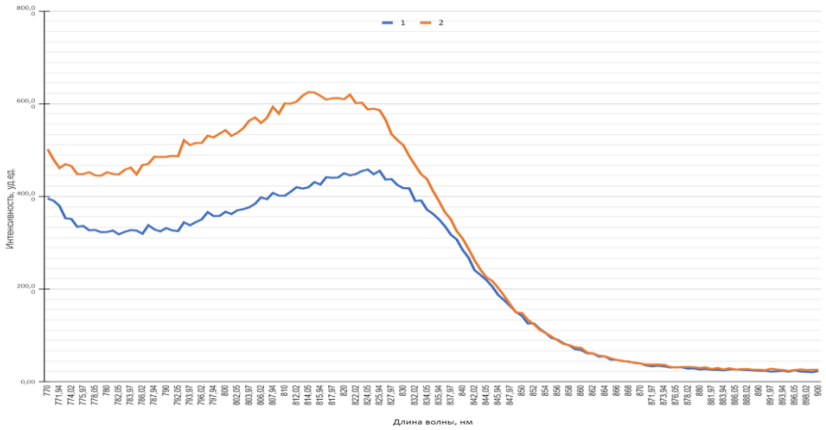
Copolymers were synthetized according to the protocol and with some modification based on the 1,3-propandiol, 1,5-pentadiol, succinic acid and citric acid. Copolymers were marked with indocyanine green and magnetic resonance agent like Gd-DOTA or Gd-citrate complex. The structure of polyester copolymers labeled with a fluorescent (indocyanine green) and paramagnetic label (gadoterate) corresponds to the structure of unlabeled polymers.

Характеристика сополимеров



FTIR 92 % of coincidence for non-marked copolymers

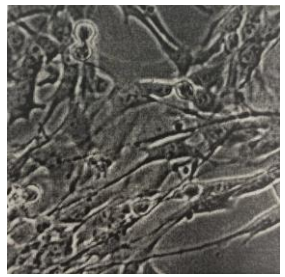


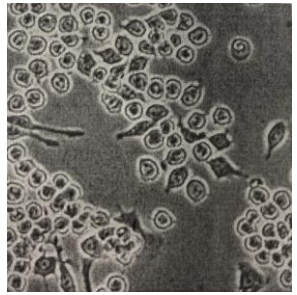


ICG and Gd citarate are included

Roadmap

1. **Cytotoxicity**





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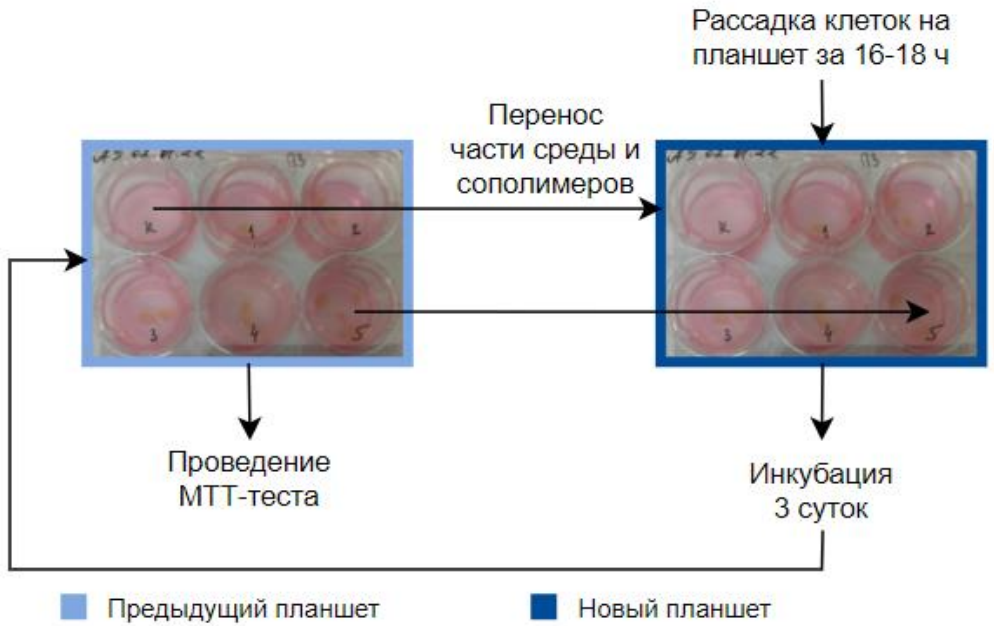
2. in vitro biodegradation modelling

