6. NANOMEDICINE

6.1. Medical Physics

3.6.1.1. Development and testing of nanoparticles for treatment of cancer cells by Curie temperature controlled magnetic hyperthermia. /A. Chirakadze, N. Mitagvaria, D. Jishiashvili, M. Devdariani, G. Petriashvili, L. Davlianidze, N. Dvali, K. Chubinidze, A. Jishiashvili, Z. Buachidze, I. Khomeriki/. Bulletin of the Georgian National Academy of Sciences. – 2021. – v. 15. – #1. – pp. 91-98. – eng.; abs.: eng., geo.

A vast amount of nanoparticles has been developed and proposed for the local hyperthermia of cancer during the last decades, but only a few of them correspond to the mandatory requirements of having therapeutic range Curie temperature (T_C = 41-45^{0}C), high-rate crystallinity and "strong" magnetic properties, strictly controlled homogeneity and dispersion of the nanoparticles, good biocompatibility and harmless decomposition products. Among them are the nickel-copper (Ni-Cu) and silver doped lanthanum manganite ($Ag_xLa_{1-x}MnO_3$) nanoparticles. The developed research showed that the materials obtained at lower than usual temperatures using microwave enhanced synthesizes and annealing can be successfully used for local hyperthermia revealing high magnetic properties. Behavioral toxicity testing of the developed nanoparticles was enhanced by blood oxygen saturation measurements using noninvasive oximetry in white rats. Both of the developed nanomaterials revealed a lower toxicity level than the commercially available Fe_2O_3 nanoparticles. Fig. 4, Ref. 14.

Keywords: Cancer, magnetic hyperthermia, behavioral tests, toxicity, nanoparticles, synthesis, magnetic properties, microwave, blood oxygen saturation

References:

1. Report on behalf of the Children, Teenagers and Young Adults Expert Advisory Group, National Cancer Registration and Analysis Service. (2018). Childhood Cancer Statistics, England. Annual report 2018: Incidence of childhood cancer, 2001 to 2015. PHE publications, Gateway number: 2018135, 31 pp. https://file:///C:/Users/593%2022-11-01/Downloads/Childhood_Cancer_Statistics_England_FINAL_updated. 20(6). pdf.
2. Ward Z.J., Yeh J.M., Bhakta N., Frazier A.L., Atun R. (2019). Estimating the total incidence of global childhood cancer: a simulation-based analysis. The Lancet Oncology: 20. 4: 483-493.
3. Ban I., Stergar J., Maver U. (2018). Ni-Cu magnetic nanoparticles: review of synthesis methods. surface functionalization approaches, and biomedical applications. Nanotechnology Review. 7. 2: 187–28.
4. Katz E. (2019). Synthesis, properties and applications of magnetic nanoparticles and nanowires - a brief introduction. Magnetochemistry. 5. 61. doi:10.3390/magnetochemistry5040061.
5. Mary J.A., Manukandani A., Kennedt L.J., Buoudina M., Sundaram R., Vijaya J.J. (2014). Structure and magnetic properties of Cu−Ni alloy nanoparticles prepared by rapid microwave combustion method. Trans. Nonferrous Met. Soc. China. 24: 1467−1479.
6. Ehi-Eromosele C.O., Ita B.I., Edobor-Osoha A., Ehi-Eromosele F.E. (2016). Low-temperature solutioncombustion synthesis and magneto-structural characterization of polycrystalline $La_{1-x}Ag_yMnO_3$ (y≤x) Manganites. International Journal of Self-Propagating High-Temperature Synthesis. 25, 1: 23–29.
7. Chirakadze A., Jishiashvili D., Shiolashvili Z., Petriashvili G., Chubinidze K. (2020). Development and testing of combined nano-based liquids for treatment of cancer cells based on nanoparticles with a therapeutic Curie temperature and liquid crystals: Georgian Experience. Abstracts of International Conferences & Meetings (AICM). Krispon Advancing Science. Edinburgh.
8. Chirakadze A., Jishiashvili D., Petriashvili G., Mitagvaria N. (2020). Development and toxicity testing of nanoliquids for cancer treatment utilizing the phosphatized nanoparticles and liquid crystals with controlled release. Abstracts of International Conferences & Meetings (AICM). Krispon Advancing Science. Edinburgh.
9. Chirakadze A., Jishiashvili D., Mitagvaria N., Lazrishvili I., Shiolashvili Z., Jishiadhvili A., Makhatadze N., Buachidze Z., Khuskivadze N. (2019). Studies of the comparatively low-temperature synthesis and

