

3. NANOBIOLOGY

3.2. Biophysics

2.3.2.1. Structural and magnetic properties of silver oleic acid multifunctional nanohybrids. /S. Khutsishvili, P. Toidze, M. Donadze, M. Gabrichidze, T. Agladze, N. Makhaldiani/. Annals of Agrarian Science. – 2019. – vol. 17. – #2. – pp. 242-250. – eng.; abs.: eng.

Sols of core-shell silver NPs are synthesized by an electrochemical method. The method provides for the ability to adjust the particle size by changing both the concentration of oleic acid and the residence time W_0 in the organic phase. We synthesized silver nanoparticles with oleic acid concentration of 0.25% (Ag&0.25%OA) and 0.75% (Ag&0.75%OA). The silver nanoparticles have been studied using modern physical-chemical methods: Transmission Electron Microscopy (TEM); Fourier Transform Infrared Spectroscopy (FT-IR); Dynamic Light Scattering (DLS); Thermogravimetric and Differential Thermal Analysis (TGA and DTA); Electron Paramagnetic Resonance (EPR). DTA curves indicate the chemical nature of bond ligand in the secondary shell. This conclusion is supported by quantum chemical simulation using the quantum-chemical software HyperChem-8 and semi-empirical calculation method ZINDO. In the EPR spectra of silver-containing sols Ag&0.25%OA and Ag&0.75%OA a complex wide asymmetric signal with several resonant lines is recorded, which is consistent with a wide-size distribution of nanoparticles. It is important to note that a change in the oleic acid layers of the nanoparticles seems to affect the dimension of the nanocrystallites that are being formed. The presence of the FMR resonance line in Ag&0.75%OA may indicate the presence of Ag-cubic cells in nanoparticles with internal magnetic fields significantly larger than the Zeeman field, the available EPR in the X-band range. Fig. 5, Tab. 2, Ref. 30.

Keywords: Core-shell, nanoparticles, oleic acid, ligand, charge, activation energy

References:

- 1 M. Donadze, M. Gabrichidze, S. Calvache, T. Agladze, Novel method of preparation of the hybrid metal (I) – metal (II) oxide nanoparticles, Int. J. Transactions of the IMF 94 (1) (2016)16-23.
- 2 J.H. Flynn, The Isoconversional method for determination energy of activation at constant heating rate, J. Therm. Anal. 27 (1) (1983) 95-102
- 3 T. A. Ozawa New method of analyzing thermo- gravimetric data, Bull. Chem. Soc. Japan 38 (1965) 1881-1886.
- 4 T. Agladze, M. Donadze, P. Toidze et al. Synthesis and Size Tuning of Metal Nanoparticles, Z.Phys. Chem. 227 (2013) 1187-1198.
- 5 D.H. Lee FTIR spectral characterization of thin film coatings of oleic acid on glasses, J. Mat. Sci. 34 (1999) 139-146.
- 6 C. Doyle, Kinetic analysis of thermogravimetric data, J. Appl. Polym. Sci. 5 (15) (1961) 285–292.
- 7 K.Yang, H.Peng, Y.Wen, N. Li, Re-examination of characteristic FTIR spectrum of secondary layer in bilayer oleic acid-coated Fe_3O_4 nanoparticles, Appl. Surf. Sci. 256 (2010) 3093–3097.
- 8 Q. Lan, C. Liu, F. Yang et al., Synthesis of bilayer oleic acid-coated Fe_3O_4 and interface nanoparticles and their application in pH- responsive Pickering emulsions, J. Coll. Sci. 310 (2007) 260–269.
- 9 L. Shen, P.E. Laibinis and T.A. Hatton, Bilayer surfactant stabilized magnetic fluids: synthesis and interactions at interfaces, Langmuir 15 (1999) 447-453.
- 10 S. Nellutla, S. Nori, S.R. Singamaneni, J.T. Prater, J. Narayan, A.I. Smirnov, Multi-frequency ferromagnetic resonance investigation of nickel nanocubes encapsulated in diamagnetic magnesium oxide matrix, J. Appl. Phys. 120 (22) (2016) 1-9.
- 11 V. Angelov, H. Velichkova, E. Ivanov, R. Kotsilkova, M.H. Delville, M. Cangiotti, A. Fattori, M.F. Ottaviani, EPR and rheological study of hybrid interfaces in gold-clay- epoxy nanocomposites, Langmuir 30 (44) (2014) 13411-13421.
- 12 M.V. Lesnichaya, B.G. Sukhov, E. Gasilova, G. Aleksandrova, T. Vakul'skaya, S. Khutsishvili, A. Sapozhnikov, I. Klimenkov, B. Trofimov, Chiroplasmonicmagneticgoldnanocomposites produced by one-step aqueousmethod using κ -carrageenan, Carbohydrate Polymers 175 (2017) 18-26.
- 13 A. Smirnov, EPR studies of nanomaterials. In: (Ed.) S. Misra, Multifrequency Willey-VCH, Verlag (2011) 825-843.
- 14 M. Schlott, H. Schaeffer, B. Elschner, Gd^{3+} -ESR in the intermediate valent cerium compounds $Ce_x La_{1-x}O_2$, Zeitschrift für Physik B Condensed Matter 63 (4) (1986) 427-436.
- 15 J. Stöhr, H. Siegmann, Magnetism: From Fundamentals to Nanoscale Dynamics, Springer- Verlag, Berlin Heidelberg, 2006.