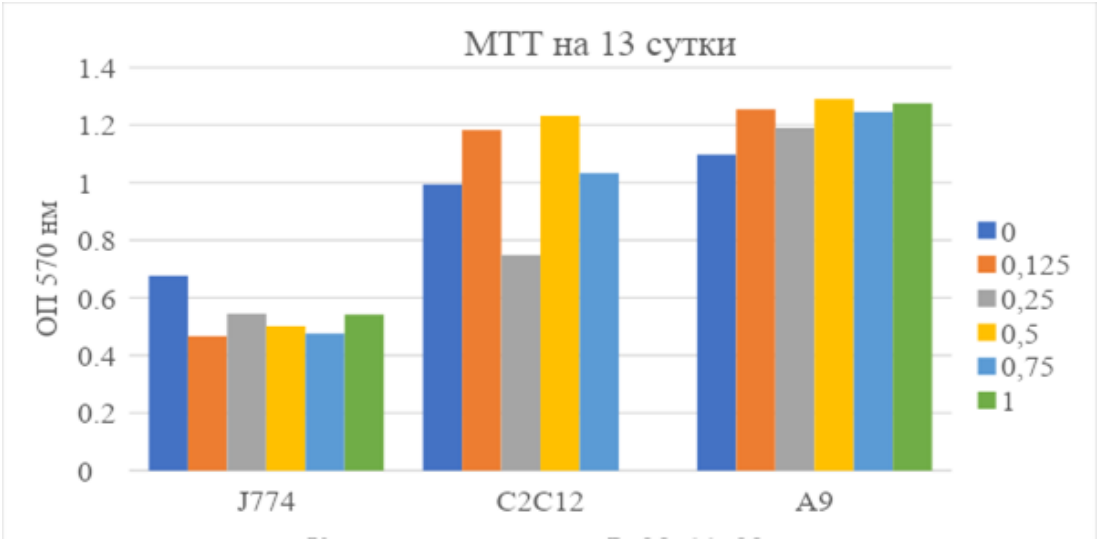
fluorescence of ICG and MRI detection

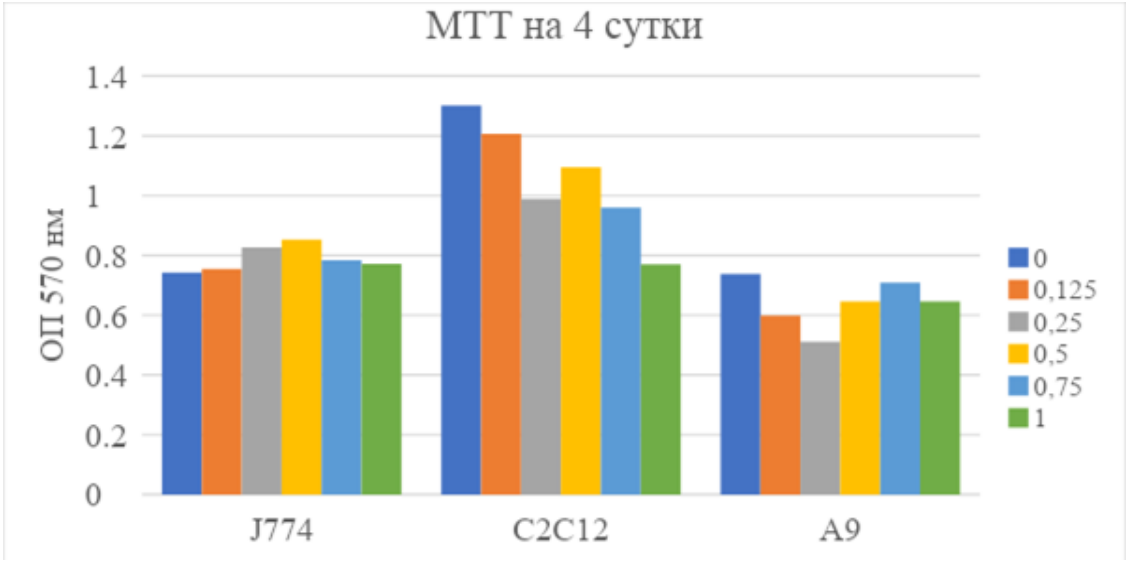
3. Next step: implantation to mice.