preliminary toxic characteristics of silver doped lanthanum manganite nanoparticles using conventional and microwave heating. Proceedings of MTP: Modern Trends in Physics. Baku. 01-03 May. 47-51.
10. Mitagvaria N., Lazrishvili I., Devdariani M., Davlianidze L., Nebieridze M., Saginadze N., Kvachakidze I., Gumberidze L., Sikharulidze N. (2015). Hormesis - a basis for homeostasis in the presence of stressors. An example of hyperthermic stress. Journal of Biological Physics and Chemistry. 15: 187-193.
11. Decker M.J., Conrad K., Strohl P. (1989). Noninvasive oximetry in the rat. Biomed Instrum. Technol. 23, 3: 222-228.
12. Gurunathan S., Kang M.H., Qasim M., Kim J.H. (2018). Nanoparticle-mediated combination therapy: two-in-one approach for cancer. Int. J. Mol. Sci. 19, 3264; doi: 10.3390/ijms19103264.
13. Petriashvili G., Devadze L., Zurabishvili T., Sepashvili N., Chubinidze K. (2016). Light controlled drug delivery containers based on spiropyran doped liquid crystal microspheres. Biomedical Optics Express.7, 2; 442-447.
14. Yagawa Y., Tanigawa K., Kobayashi Y., Yamamoto M. (2017). Cancer immunity and therapy using hyperthermia with immunotherapy, radiotherapy, chemotherapy and surgery. J. Cancer Metastasis Treat. 3: 218-230.

3.6.1.2. Information about artificially intelligent nanoarray for detection of various diseases in nanomedicine. /V.M. Aroutiounian/. Armenian Journal of Physics. – 2021. – vol. 14. – #3. – pp. 148-150. – eng.; abs.: eng.

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In brief is summarized information about artificially intelligent nanoarray for detection of various diseases in nanomedicine. Ref. 20.

Keywords: artificially intelligent nanoarray, detection of various diseases, nanomedicine

References:

1. V.M. Aroutiounian, Journal of Nanomedicine & Nanotechnology 11 (2020) 1.
2. Ji.W. Yoon, J.H. Lee, Lab on a chip. 1 (2017) 8.
3. V.M. Aroutiounian, J. Cont. Phys.-Arm. Acad. Sci. 54 (2009) 324.
4. N. Nasiri, Ch. Clark, Biosensors 9 (2019) 43.
5. M. Nakhleh, Y. Broza, H. Haick, Nanomedicine 9 (2014) 1991.
6. Y.Y. Broza, H. Haick, Nanomedicine 8 (2013) 785.
7. R. Vishinkin, H. Haick, Small 11 (2015) 6142.
8. G. Konvalina, H. Haick, Acc. Chem. Res. 47 (2014) 66.
9. P.I. Gouma, K. Kalyanasundaram, Appl. Phys. Lett. 93 (2008) 244102.
10. W. pel, Sens. Actuators B 4 (1991) 7.
11. N. Shehada, J.C. Cancilla, J.S. Torrecilla et al, ACS Nano 10 (2016) 7047.
12. B. Wang, J.C. Cancilla, J.S. Torrecilla et al, Nano Lett. 14 (2014) 933.
13. M.K. Nakhleh, S. Baram, R. Jeries et al, Adv. Mater. Technologies 1 (2016) 1600132.
14. E. Homede, M. Abo Jabal, R. Ionescu et al, Adv. Funct. Mater. 26 (2016) 6359.
15. N. Shehada, G. r nstrup, K. Funka et al, Nano Lett. 15 (2015) 1288.
16. B. Wang, T.-P. Huynh, W. Wu et al, Adv. Mater. 28 (2016), 4012.
17. R. Ionescu, Y. Broza, H. Shaltieli et al, ACS Chem. Neurosci. 2 (2011) 687.
18. M.K. Nakhleh, H. Amal, R. Jeries et al, ACS Nano 11 (2017) 112.
19. G. Peng, U. Tisch, O. Adams et al, Nat. Nanotechnol. 4 (2009) 669.
20. E. Dovgolevsky, G. Konvalina, U. Tisch, H. Haick, J. Phys. Chem. C 114 (2010) 14042.