- 16 P. Venegas, P. Netto, Exchange narrowing effects in the EPR linewidth of Gd diluted in Ce compounds, *J. Appl. Phys.* 83 (11) (1998) 6958-6968.
- 17 P. Shin, S. Wu, Magnetic anisotropic energy gap and strain effect in Au nanoparticles, *Nanoscale Research Letters* 5 (2010) 25-30.
- 18 M. Kakazey, N. Ivanova, G. Sokolsky, J. Gonzalez-Rodriguez, Electron paramagnetic resonance of MnO₂ powders, *Electrochemical and Solid-State Letters* 4 (5) (2001) 1-4.
- 19 F. Blatter, K. Blazey, Conduction electron spin resonance of silver in zeolite AgY, *Z. Phys. D - Atoms, Molecules and Clusters* 18 (1991) 427-429.
- 20 S. Sako Kimura, K. Size, Effect in CESR of magnesium and calcium small particles, *Surface Sci.* 156 (1985) 511-515.
- 21 X. Li, A. Vannice, ESR studies of well-dispersed Ag crystallites on SiO₂, *J. Catalysis* 151 (1995) 87-95.
- 22 M. Ali, A. Shames, S. Gangopadhyay, B. Saha, D. Meyerstein, Silver(II) complexes of tetrazamacrocycles: studies on e.p.r. and electron transfer kinetics with thiosulfate ion, *Transition Metal Chemistry (Dordrecht, Neth.)* 29 (2004) 463-470.
- 23 M. Kester, A. Allred, Ligand-induced disproportionation of silver (I), *J. American Chemical Society* 94 (1972) 7189-7189.
- 24 S. Khutsishvili, T. Vakul'skaya, N. Kuznetsova, T. Ermakova, A. Pozdnyakov, G. Prozorova, Formation of stable paramagnetic nano-composites containing zero-valence silver and copper in a polymeric matrix, *J. Phys. Chem. C* 118 (33) (2014) 19338-1701
- 25 J. McMilan, B. Smaler, Paramagnetic resonance of some silver(II) compounds. *J. Chem. Phys.* 35 (1961) 1698-1701.
- 26 H. Moon, J. Kim, M. Suh, Redox-active porous organic framework Chemie producing silver nanoparticles from Ag^I ions at room temperature, *Angew. Chem. Int. Ed.* 44 (2005) 1261-1265.
- 27 G. Deligiannakis, Y. Trapalis, C. Boukos, N. Kordas, CW and pulsed EPR study of silver nanoparticles in SiO₂ matrix, *J. Sol-Gel Science Technology* 13 (1998) 503-508.
- 28 S. Khutsishvili, T. Vakul'skaya, G. Aleksandrova, B. Sukhov, Stabilized silver nanoparticles and clusters Ag_n of humic-based bioactive nanocomposites, *J. Cluster Sci.* 28 (2017) 3067-3074.
- 29 V. Timoshenko, T. Shabatina, Yu. Morozov, G. Sergeev, Complexation and chemical transformations in the ternary system silver-carbon tetrachloride- mesogenic cyanobiphenyl at low temperatures, *J. Struc. Chem.* 47 (1) (2006) 145-150.
- 30 J. Michalik, H. Yamada, D. Brown, L. Kevan, Small silver clusters in smective clay interlayers, *J. Phys. Chem.* 100 (1996) 4213-4218.250.