fluorescence of ICG and MRI detection

Cytotoxicity

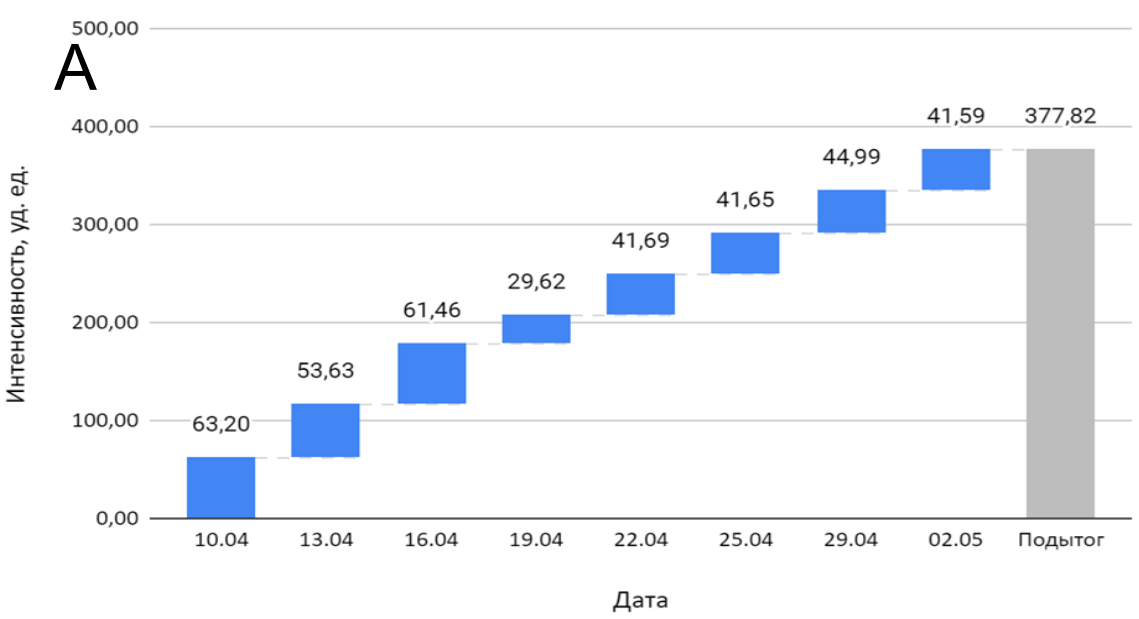


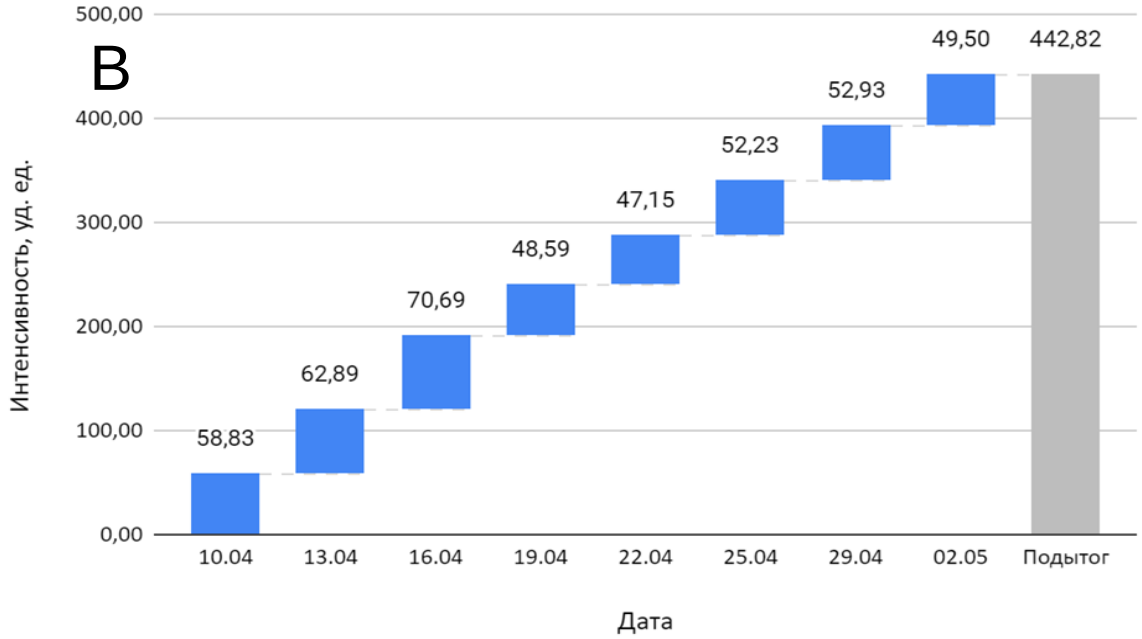




Release rate of paramagnetic label*

T1 paramagnetic signal intensity (SNR) of Gd-DOTA label release in blood serum (A) and in blood serum with enzyme (B) cumulatively