6.2. Medical Chemistry

3.6.2.1. Pseudoprotein-based nanoparticles show promise as carriers for ophthalmic drug delivery. /Tem. Kantaria, Ten. Kantaria, S. Kobauri, W. Zhang, N. Eter, P. Heiduschka, A. Kezeli, G. Chichua, D. Tugushi, R. Katsarava/. Annals of Agrarian Science. – 2020. – v. 18. – #1. – pp. 43-53. – eng.; abs.: eng.

Drug delivery used to treat ocular disease still poses a challenge to modern ophthalmology. Well-established intravitreal injections imply discomfort to the patients and risk of ocular complications. Therefore, opportunities to deliver drugs by topical administration are investigated thoroughly. Despite its seemingly easy accessibility, the eye is well protected by efficient mechanisms that rapidly remove drugs after instillation on the eye surface. Hence, eye drops are less effective for the treatment of various diseases, which necessitates a risk-containing procedure of intravitreal injection. One of the rational ways to overcome the problem is the application of drug-loaded polymeric nanoparticles (NPs) that are able to penetrate through ocular barriers when administered topically. Pseudo-proteins (PPs) - amino acid-based biodegradable polymers are one of the most suitable materials for the design of drug delivering NPs. One of the most important features of such kind of nanovehicles is “disappearance” from the body after their function is fulfilled. We have prepared biodegradable NPs of various types by nanoprecipitation of the PEA-class of PP composed of L-leucine, 1,6-hexanediol and sebacic acid (8L6). The originally designed arginine-based cationic PEA and comb-like PEA containing lateral PEG-2000 chains along with 8L6 anchoring fragments in the backbones were used to construct positively charged and PEGylated NPs. The NPs were loaded with fluorescein diacetate (FDA) as a fluorescent probe to detect if the NP penetrated through the ocular barriers. A preliminary in vivo study on intraocular infiltration of the NPs has been done using wild-type C57BL/6 mice. After penetrating into the cellular lysosomes, FDA probes became visible due to the hydrolysis of the diacetate groups, thus allowing for the detection of the NPs as tiny fluorescent spots inside the tissues. One day after administration, fluorescent dots were found at various sites - always in the peripheral cornea and the sclera, and in different layers of the outer retina depending on the type of NPs used. Four days after administration, fluorescent dots were still visible in the peripheral cornea and the sclera with some of the NPs. These results show that the new type of NPs infiltrate the ocular tissues after topical administration and are taken up by the cells. This raises hope that the NPs may be useful carriers for ocular delivery of therapeutic agents. Fig. 4, Tab. 3, Ref. 35.

Keywords: biodegradable polymers, pseudo-proteins, nanoparticles, biodegradable surfactant, PEGylation, ocular penetration

References:

1. S. Resnikoff, D. Pascolini D. Etya’ale et al. Global data on visual impairment in the year 2002. Bull. World Health Organ. 82 (2004) 844–851.
2. R. Gaudana, H.K. Ananthula, A. Parenky et al. Ocular drug delivery. AAPS J. 12 (2010) 348–360.
3. A. Urtti, Challenges and obstacles of ocular pharmacokinetics and drug delivery, Adv. Drug Deliv. Rev. 58 (2006) 1131–1135.
4. R. Herrero-Vanrell, M. Vicario-de-la-Torre, V. Andrés-Guerrero et al. Nano and microtechnologies for ophthalmic administration, an overview. J. Drug Deliv. Sci. Technol. 23 (2013) 27.
5. E.M. Del Amo A. Urtti, Current and future ophthalmic drug delivery systems. A shift to the posterior segment. Drug Discov. Today. 13 (2008) 135–143.
6. M. Kropp K.M., Morawa G., Mihov A.K., Salz N., Harmening A. Franken, A. Kemp A.A., Dias, J. Thies, S. Johnen, G. Thuman. Biocompatibility of Poly(ester amide) (PEA) Microfibrils in Ocular Tissues. Polymers 6 (2014) 243-260.
7. V. Andrés-Guerrero M. Zongc, E. Ramsay et al., Novel biodegradable polyesteramide microspheres for controlled drug delivery in Ophthalmology. J. Contr. Release 211 (2015) 105–117.

8. L.L. Zhang, C.D. Xiong, X. M. Deng. Biodegradable polyester blends for biomedical application. J. Appl. Polym. Sci. 56 (1995) 103–112.
9. D. Eglin, D. Mortisen, M. Alini, Degradation of synthetic polymeric scaffolds for bone and cartilage tissue repairs. Soft Matter 5 (2009) 938–947.
10. K. Hemmrich, J. Salber M., Meersch U., Wiesemann T., Gries N., Pallua D. Klee, Three dimensional nonwoven scaffolds from a novel biodegradable poly(ester amide) for tissue engineering applications. J. Mater Sc. Mater Med. 19 (2008) 257–267.
11. P. Karimi A.S., Rizkalla K., Mequanint, Versatile Biodegradable Poly(ester amide)s Derived from α-Amino Acids for Vascular Tissue Engineering. Materials 3 (2010) 2346-2368.
12. D.K. Knight, E.R. Gillies, K. Mequanint, Strategies in Functional Poly(ester amide) Syntheses to Study Human Coronary Artery Smooth Muscle Cell Interactions. Biomacromolecules. 12 (2011) 2475–2487.
13. S.P. Higgins, A.K. Solan, L.E. Niklason. Effects of polyglycolic acid on porcine smooth muscle cell growth and differentiation. J Biomed Mater Res A. 67 (2003) 295–302.
14. S. Kobauri, Tem. Kantaria, N. Kupatadze, N. Kutsiava, D. Tugushi, R. Katsarava. Pseudo-proteins: A new family of biodegradable polymers for sophisticated biomedical applications. Nano technology & nano science J. 1 (2019). 37-42.
15. R. Katsarava, Ten. Kantaria, S. Kobauri. Pseudo-proteins and related synthetic amino acid based polymers (Review). Journal of Materials Education (in press).
16. N. Zavradashvili, J. Puiggali, R. Katsarava. Synthetic analogues of proteins – poly (amino acid)s, pseudo-poly(amino acid)s. poly(depsipeptide)s, and pseudoproteins. Current Pharmaceutical Design (in press).
17. G. Jokhadze, M. Machaidze, H. Panosyan, C.C. Chu, R. Katsarava. Synthesis and characterization of functional elastomeric poly (ester amide) co-polymers. J. Biomater. Sci. Polym. Ed., 18 (2007). 411. C.C. Chu/. R. Katsarava. Elastomeric functional biodegradable copolyester amides and copolyester urethanes. (accessed on 5 August 2008) http://www.google.tl/patents/US7408018.
18. A. Zimmer, J. Kreuter. Microspheres and nanoparticles used in ocular delivery systems. Adv. Drug Delivery Reviews. 16 (1995). 61-73.
19. S.K. Sahoo, F. Dilnawaz, S. Krishnakumar. Nanotechnology in ocular drug delivery. Drug Discovery Today. 13 (2008). 144-151. A. Bochot, E. Fattal, V. Boutet, J.R. Deverre, et al. Intravitreal delivery of oligonucleotides by sterically stabilized liposomes. Invest. Oph-Annals of Agrarian Science 18 (2020) 43–53. T. Kantaria et al. 53thalmol. Vis. Sci. 43 (2002). 253–259. J.M. Irache, M. Merodio, A. Arnedo et al. Albumin nanoparticles for the intravitreal delivery of anticytomegaloviral drugs. Mini Rev. Med. Chem. 5 (2005). 293–305. R. Pignatello, C. Bucolo, G. Spedalieri et al. Flurbiprofen-loaded acrylate polymer nanosuspensions for ophthalmic application. Biomaterials, 23 (2002) 3247–3255. V. Vidmar, S. Pepeljnjak, J. Jalseniak. The in vivo evaluation of poly(lactic acid) microcapsules of pilocarpine hydrochlo-ride. J. Microencapsulation. 2 (1985). 289-292.
20. R. Katsarava, Z. Gomurashvili. Biodegradable polymers composed of naturally occurring α-amino acids. in: A. Lendlein, A. Sisson (Eds.), Handbook of Biodegradable Polymers—Isolation. Synthesis. Characterization and Applications. Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim. Germany. 2011.
21. Tem. Kantaria, Teng. Kantaria, S. Kobauri, M. Ksovreli, T. Kachlishvili, N. Kulikova, D. Tugushi, R. Katsarava. Biodegradable nanoparticles made of amino acid based ester polymers: preparation, characterization, and in vitro bio-compatibility study. Appl. Sci. 6 (2016). 444. doi:10.3390/app6120444
22. T. Memanishvili, N. Zavradashvili, N. Kupatadze, D. Tugushi, M. Gverdtsiteli, V.P. Torchilin, C. Wandrey, L. Baldi, S.S. Manoli, R. Katsarava. Arginine-based biodegradable ether-ester polymers of low cytotoxicity as po-tential gene carriers. Biomacromolecules 15 (2014). 2839-2848.
23. Tem. Kantaria, Ten. Kantaria, S. Kobauri, M. Ksovreli, T. Kachlishvili, N. Kulikova, D. Tugushi, R. Katsarava. A new generation of biocompatible nanoparticles made of resorbable poly(ester amide)s, J. Annals of Agrarian Science. 17 (2019). 49-58.