3.3. Biochemistry

2.3.3.1. Revealing a Nonergodic Mechanistic Pattern for Electron Exchange between Azurin and Electrodes Coated by Nanofilms under the Glassy Environmental Conditions. /T. Dolidze, R. van Eldik, D. Khoshtariya/. *Bulletin of the Georgian National Academy of Sciences.* – 2019. – vol. 13. – #4. – pp. 97-103. – eng.; abs.: eng., geo.

Fast-scan protein-film voltammetry was applied to explore interfacial biomimetic electron exchange under the environmental glass forming conditions. Gold electrodes were coated with 1-pentanethiol SAM-azurin (Az, blue cupredoxin) assemblies and placed in contact with a water-doped and buffered protic ionic melts of choline dihydrogen phosphate ([ch][dhp]), served as electrolyte media, allowing for a necessary cell conductivity under the virtually solid, semi-solid and liquid electrolyte conditions over 273–353 K, within which the electron exchange rate was studied as a function of the water amount and temperature. Exposure of the Az films to the semi-solid electrolyte greatly affected the protein's conformational dynamics, hence the ET rate, via the mechanism occurring in the extra complicated dynamically-controlled regime. Results are compared to the earlier studies on the reference system with a conventional electrolyte, allowing for the disclosure of mutually-entangled mechanistic motifs. Under the "standard" condition (with no [ch][dhp] added), the Az biomolecule may reside in an apparently ergodic state, whereas upon adding of [ch][dhp] to allow water content ranging between 6 to 15 waters per [ch][dhp], system displays anomalous temperature dependences, suggesting that the reactive system crosses a broad, well-manifested nonergodic zone which arises from the continuous interplay (freezing/unfreezing) of ET-coupled highly cooperative conformational modes of the Az protein, inherently linked to the electrolyte's

slowest collective relaxation(s). Above this [ch][dhp] concentration, allowing the water content between 1.65 to 3.7 waters per ion pair, the system returns to a series of new, quasi-ergodic states, with each displaying virtually linear Arrhenius patterns yet with distinct parameters. Fig. 2, Tab. 3, Ref. 22.

Keywords: redox protein, electron exchange, interphase, self-assembly, nonergodicity

References:

1. Ellis R.J. (2001) Macromolecular crowding: an important but neglected aspect of the intracellular environment. *Curr. Opin. Struct. Biol.* 11:114–119.
2. Zhou H.-X., Rivas G., Minton A.P. (2008) Macromolecular crowding and confinement: biochemical, biophysical and potential physiological consequences. *Annual Rev. Biophys.*, 37:375–397.
3. Mittal S., Chowhan R.K., Singh L.R. (2015) Macromolecular crowding: macromolecules' friend or foe. *Biochim. Biophys. Acta* 1850:1822–1831.
4. Frauenfelder H., et al. (2009) A unified model of protein dynamics. *Proc. Natl. Acad. Sci. USA* 106:5129–5134.
5. Jansson H., Bergman R., Swenson J. (2011) Role of solvent for the dynamics and the glass transition of proteins. *J. Phys. Chem. B* 115:4099–4109.
6. Lee A.G. (2004) How lipids affect the activities of integral membrane proteins. *Biochim. Biophys. Acta* 1666:62–87.
7. Bondar A.-N., White S.H. (2004) Hydrogen bond dynamics in membrane protein function. *Biochim. Biophys. Acta* 1818:942–950.
8. Belieres J.-P., Angell C.A. (2007) Protic ionic liquids: preparation, characterization and proton free energy level representation. *J. Phys. Chem. B* 111:4926–4937.
9. Rana U.A., et al. (2010) Proton transport in choline dihydrogen phosphate/H₃PO₄ mixtures. *Phys. Chem. Chem. Phys.* 12:11291–11298.
10. Fujita K., Ohno H. (2010) Enzymatic activity and thermal stability of metalloproteins in hydrated ionic liquids. *Biopolymers* 93:1093–1099.
11. Khoshtariya D.E., et al. (2006) Kinetic, thermodynamic, and mechanistic patterns for free (unbound) cytochrome C at Au/SAM junctions: impact of electronic coupling, hydrostatic pressure, and stabilizing/denaturing additives. *Chemistry – A European J.* 12:7041–7056.
12. Khoshtariya D.E., et al. (2010) Fundamental signatures of short and long-range electron transfer for the blue copper protein azurin at Au/SAM junctions. *Proc. Natl. Acad. Sci. USA* 107:2757–2762.
13. Khoshtariya D.E. et al. (2014) Long-range electron transfer with myoglobin immobilized at Au/Mixed–SAM junctions: mechanistic impact of the strong protein confinement. *J. Phys. Chem. B* 118:692–706.
14. Weber K., Hockett L., Creager S. (1997) Long-range electronic coupling between ferrocene and gold in alkanethiolate-based monolayers on electrodes. *J. Phys. Chem. B* 101:8286–8291.
15. Palmer R.G. (1982) Broken ergodicity. *Adv. Phys.* 31:669–735.
16. Mauro J.C., Gupta P.K., Loucks R.J. (2007) Continuously broken ergodicity. *J. Chem. Phys.* 126:184511 (11 p.).
17. Mallamace F., et al. (2011) The role of the dynamic crossover temperature and the arrest in glass-forming fluids. *Eur. Phys. J. E* 34:94 (94 p).
18. Lebard D.N., Matyushov D.V. (2010) Protein-water electrostatics and principles of bioenergetics. *Phys. Chem. Chem. Phys.* 12:15335–15348.
19. Matyushov D.V. (2011) Nanosecond stokes shift dynamics, dynamical transition, and gigantic reorganization energy of hydrated heme proteins. *J. Phys. Chem. B*, 115:10715–10724.
20. Matyushov, D.V. (2013) Protein electron transfer: dynamics and statistics. *J. Chem. Phys.* 139:025102 (12 p.).
21. Zusman L.D. (1994) Dynamic solvent effects in electron transfer reactions. *Z. Phys. Chem.* 186:1–29.
22. Bixon M., Jortner J. (1999) Electron transfer – from isolated molecules to biomolecules. *Adv. Chem. Phys.* 106:35–202.

2.3.3.2. A new generation of biocompatible nanoparticles made of resorbable poly(ester amide)s. /T. Kantaria, T. Kantaria, G. Titvinidze, S. Kobauri, M. Ksovreli, T. Kachlishvili, N. Kulikova, D. Tugushi and R. Katsarava/. *Annals of Agrarian Science.* – 2019. – vol. 17. – #1. – pp. 49-58. – eng.; abs.: eng.