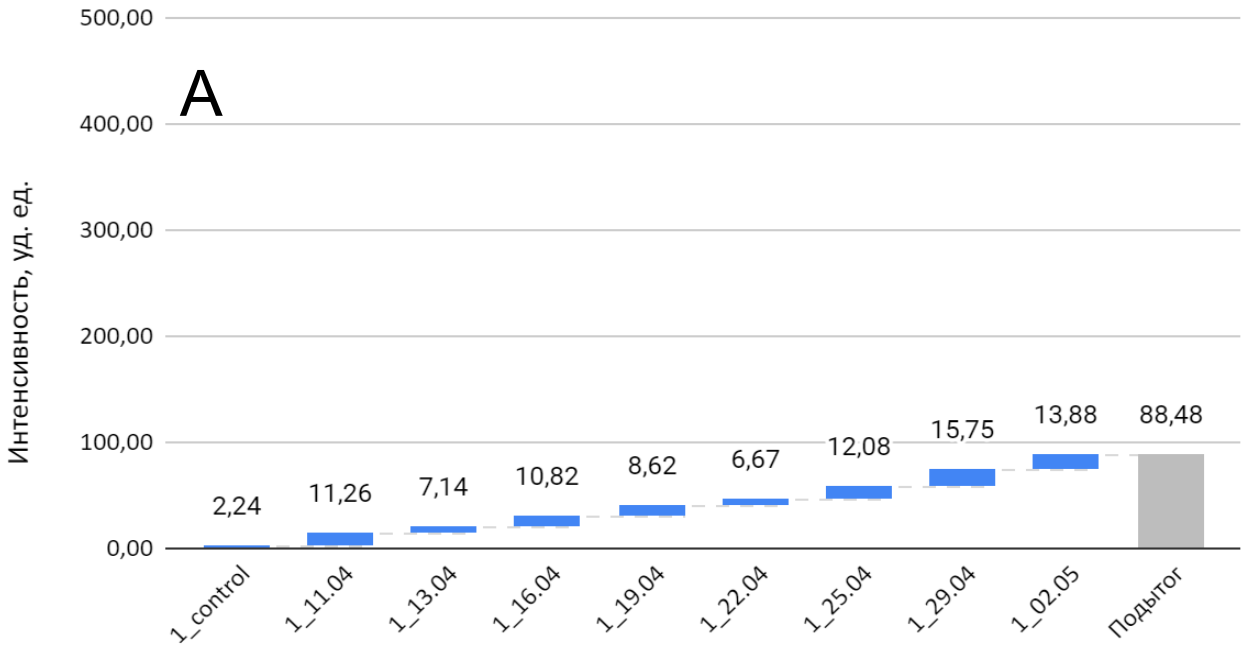


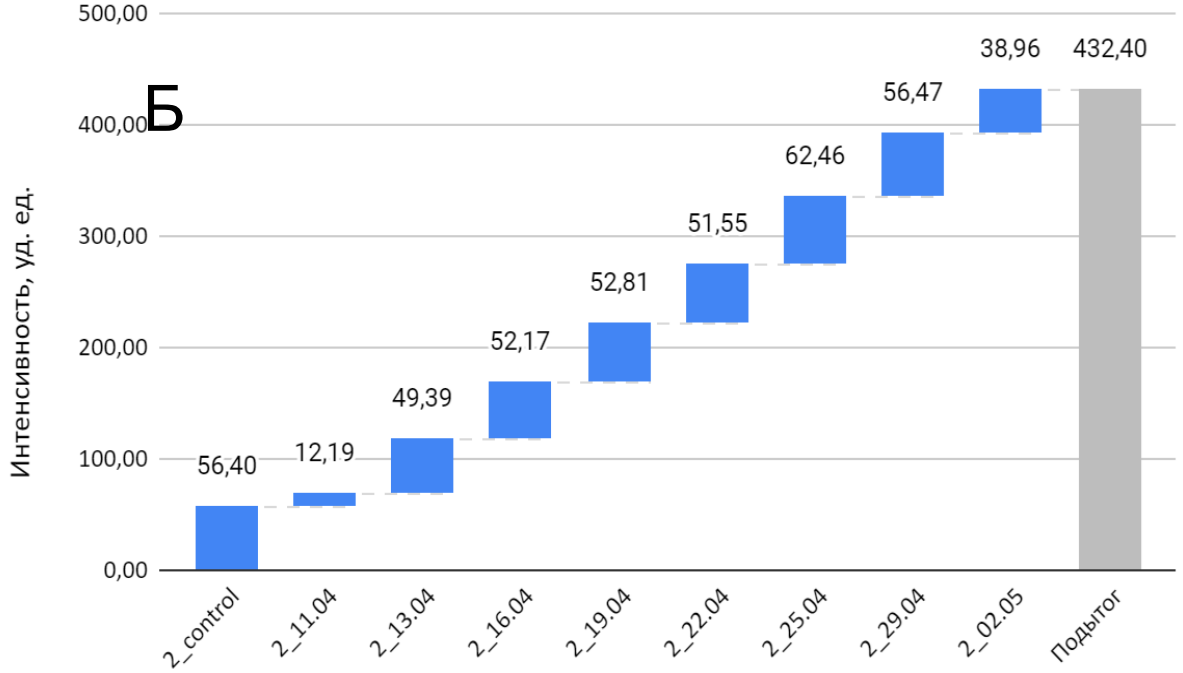


* The lipase activity in the solution is 1750 units/l, which is 11 times more than the lipase activity in human blood and 175 times more than the activity in mice.

Release rate of fluorescent label*

Fluorescence intensity of the ICG label when it is released in blood serum (A) and in blood serum with the enzyme (B) cumulatively