24. C. Le Bourlais, L. Acar H., Zia P.A., Sado T., Needham, R. Leverge. Ophthalmic Drug Delivery Systems—Recent Advances. Prog. Retin. Eye Res. 17 (1998). 33–58.
25. M. Mudgil, N. Gupta M., Nagpal, P. Pawar. Nanotechnology: a new approach for ocular drug delivery system. Int. J. Pharm. Pharm. Sci. 4 (2012) 105–112.
26. S. Laurent, L.H. Yahia. Protein corona: Applications and challenges. Springer Series in Biophysics. Martinac B. editor. 2013. pp 45-63.
27. B. Sahoo, M. Goswami, S. Nag et al. Spontaneous formation of a protein corona prevents the loss of quantum dot fluorescence in physiological buffers. Chem Phys Lett. 445 (2007) 217.
28. C. Giannavola, C. Bucolo, A. Maltese et al. Influence of Preparation Conditions on Acyclovir-Loaded Poly-d,l-Lactic Acid Nanospheres and Effect of PEG Coating on Ocular Drug Bioavailability. Pharmaceutical Research. 20 (2003) 584-590.
29. P. Breeuwer, J.L. Drocourt, N. Bunschoten, M.H. Zwietering, F.M. Rombouts, T. Abee. Characterization of Uptake and Hydrolysis of Fluorescein Diacetate and Carboxy fluorescein Diacetate by Intracellular Esterases in Saccharomyces cerevisiae. Which Result in Accumulation of Fluorescent Product. Appl. Envitron. Microbiol. 61 (1995) 1614–1619.
30. R. Katsarava, N. Kulikova, J. Puiggalí, Amino acid based biodegradable polymers—promising materials for the applications in regenerative medicine. J.J. Regener. Med. 1 (2016) 012.
31. S. Laurent L.H. Yahia. Protein corona: Applications and challenges. Springer Series in Biophysics. Martinac B, editor. 2013. pp 45-63.
32. B. Sahoo, M. Goswami, S. Nag et al. Spontaneous formation of a protein corona prevents the loss of quantum dot fluorescence in physiological buffers. Chem Phy Lett. 445 (2007) 217.
33. C. Giannavola, C. Bucolo, A. Maltese et al. Influence of Preparation Conditions on Acyclovir-Loaded Poly-d,l-Lactic Acid Nanospheres and Effect of PEG Coating on Ocular Drug Bioavailability. Pharmaceutical Research. 20 (2003) 584-590.
34. P. Breeuwer, J.L. Drocourt, N. Bunschoten, M.H. Zwietering, F.M. Rombouts, T. Abee. Characterization of Uptake and Hydrolysis of Fluorescein Diacetate and Carboxy fluorescein Diacetate by Intracellular Esterases in Saccharomyces cerevisiae. Which Result in Accumulation of Fluorescent Product. Appl. Envitron. Microbiol. 61 (1995) 1614–1619.
35. R. Katsarava, N. Kulikova, J. Puiggalí, Amino acid based biodegradable polymers—promising materials for the applications in regenera-tive medicine. J.J. Regener. Med. 1 (2016) 012.