A new generation of resorbable nanoparticles (NPs) were prepared on the basis of amino acid-based biodegradable (AABB) poly (ester amide)s (PEAs) for drug delivery application. The NPs were fabricated by cost-effective polymer deposition/solvent displacement (nanoprecipitation) method on the basis of three different AABB PEAs recently developed by our group: (i) PEA composed of amino acid leucine as a basic component, (ii) cationic PEA composed of amino acid arginine for imparting positive charge, and (iii)

functional PEA composed of amino acid leucine and lateral poly(ethylene glycol) groups acting as surfactant as well as PEGylating agent. The mean particle diameter (MPD), polydispersity index (PDI) and zeta-potential (ZP) were determined by Dynamic Light Scattering (DLS). Moreover, the stability (resuspendability) of the NPs over time at low temperature was investigated. The NPs were studied for *in vitro* cell compatibility using four different stable cell lines: A549 (human), U937 (human), RAW264.7 (murine), Hepa 1-6 (murine). The produced nanoparticles exhibit high stability and cell compatibility and have potential for the application as drug delivery devices. Fig. 2, Ref. 37.

Keywords: Biodegradable polymers; nanoprecipitation; nanoparticles; biodegradable surfactant; PEGylation; *in vitro* cell compatibility

References:

- 1 R. Bisht, A. Mandal, J.K. Jaiswal, I.D. Rupenthal, Nanocarrier mediated retinal drug delivery: overcoming ocular barriers to treat posterior eye diseases, *Advanced review* 10 (2018) e1473. doi: 10.1002/wnan.1473.
- 2 L. Zhang, F.X. Gu, J.M. Chan, A.Z. Wang, R.S. Langer, O.C. Farokhzad, Nanoparticles in medicine: therapeutic applications and developments, *Clin. Pharmacol. Ther.* 83 (2018) 761–769.
- 3 S. Mallakpour, V. Behranvand, Polymeric nanoparticles: recent development in synthesis and application, *Express Polym. Lett.* 10 (2016) 895–913.
- 4 S. Schubert, J.T. Delaney Jr, U.S. Schubert, Nanoprecipitation and nanoformulation of polymers: from history to powerful possibilities beyond poly(lactic acid), *Soft Matter* 7 (2011) 1581–1588.
- 5 R. Liang, L. Dong, R. Deng, J. Wang, K. Wang, M. Sullivan, J. Tao, Surfactant-free biodegradable polymeric nanoparticles generated from self-organized precipitation route: Cellular uptake and cytotoxicity, *Eur. Polym. J.* 57 (2014) 187–201.
- 6 L.A. Dailey, E. Kleemann, M. Wittmar, T. Gessler, T. Schmehl, C. Roberts, W. Seeger, T. Kissel, Surfactant-free, biodegradable nanoparticles for aerosol therapy based on the branched polyesters, DEAPA-PVAL-g-PLGA. *Pharm. Res.* 20 (2003) 2011–2020.
- 7 K. Ulbrich, K. Hola, V. Subr, A. Bakandritsos, J. Tucek, B. Zboril, Targeted drug delivery with polymers and magnetic nanoparticles: covalent and noncovalent approaches, release control, and clinical studies, *Chem. Rev.* 116 (2016) 5338–5431.
- 8 E. Marin, M.I. Briceno, C. Caballero-George, Critical evaluation of biodegradable polymers used in nanodrugs, *Int. J. Nanomedicine.* 8 (2013) 3071–3091.
- 9 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.
- 10 M. Jacoby, Custom-made biomaterials. *Chem. Eng. News.* 79 (2001) 30–35.
- 11 N. Arabuli, G. Tsitlanadze, L. Edilashvili, D. Kharadze, T. Gogvadze, V. Beridze, Z. Gomurashvili, R. Katsarava, Heterochain polymers based on natural α -amino acids. Synthesis and enzymatic hydrolysis of regular poly(ester amide)s based on bis(L-phenylalanine) α,ω -alkylene diesters and adipic acid, *Macromol. Chem. Phys.* 195 (1994) 2279–2289.
- 12 T. Kartvelishvili, G. Tsitlanadze, L. Edilashvili, N. Japaridze, R. Katsarava, Amino acid based bioanalogous polymers. Regular poly(ester urethane)s and poly(ester urea)s based on bis(phenylalanine)- α,ω -alkylene diesters, *Macromol. Chem. Phys.* 198 (1997) 1921–1932.
- 13 R. Katsarava, D. Tugushi, Z. Gomurashvili, Poly (ester urea) polymers and methods of use. US Patent No. 8,765,164 (accessed on 1 July 2014) <https://www.google.ch/patents/US8765164>.
- 14 R. Katsarava, Active polycondensation: from peptide chemistry to amino acid based biodegradable polymers, *Macromol. Symp.* 199 (2003) 419–429.
- 15 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, pp. 107–131.
- 16 K. Defife, K. Grako, G. Cruz-Aranda, S. Price, R. Chantung, K. Pacpherson, R. Koshabeh, S. Gopalan, W.G. Turnell, Poly(ester amide) co-polymers promote blood and tissue compatibility, *J. Biomater. Sci.* 20 (2009) 1495–1511.
- 17 H. Sun, F.M. Meng, A.A. Dias, M. Hendriks, J. Feijen, Z. Zhong, α -Amino acid containing degradable polymers as functional biomaterials: rational design, synthetic pathway, and biomedical applications, *Biomacromolecules.* 12 (2011) 1937–1955.