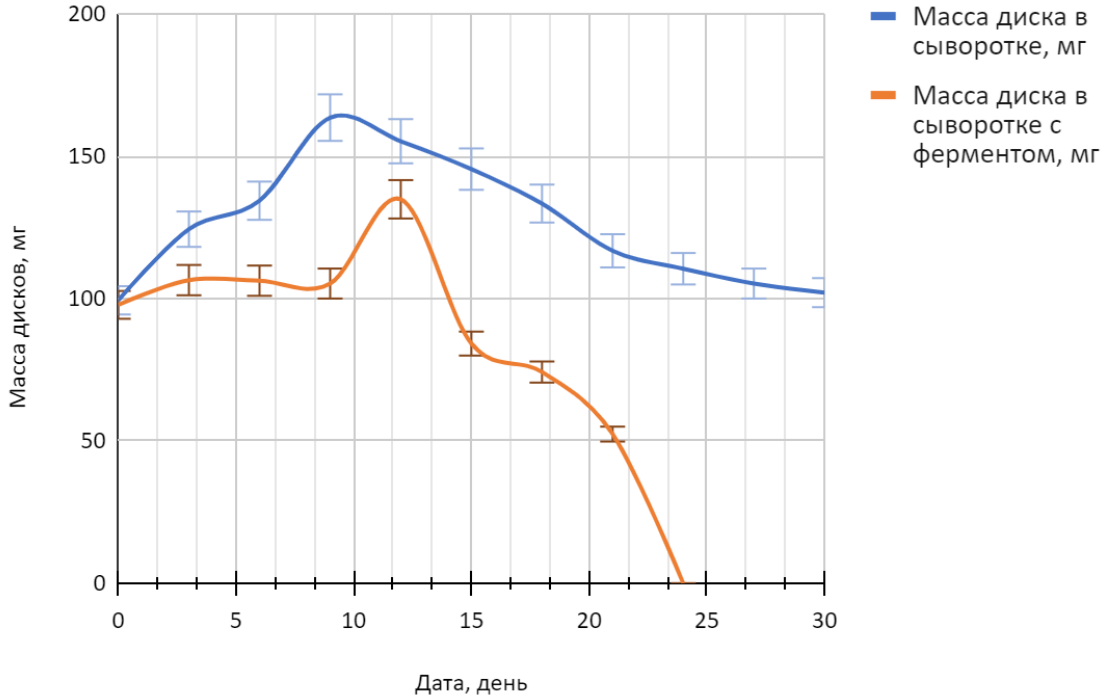




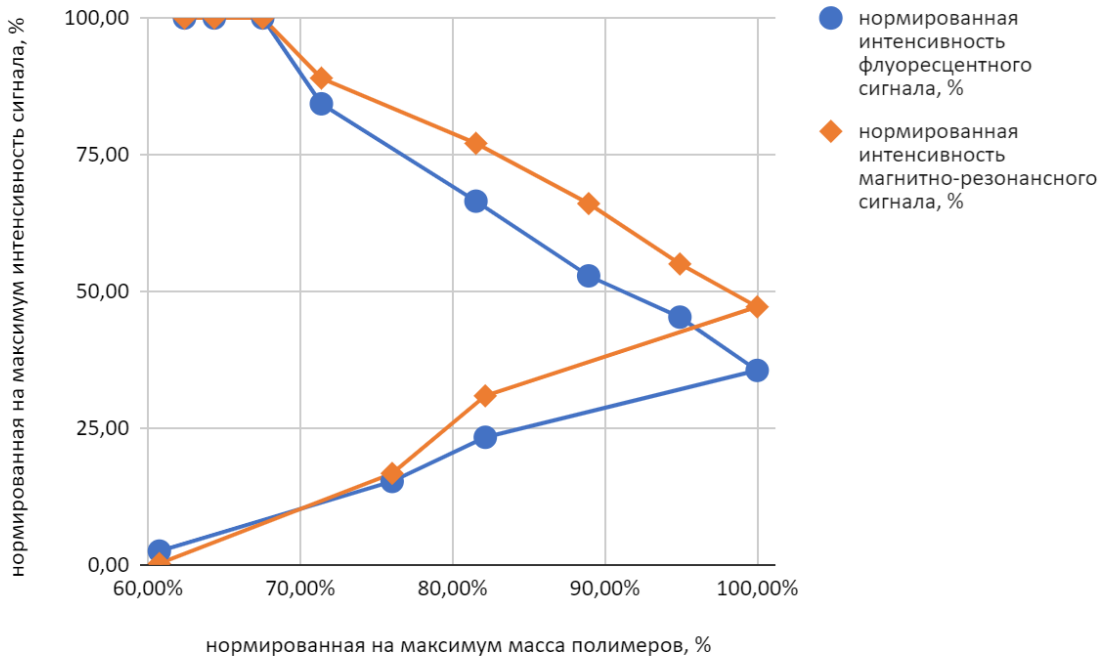
* The lipase activity in the solution is 1750 units/l, which is 11 times more than the lipase activity in human blood and 175 times more than the activity in mice.

Correlation of Changes in Polymer Weight, Fluorescence Intensity, and MR Signal in the Study of In Vitro Degradation

Change in the mass of copolymer discs in model serum solutions



Dependence of the change in the intensities of the MR signal and the fluorescent signal normalized to the maximum on the mass of the polymer normalized to the maximum



Conclusions

- During the degradation of polymers in buffer solutions, hydrolysis predominates; it also contributes to the enzyme-mediated cleavage of polyester bonds by esterases (lipases). In blood serum, only 60% of the initial mass of copolymers biodegraded in 70 days, while under the action of enzymes, complete biodegradation occurred on the 24th day of the experiment, which is 3 times slower than in the buffer, which is presumably due to the stabilizing role of proteins present in blood serum.

- The process of release of fluorescent and paramagnetic labels in vitro takes place in two phases: a) phase 1 - moderate yield of degradation products - with swelling of the copolymers and with a moderate rate of polymer degradation; b) phase 2 - fast release of degradation products - with a higher rate of degradation of polymers. It has been established that the release of the paramagnetic and fluorescent labels correlates with the change in the weihgt of the copolymers.

Funding
This research was funding by Ministry of Science and Higher Education of the Russian Federation grant № 13.2251.21.0009 from 29.09.2021 (Agreement № 075-15-2021-942).