3.6.2.2. Biopharmaceutical understanding of formulation preparation variability of PLGA nanoparticles loaded with erysimum extract. /L. Ebralidze, A. Tsertsvadze, L. Bakuridze, D. Berashvili, A. Bakuridze/. Georgian Medical News (GMN). – 2021. – #2(311). – pp. 173-177. – eng., abs.: eng., geo., rus.

The purpose of this study was to evaluate effect of process and formulation variables on the preparation of Erysimum extract loaded PLGA nanoparticles. The influence of the various biopharmaceutical factors such as type of organic solvent, type and concentration of surfactant, polymer concentration in the organic phase, ratio of organic phase and water phase were studied. Modified emulsification solvent evaporation method was used for preparation of nanoparticles. Based on the performed experiments optimal formulation of nanocomposite is suggested. Nanoparticle size, size distribution and entrapment efficiency were determined. Among five non-ionic surfactants polyvinyl alcohol provided more stable nanocomposite. Influence mechanisms of different surfactants on nanoparticle formation are provided. Water miscible organic solvent, acetone obtained 232 nm nanoparticles with improved size distribution. Entrapment efficiency was increased to 73% by reducing ratio of organic and water phases. Based on experiments nanoparticles with stable, reproducible properties are fabricated. Fig. 9, Tab. 4, Ref. 9.

Keywords: polymeric nanoparticle, PLGA, formulation variables, endemic plant species

References:

1. E. Sah and H. Sah. Recent Trends in Preparation of Poly (lactide-coglycolide) Nanoparticles by Mixing Polymeric Organic Solution with Antisolvent. vol. 2015. 2015.
2. B. L. Banik, P. Fattahi, and J. L. Brown. Polymeric nanoparticles: The future of nanomedicine. Wiley Interdiscip. Rev. Nano-medicine Nanobiotechnology. vol. 8. no. 2. pp. 271–299, 2016.
3. W. Mccarthy. Polymeric Drug Delivery Techniques. Aldrich Mater. Sci. no. 5. pp. 2–5, 2016.
4. C.I.C. Crucho and M.T. Barros. Polymeric nanoparticles: A study on the preparation variables and characterization methods. Mater. Sci. Eng. C. vol. 80. pp. 771–784. 2017.
5. S.M.I. Mors. Review Article Role of Surfactants in Nanotechnology and Their Applications. vol. 3. no. 5. pp. 237–260. 2014.
6. M. Silva, A. Santini, and E.B. Souto. Polymeric Nanoparticles: Production. 2020.
7. Rao J.P., Geckeler K. E. Polymer nanoparticles: Preparation techniques and size-control parameters. Prog. Polym. Sci. vol.36. no. 7. pp. 887–913. 2011.
8. R. Article. International Journal of Pharmacology and Review Article Recent biomedical applications and patents on biodegradable polymer. pp. 30–42. 2014.
9. Türk C.T.Ş., Bayindir Z.S., Badilli U. Preparation of polymeric nanoparticles using different stabilizing agents 2009; vol. 38. no. 4. 257–268.