- 18 A. Ghaffar, G.J.J. Draaisma, G. Mihov, A.A. Dias, P.J. Schoenmakers, S.J. van der Val, Monitoring the in vitro enzyme-mediated degradation of degradable poly(ester amide) for controlled drug delivery by LC-ToF-MS, *Biomacromolecules*. 12 (2011) 3243–3251.
- 19 M. Trollsas, B. Maslanka, N. Pham, Q. Lin, S. Hossainy, H.L. Hsu, M.H. Ngo, Polyesteramide coatings for drug eluting stents: controlling drug release by polymer engineering, *Stud. Mechanobiol. Tissue Eng. Biomater.* 8 (2011) 127–143.
- 20 R. Katsarava, N. Kulikova, J. Puiggali, Amino acid based biodegradable polymers—promising materials for the applications in regenerative medicine, *J. J. Regener. Med.* 1 (2016) 012.
- 21 K. Markosishvili, G. Tsitlanadze, R. Katsarava, J.G. Jr. Morris, A. Sulakvelidze, Novel sustained-release matrix based on biodegradable poly(ester amide)s and impregnated with bacteriophages and an antibiotic shows promise in management of infected venous stasis ulcers and other poorly healing wounds, *Int. J. Dermatol.* 41 (2002) 453–458.
- 22 D. Jikia, N. Chkhaidze, E. Imedashvili, I. Mgaloblishvili, G. Tsitlanadze, R. Katsarava, J.Jr. Glenn Morris, A. Sulakvelidze, The use of a novel biodegradable preparation capable of the sustained release of bacteriophages and ciprofloxacin, in the complex treatment of multidrug-resistant staphylococcus aureus-infected local radiation injuries caused by exposure to Sr90, *Clin. Exp. Dermatol.* 30 (2005) 23–26.
- 23 C.C. Chu, R. Katsarava. Elastomeric functional-biodegradable copolyester amides and copolyester urethanes (accessed on 5 August 2008) <http://www.google.tl/patents/US7408018>.
- 24 S.H. Lee, I. Szinai, K. Carpenter, R. Katsarava, G. Jokhadze, C.C. Chu, Y. Huang, E. Verbeken, O. Bramwell, I. De Scheerder, M.K. Hong, In vivo biocompatibility evaluation of stents coated with a new biodegradable elastomeric and functional polymer, *Coron. Artery Dis.* 13 (2002) 237–241.
- 25 Z. Gomurashvili, H. Zhang, J. Da, T.D. Jenkins, J. Hughes, M. Wu, L. Lambert, K.A. Grako, K.M. DeFife, K. MacPherson, V. Vassilev, R. Katsarava, V.G. Turnell, From drug-eluting stents to biopharmaceuticals: poly(ester amide) a versatile new bioabsorbable biopolymer. in: A. Mahapatro, A.S. Kulshrestha (Eds.), *ACS Symposium Series 977: Polymers for Biomedical Applications*, Oxford University Press: Oxford, UK, 2008, pp. 10–26.