3.6.2.3. Formulation thermoresponsive nanocomposite hydrogel with embedded PLGA nanoparticles containing cytotoxic agent. /L. Ebralidze, A. Tsertsvadze, L. Bakuridze, D. Berashvili, A. Bakuridze/. Georgian Medical News (GMN). – 2021. – #3(312). – pp.133-138. – eng., abs.: eng., geo., rus.

The aim of the study was to develop and characterize the nanocomposite in-situ hydrogel as local drug delivery system of cytotoxic agent. In-situ hydrogel consisting of 15% ther- mosensitive (Poloxamer 407) and 1% mucoadhesive (sodium alginate) polymers was selected as the optimal formulation by the conducted studies. The influence of nanoparticle concentration on gelation time and temperature has been experimentally established. As a result, the optimum concentration of nanoparticles (5%) is selected, which does not alter the gel forming process. The resulting nanocomposite hydrogel was characterized through Fourier transform infrared spectroscopy (FT-IR), scanning electron microscopy (SEM), rotational viscometer (LVDV- 1T). FT-IR spectra confirmed the PLGA nanoparticles pres- ence within the hydrogel matrix through the absorption peak located at 1750 cm^{-1}. SEM images allowed observing the nanoparticles to be homogenously dispersed. The release pattern of the active substance from the nanocomposite hydrogel is following: at 72 h, 64% and 78% of the active substance were released into the phosphate buffer and cell culture area, respectively. Irritation test on hen's egg model revealed that formulated nanocomposite hydrogel did not show damage of vascular system. Fig. 10, Tab. 1, Ref. 9.

Keywords: Nanocomposite, thermosensitive hydrogel, PLGA nanoparticles

References:

1. Lu Y., Mahato R.I. Pharmaceutical perspectives of cancer therapeutics. 2009.
2. GLOBOCAN. The Global Cancer Observatory - All cancers. Int. Agent Res. Cancer – WHO 2020. 419: 199–200.
3. Vashist A. et al. Nanocomposite Hydrogels: Advances in Nanofillers Used for Nanomedicine. Gels 2018. 4(3): 75. doi: 10.3390/gels4030075.
4. Rafieian S., Mirzadeh H., Mahdavi H., Masoumi M.E. A review on nanocomposite hydrogels and their biomedical applications. IEEE J. Sel. Top. Quantum Electron. 2019. 26(1): 154–174, 2019. doi: 10.1515/secm-2017-0161.

5. Matsumura K. Special issue: Nanocomposite hydrogels for biomedical applications. Appl. Sci. 2020. 10(1): 15–16, 2020. doi: 10.3390/app10010389.
6. Nirmal H.B., Bakliwal S.R., Pawar S.P. In-Situ gel: New trends in controlled and sustained drug delivery system. Int. J. PharmTech Res. 2010. 2(2): 1398–1408.
7. Bakuridze A., Beridze D., Jokhadze M., Metreveli M. The Study of Ajara and Ajara-Lazica Endemics on the Content of Biologically Active Compound Coumarin 2016. 4: 76–83.
8. Beridze D., Jokhadze M., Bakuridze A., Metreveli M., Manvelidze Z. Gas chromatography - mass spectrometry (GC-MS) analysis of bioactive compounds of Ajara and Ajara-Lazica endemic species. International Journal of Current Research 2016. vol. 8. issue 09: 38939-38944.
9. Metreveli M. North American Multi-Purpose Dear Introducent Plants in Western Georgia Humid Subtropical Conditions. Am. J. Environ. Prot. 2015. 4(3): 168. 2015, doi: 10.11648/j. ajep.s.2015040301.36.