- 26 M. Kropp, K.-M. Morawa, G. Mihov, A.K. Salz, N. Harmening, A. Franken, A. Kemp, Dias, J. Thies, S. Johnen, G. Thumann, Biocompatibility of poly(ester amide) (PEA) microfibrils in ocular tissues, *Polymers*. 6 (2014) 243–260.
- 27 V. Andrés-Guerrero, M. Zongc, E. Ramsay, R. Rojas, S. Sarkhel, B. Gallego, R. de Hoz, A.I. Ramirez, J.J. Salazar, A. Trivino, J.M. Ramirez, E.M. Del Amo, N. Cameron, B. de-Las Heras, A. Urtili, G. Mihov, A. Dias, R. Herrero-Vanrell, Novel biodegradable polyesteramide microspheres for controlled drug delivery in ophthalmology, *J. Control. Release*. 211 (2015) 105–117.
- 28 S. Laurent, L.H. Yahia, Protein corona: applications and challenges, in: B. Martinac (Ed.), *Protein-Nanoparticle Interactions*, Springer-Verlag Berlin Heidelberg, 2013, <https://doi:10.1007/978-3-642-37555-2>.
- 29 B. Sahoo, M. Goswami, S. Nag, S. Maiti, Spontaneous formation of a protein corona prevents the loss of quantum dot fluorescence in physiological buffers, *Chem Phys Lett.* 445 (2007) 217–220.
- 30 C. Le Boultais, L. Acar, H. Zia, P.A. Sado, T. Needham, R. Leverage, Ophthalmic drug delivery systems—recent advances, *Prog. Retin. Eye Res.* 17 (1998) 33–58.
- 31 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.
- 32 P. Dandagi, S. Kerur, V. Mastiholmath, A. Gadad, A. Kulkarni, Polymeric ocular nanosuspension for controlled release of acyclovir: in vitro release and ocular distribution, *Iranian J. Pharm. Res.* 8 (2009) 79–86.
- 33 C. Giannavola, C. Bucolo, A. Maltese, D. Paolino, M.A. Vandelli, G. Puglisi, V.H.L. Lee, M. Fresta, 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 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, characteriation, and in vitro biocompatibility study, *Appl. Sci.* 6 (2016) <https://doi:10.3390/app6120444>.
- 35 T. Memanishvili, N. Zavrashvili, N. Kupatadze, D. Tugushi, M. Gverdtsiteli, V.P. Torchilin, C. Vandrey, L. Baldi, S.S. Manoli, R. Katsarava, Arginine-based biodegradable ether-ester polymers of low cytotoxicity as potential gene carriers, *Biomacromolecules*. 15 (2014) 2839–2848.
- 36 N. Zavrashvili, G. Jokhadze, M. Gverdtsiteli, G. Otinashvili, N. Kupatadze, Z. Gomurashvili, D. Tugushi, R. Katsarava, Amino acid based epoxy-poly(ester amide)s – a new class of functional biodegradable polymers: synthesis and chemical transformations, *J. Macromol.Sci., Part A, Pure & Appl. Chem.* 50 (2013) 449–465.
- 37 T. Mosmann, Rapid colorimetric assay for cellular growth and survival: Application to proliferation and cytotoxicity assays, *J. Immunol. Methods*. 65 (1983) 55–63.